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Virtual Congress

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Oral Sessions

Saturday, May 23 2020

Infectious diseases

O1001

Progressive multifocal leukoencephalopathy associated with lymphopenia and T-cell exhaustion successfully treated with interleukin-7

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is a devastating brain infection caused by the JC polyomavirus (JCPyV). Subjects who are immunocompromised are at risk. Survival depends on immune recovery. We have previously used interleukin-7 (IL-7) with success to treat a patient with PML and idiopathic T-cell lymphopenia (ICL). Here we describe a second case.

Methods: A 78-year-old woman who had been treated with corticosteroids for pulmonary sarcoidosis 25 years earlier developed PML associated with severe ICL characterized by expression of programmed cell death-1 (PD-1) receptors on the majority of her total circulating CD4+ and CD8+ T-cells. This is a potential state of T-cell hypo-responsiveness (loss of effector cytokines), so called T-lymphocyte exhaustion.

Results: Mirtazapine, to block serotonin receptors needed for viral cell entry, was started, but the disease progressed. She was then treated with IL-7, which is a cytokine essential for T-cell proliferation. A month later, signs of recovery were observed. The patient continued to improve remarkably, both clinically and radiologically, and along with increasing peripheral lymphocytes and declining PD-1 expression. Viral clearance of CSF was achieved, and repeated FDG-PET scan showed evidence of re-myelination.

Conclusion: Complementary and tailored treatments to enhance the host defense against JCPyV in PML are promising. IL-7 therapy in PML when lymphopenia is present could be offered. The IL-7 treatment reversed PD-1 up-regulation in our patient suggests also the possibility of combining IL-7 with PD-1 blockade in future research studies.

Disclosure: Nothing to disclose

O1002

Infectious encephalitis and myelitis in a tropical area during 2012-2018: Influence of emerging viral infections and rare causes

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Background and aims: The frequency of infectious encephalitis and the distribution of causative pathogens in the Caribbean are unknown and might be influenced by emerging arbovirus infections.

Methods: Using a hospital database, we retrospectively collected detailed information on a comprehensive series of immunocompetent patients with acute infectious myelitis and encephalitis over the 2012-2018 period.

Results: From 259 suspected cases with acute central nervous system (CNS) infection, we included for analysis 175 cases, comprising 145 encephalitis, 22 myelitis, and 8 encephalomyelitis. The annual incidence peaked at 15.2/100 000 during the Zika 2016 outbreak. Children accounted for 21.7% of cases. Ten adults died during hospital stay, all encephalitis. Infectious agents were identified in 105 cases (60.0%), including 39 confirmed cases (37.1%), 48 probable cases (45.7%), 15 possible cases (14.3%) and 3 clinical cases (2.9%). Among 175 cases, the most frequent etiologic agents were Zika virus in 23 cases (13.1%), herpes simplex in 12 (6.9%), varicella zona virus in 11 (6.3%), dengue virus in 11 (6.3%) and leptospirosis in 11 (6.3%). Pathogens unidentified until then in Guadeloupe were found.

Conclusion: Zika outbreak had a major influence on the annual incidence of acute CNS infection. Acute neuroleptospirosis was over-represented in our series. It is important for clinical practice in tropical areas since neuroleptospirosis has a good prognosis when early treated. Further efforts are mandatory to develop new diagnosis tools for pathogen profiling.

Disclosure: Nothing to disclose

O1003

Retinal changes in cerebral malaria among Sudanese patients in Khartoum state, Sudan

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Background and aims: It is thought that Malaria parasites live in red blood cells and make them stick to the inside of small blood vessels, particularly this causes the unique whitening of eye blood vessels. The light-sensitive tissue in the eye is also affected because the parasites disrupt the supply of oxygen and nutrients. These changes, known as malarial retinopathy, include white, opaque patches, whitening of the infected blood vessels, bleeding into the retina and swelling of the optic nerve.

Objectives: Our study aims to demonstrate malarial retinopathy in patients presented with neurological manifestations of malaria.

Methods: A cross-sectional Hospital based study included all patients with malaria seen during the period between 1-1-2019 and 25-4-2019.

Results: Almost 40 patients with neurological manifestations of malaria were included in the study (29 having cerebral malaria, 3 with post malarial cerebellar ataxia, 2 with post malarial syndrome and abnormal movement, one with peripheral neuropathy, one with proximal myopathy, one had cerebral infarction, one had cerebral haemorrhage, one had sagittal sinus thrombosis and one had six nerve palsy. Out of 29 patients with cerebral malaria 14 were children and 15 were adult. Malarial retinopathy changes were detected only among those with cerebral malaria (7 children and 3 Adult).

Conclusion: The eye can provide a very reliable way of diagnosing cerebral malaria. By looking at the changes to the retina our research demonstrates that the detection of malarial retinopathy is a much needed diagnostic tool in cerebral malaria, and can identify those children at most risk of death.

Disclosure: Nothing to disclose

O1004

Tumor necrosis factor-alpha signaling may contribute to chronic west Nile virus post-infectious proinflammatory state

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Background and aims: West Nile virus (WNV) causes human disease ranging from a febrile illness (WNV fever) to severe neuroinvasive disease (meningitis, encephalitis, acute flaccid paralysis). Since WNV became a global Public Health concern, clinicians caring for WNV survivors have observed persistent neurological symptoms occurring long-after the production of neutralizing antibodies and clearance of the virus. Alternative pathogeneses other than direct viral invasion have been hypothesized to explain these post-infectious symptoms. A dominant hypothesis is that antiviral responses triggered initially to clear WNV may persist to promote a post-infectious proinflammatory state.

Methods: In 4 serologically-confirmed WNV patients with persistent post-infectious symptoms (3 WNV fever, 1 neuroinvasive disease), we ordered a comprehensive cytokine panel at weeks 8, 10, 12 and 36 months post-onset of illness, respectively, to better understand the pathophysiology of the protracted symptoms.

Results: All 4 patients had abnormally elevated tumor necrosis factor alpha (TNF- α), a major molecule triggering antiviral cytokines and chronic inflammation in many human autoimmune diseases, but heretofore not reported to be upregulated in human WNV infection. Three patients also had elevations of other proinflammatory proteins. Major symptoms included fatigue, arthralgias, myalgias, generalized or multifocal pain or weakness, imbalance, headaches, cognitive problems, and symptoms of dysautonomia.

Conclusion: The findings provide support for an extended post-infectious proinflammatory state that may contribute to chronic inflammation and long-term morbidity in some WNV survivors and further suggest that TNF- α may play a pathogenic role in initiating this inflammatory environment. Clinical trials are warranted to determine if TNF- α inhibitors or other immunosuppressive agents can improve patient outcomes.

Disclosure: Dr. Leis receives funding from the Mosquito Illness Alliance (mosquitoillnessalliance.org) and the Wilson Research Foundation, Jackson, MS.

O1005

Impact of brain biopsy on management of nonneoplastic brain disease

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Background and aims: Diagnostic yield of brain biopsy in neoplastic brain disease is high and its clinical impact is well established. In non-neoplastic brain disease with negative conventional investigation, decision to undergo invasive procedures is difficult due to its inherent risk. This study aimed to assess clinical impact of brain biopsy results on management of non-neoplastic brain disease.

Methods: A multidisciplinary team retrospectively reviewed and included all non-neoplastic brain disease cases submitted to biopsy between 2009-2019, in a tertiary hospital in Lisbon. Baseline characteristics were registered, including immunosuppression status, diagnostic workup and treatment prior to biopsy. Diagnostic yield, clinical impact and in-hospital complication rates were assessed.

Results: 64 patients were included, 20 (31.3%) of them immunosuppressed (15 HIV+ patients). 35 (67.7%) were previously treated with corticosteroids or anti-infectious agents, with higher percentage (93.3%) in the immunosuppressed group. Biopsy results were diagnostic in 48 (75%) cases. More frequent diagnosis were infectious diseases in 20 (31.2%), inflammatory diseases in 13 (20.3%) and neoplastic in 12 (20%). Brain biopsy resulted on impact on patient's clinical management in 56 (87.5%), of which 69.8% were submitted to treatment change. In-hospital complications were registered in 4 (6.6%) patients. All cause in-hospital mortality was 3.3%.

Conclusion: Brain biopsy had clinical impact, including a change in treatment, in the majority of patients studied, and may be considered a useful diagnostic option in nonneoplastic brain disease. However, associated complication rate is not negligible, and previous thorough workup, patient selection and risk-benefit assessment are important.

Disclosure: Nothing to disclose

O1006

Recurrent community-acquired bacterial meningitis in adults

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Background and aims: Recurrent episodes of bacterial meningitis have previously been described in 5% of cases and has been associated with a relatively favorable prognosis. Recent changes in epidemiology of bacterial meningitis may have changed the risk factors and characteristics. Furthermore, it is unclear whether vaccines failures occur.

Methods: We analyzed adults with recurrent episodes from a prospective nationwide cohort study of community-acquired bacterial meningitis.

Results: We identified 143 recurrent episodes of community-acquired bacterial meningitis out of 2264 episodes (5%) in 123 patients. The median age was 57 years (IQR 43-66) and 57 episodes (46%) occurred in men. The median duration between the first and the current episode was 5 years (IQR 1-15). For 82/123 patients (67%) it was the first recurrent episode, 30 patients had 2-5 previous episodes (24%), 2 had 6-10 episodes (2%), and 2 had >10 episodes. Predisposing factors were identified in 86/123 patients (70%), most commonly consisted of ear or sinus infections (45/123 [37%]) and cerebrospinal fluid leakage (36/122 [30%]). The most common pathogens were *Streptococcus pneumoniae* (80/123 [65%]) and *Haemophilus influenzae* (16/123[13%]). The outcome was unfavorable (Glasgow outcome scale score<5) in 22 patients with recurrent meningitis (18%) versus 806 (40%) for non-recurrent meningitis patients (p<0.001). Five versus 363 patients died (4% vs. 18%, p<0.001).

Conclusion: Recurrent meningitis frequently occurs due to predisposing factors, most commonly ear or sinus infections and CSF leakage. Recurrent episodes are predominantly caused by *S. pneumoniae* and *H. influenzae*. The disease course is less severe with a lower mortality rate compared with non-recurrent meningitis patients.

Disclosure: Nothing to disclose

O1007

Molecular epidemiology, incidence and mortality of neonatal group B streptococcal meningitis and sepsis in the Netherlands

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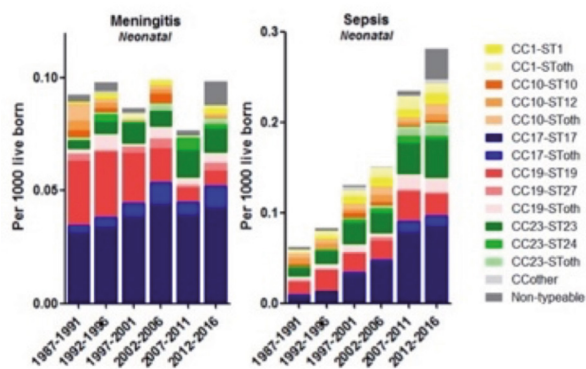
Background and aims: Group B streptococcus (GBS) is the most common cause of neonatal meningitis and sepsis. We assessed the molecular epidemiology, incidence and mortality of invasive neonatal GBS infections in the Netherlands.

Methods: Culture positive GBS cases in patients 0-3 months old between 1987 and 2016 were identified through Netherlands Reference Laboratory for Bacterial Meningitis. Serotyping was performed by latex agglutination. Sequence types (ST) were determined using whole genome sequencing. Outcome data was obtained through the Municipal Personal Records Database.

Results: 1396 episodes in 1386 patients were identified; 177 (13%) were cultured from cerebrospinal fluid (CSF), 344 (25%) from CSF and blood, and 875 (63%) from blood only. The annual incidence of meningitis remained stable, due to a decline in ST19 cases ($b=-0.001$, $p<0.001$) with a concurrent non-significant increase of ST17. The incidence of sepsis increased from 0.06 in 1987 to 0.29 per 1000 livebirths in 2016 ($b=0.009$, $p<0.001$), mainly due to a rise in ST17 ($b=0.003$, $p<0.001$). Serotype III was associated with meningitis, causing 403/508 (79%) of the meningitis and 433/838 (52%) of the sepsis cases ($p<0.001$). Mortality rate was 8% (27/323) in meningitis cases and 6% (39/656) in sepsis cases ($p=0.175$). Serotype Ib was associated with mortality in meningitis (OR 8.78 95%CI 1.92-40.05) compared to serotype III, even after correcting for multiple testing.

Conclusion: The overall incidence of GBS meningitis remained stable. The incidence of sepsis increased mainly due to the rise of ST17.

Disclosure: Nothing to disclose



O1008

Central Nervous System Vasculitis in Whipple Disease: a Case Report

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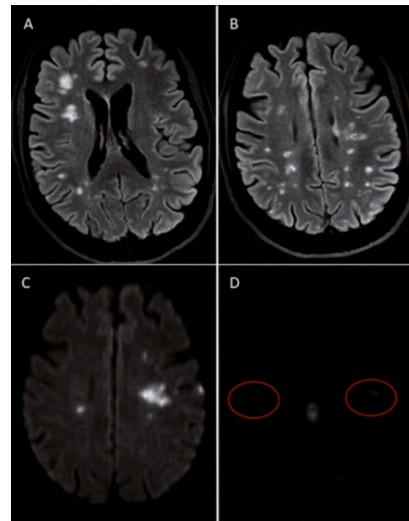
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Background and aims: Whipple disease (WD) is a rare systemic infection with possible involvement of the central nervous system (CNS). The neurological manifestations of the disease are various and can mimic any neurologic condition.

Methods: Case report.

Results: A 46-year-old woman developed acute right-sided hemiparesis and dysarthria. She had a 10-year history of diffuse arthralgias, episodic fever and rash of unclear etiology poorly responsive to different immunotherapies. Brain MRI demonstrated multiple anterior circulation infarctions and stenosis of the bilateral M1 segments of the middle cerebral artery on MR angiography. Black blood sequences revealed contrast enhancement of the vessel walls consistent with vasculitis (Figure 1). Cerebrospinal fluid (CSF) analysis was unrevealing, including PCR for viruses and bacteria. A working diagnosis of primary CNS vasculitis and progressive neurologic deterioration with abnormal behavior and altered mental status prompted the initiation of intravenous (IV) methylprednisolone followed by cyclophosphamide without significant improvement. Re-evaluation of the long-standing history of ill-defined rheumatologic manifestations unresponsive to immunotherapy led to wide-spectrum investigations. PCR for *Tropheryma Whipplei* was positive in stool, urine, blood and CSF, and duodenal mucosal biopsies confirmed the diagnosis. A combination of ceftriaxone, doxycycline, and hydroxychloroquine was initiated. Three days later the patient developed periocular burning pain and cutaneous vesicles consistent with shingles. Varicella-zoster virus DNA was detected in CSF and IV acyclovir was started. At 3 months follow-up neurologic examination was unremarkable except for a slightly fatuous behavior.



Brain MRI FLAIR sequences revealing hyperintense lesions in the subcortical white matter of both hemispheres (A-B). C, DWI sequences showing several recent ischemic lesions bilaterally with prominent involvement of the left frontal lobe. D, black blood sequences documenting enhancement and thickening of the wall vessel of both MCAs (red circles).

Conclusion: Recognition of rare manifestations of WD is important to avoid diagnostic delay and inappropriate, potentially harmful treatments.

Disclosure: Dr. Matteo Tagliapietra receives training grant from Pfizer

Neuromuscular junction diseases; peripheral nerve disorders

O1009

Zilucoplan, an investigational peptide inhibitor of complement component 5, blocked muscle weakness in a humanized passive transfer model of immune-mediated necrotizing myopathy

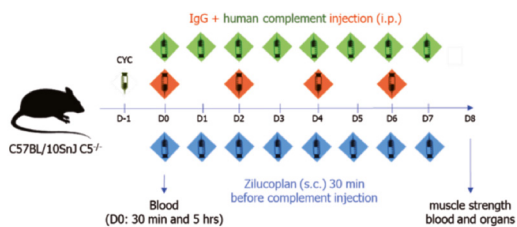
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Background and aims: Immune-mediated necrotizing myopathy (IMNM) is a rare and severe inflammatory myopathy. On biopsy, necrosis of skeletal muscle fibers, prominent complement activation and deposition of C5b-9 membrane attack complex (MAC) is observed. Autoantibodies against signal recognition particle and hydroxy-3-methylglutaryl-CoaA reductase (HMGCR) are associated with IMNM subtypes. Zilucoplan is a convenient, subcutaneously self-administered macrocyclic peptide inhibitor of complement component 5 (C5) developed by Ra Pharma, currently in Phase 2 development for IMNM and in Phase 3 development for acetylcholine receptor-positive generalized myasthenia gravis (gMG).

In this study, we provide preclinical evidence of the protective role for C5 inhibition by Zilucoplan in a humanized murine model of IMNM.

Methods: C5-deficient B10.D2/oSn mice received daily intraperitoneal injections of IgG-depleted human serum as source of human complement. Disease was induced by injection of IgG purified from an anti-HMGCR+ IMNM patient or healthy donor as control every other day. A subgroup was treated with daily subcutaneous injections of zilucoplan (Figure 1). Muscle strength following sciatic nerve electrostimulation of a gastrocnemius and markers of C5 activation in sera and muscle tissue sections were measured at day 8.



To reduce anti-human xenogeneic immune responses, mice received a single dose of 300 mg/kg of cyclophosphamide at day-1. A total of 24 mice for a n=8 per group was used.

Figure 1: Description of dosing-regimen for the IMNM passive transfer model

Results: Administration of zilucoplan completely prevents the decrease in muscle strength observed following co-administration of human complement and anti-HMGCR autoantibodies (Figure 2). C5 activation is inhibited in the sera of animals treated with zilucoplan. Histological data (ongoing) will be provided.

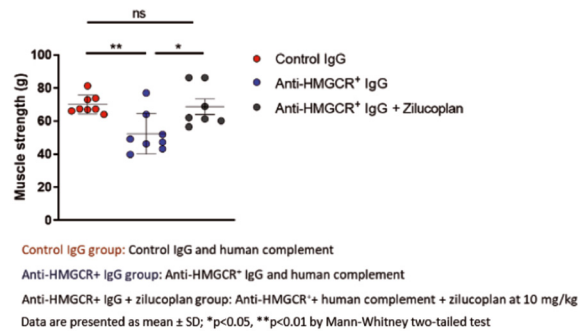


Figure 2: Zilucoplan completely prevents muscle weakness following passive transfer of anti-HMGCR and human complement to C5-deficient B10.D2/oSn mice

Conclusion: Our data establish a central role for C5 activation in a preclinical IMNM model, supporting the therapeutic evaluation of zilucoplan in an ongoing multicenter Phase 2 IMNM clinical trial (NCT04025632).

Disclosure: This work received financial support from Ra Pharmaceuticals. SR, AR, CS, and DV are employees and shareholders of Ra Pharmaceuticals.

O1010

Clinical correlations and progression rate of patients with late-onset dysferlinopathy (≥ 30 years): a French nationwide retrospective study

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Background and aims: Dysferlinopathies are a group of muscle disorders caused by mutations in the DYSF gene. Onset of disease is rarely beyond 30 years. With the advent of NGS technologies, patients with late-onset dysferlinopathy are recognized more frequently, although descriptions as a group are lacking. The aim of this study is to characterize this subgroup of “milder” forms of the disease and to define clinical correlations and progression.

Methods: Nation-wide retrospective study of French neuromuscular network (FILENEMUS) centers. Inclusion criteria are i) symptomatic patients ii) onset ≥ 30 years iii) absent dysferlin on muscle immunoblot/western-blot iv) 2 DYSF gene mutations. Clinical, paraclinical and functional data will be collected (at first and last visits). Patients from the international dysferlinopathy cohort from the JAIN foundation will be ascertained following the same criteria.

Results: 22 patients were ascertained in France and 20 (90.9%) already included. Mean age is 59.8 ± 9.52 SD years and 63.2% are females. Symptom onset was at 39.5 ± 9.1 SD years, 12 between 30-39 years (late-onset) and 8 after 40 years (very-late-onset). Phenotypes at onset encompass Miyoshi myopathy (40%), pseudometabolic (40%) and axial (20%). 73.3% showed proximal lower-limb weakness on follow-up (at 12.9 ± 5.9 SD years). One patient has lost ambulation, and one patient presents respiratory insufficiency. Genetic heterogeneity was noticed. Furthermore, 19 patients fulfilling inclusion criteria from the JAIN international cohort will be added.

Conclusion: We will provide a full characterization of

patients with late-onset dysferlinopathy with the goal of better understanding this subgroup of patients who will influence power and design of clinical trials.

Disclosure: Nothing to disclose

O1011

Role of next generation sequencing in the diagnosis of congenital neuromuscular diseases: the experience of an Italian centre

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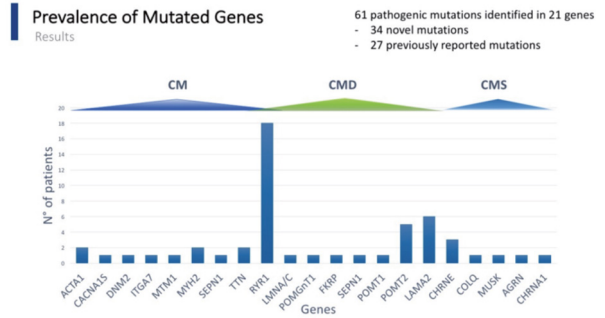
Policlinico, Milan, Italy, ⁴Dino Ferrari Centre, Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, IRCCS Foundation Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy., Milan, Italy,

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Background and aims: Congenital myopathy (CM), congenital muscular dystrophies (CMD) and congenital myasthenic syndromes (CMS) are heterogeneous groups of genetic disorders. In last years, genetic techniques developed from Sanger to Next Generation Sequencing (NGS) and Whole Exome/Genome Sequencing allowing the discovery of disease-related genes and a better understanding of molecular disease-basis.

Methods: We analysed our 10-year experience in the diagnosis of congenital neuromuscular diseases from a clinical, histopathologic and genetic point of view. We select a cohort of 90 patients/86 probands with a clinical suspect of congenital neuromuscular disease, which underwent extensive genetic analysis; most of patients underwent muscle biopsy prior to genetic testing.

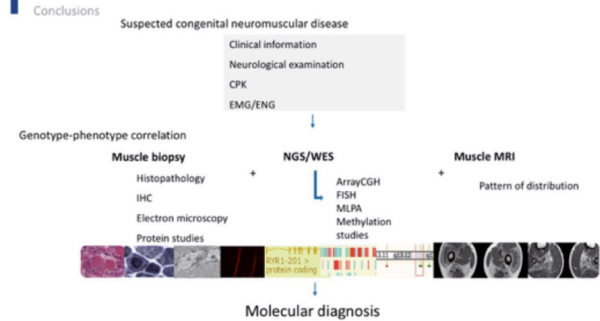
Results: The cohort presented 54 CM (60%), 26 CMD (29%) and 10 CMS (11%). 60% of patients manifested early-onset disease (6±7 m), 6 patients in infantile age (7.3±2.7 y), 33% was adult-onset (42±15 y). A molecular diagnosis was reached in the 59% (53/90): among CM 28 mutations were identified in 9 genes (14 novel mutations); in CMD 24 mutations in 9 genes (15 novel mutations); in CMS 8 novel mutations in 5 genes (6 novel mutations). NGS was applied in 52% (47/90) of patients and was diagnostic in 44%. In undiagnosed group we identified 92 variants of unknown significance in 31 genes.



Prevalence of mutated genes and their distribution in CM, CMD and CMS.

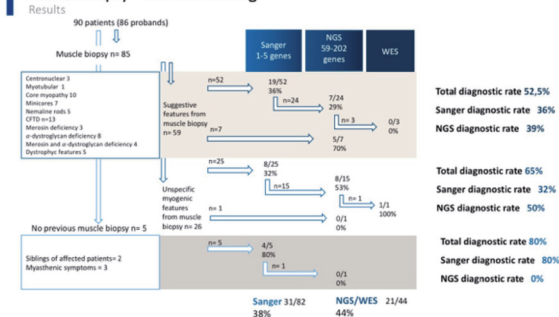
Conclusion: NGS panels reached a molecular diagnosis in a higher number of patients and identified overlapping genes and phenotypes; however, many patients remain without a molecular diagnosis: this will be fundamental for patient's selection for treatments under development. Finally, we propose a diagnostic algorithm for congenital neuromuscular diseases.

Diagnostic Algorithm



Disclosure: Nothing to disclose

Muscle Biopsy – Genetic Testing



Flow diagram to visualize the step-wise diagnostic workup and the number of positive genetic results (absolute number and frequency) for all patients. Biopsy findings and clear phenotypic data that guided the targeted testing are mentioned in detail and in their frequency.

O1012

Exploring possible predictors of clinical outcomes following nusinersen treatment of Spinal Muscular Atrophy (SMA): interim results from the Phase 2 NURTURE Study

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Background and aims: NURTURE is an ongoing open-label study (NCT02386553) examining the efficacy and safety of intrathecal nusinersen initiated in presymptomatic infants with 2 or 3 SMN2 copies.

Methods: Enrolled infants were age ≤ 6 weeks at first dose, clinically presymptomatic, and genetically diagnosed with SMA. Primary endpoint is time to death or respiratory intervention (invasive/non-invasive ventilation for ≥ 6 hours/day continuously for ≥ 7 days or tracheostomy). Cerebrospinal fluid (CSF) was drawn prior to nusinersen administration to assess phosphorylated neurofilament heavy chain (pNF-H) levels on Days 1, 15, 29, 64, 183 and every 119 days subsequently. Correlations (Spearman's rho) were determined between pNF-H levels and HINE-2 motor milestone total score and WHO motor milestone walking alone, with additional correlational analyses.

Results: NURTURE enrolled 25 infants (2 copies SMN2, n=15; 3 copies, n=10). As of 29 March 2019 interim analysis, median age at last visit was 34.8 (range 25.7–45.4) months. All infants were alive and none required permanent ventilation. CSF pNF-H levels rapidly declined after initiation of nusinersen before stabilizing at lower plateau levels. CSF pNF-H levels at Baseline and Day 64 in the overall population were significantly correlated with earlier achievement of WHO motor milestone walking alone and HINE-2 total score at Day 302. In participants with 2 SMN2 copies, Day 64 weight for age and CMAP amplitude were correlated with achievement of WHO walking alone and HINE-2 total score at Day 302.

Conclusion: CSF and plasma pNF-H levels following nusinersen loading may predict future motor function in NURTURE participants.

Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Fairfield, CT, US): funding was provided by Biogen.

O1013

Knockdown and replacement of MFN2: a gene therapy to treat dominantly inherited peripheral neuropathy CMT2A

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Background and aims: Charcot-Marie-Tooth type 2A (CMT2A) is an inherited, debilitating sensory-motor neuropathy caused by missense mutations in the MFN2 (Mitofusin2) gene. MFN2 mutations appear to induce the disease with a dominant-negative mechanism, where the expression of the wild-type MFN2 allele is negatively regulated by the mutant protein. Although no effective treatment exists, the molecular silencing of the mutant pathological protein, in combination with the replacement of wild-type activity, represents a possible treatment for this disease.

Methods: We produced an adenovirus associated type 9 co-expressing short hairpin (sh)-RNA targeting MFN2 for degradation and shRNA-resistant MFN2 cDNA. This vector has been tested in in vitro (patient-specific induced pluripotent stem cell (iPSCs)-derived motor neurons (MN)) and in vivo (MitoCharc1 mice) disease models, evaluating the rescue of disease hallmarks previously identified (Rizzo et al., 2016; Cartoni et al., 2010).

Results: We demonstrated the correct silencing of MFN2 endogenous alleles and their replacement with an exogenous copy of the functional wild-type gene. This approach significantly rescues the CMT2A MNs phenotype in vitro, promoting correct mitochondrial axonal transport and mitophagy process. Finally, we demonstrated that this approach allows proper MFN2 therapeutic correction also in vivo in MitoCharc1 transgenic mice.

Conclusion: This study yields proof-of-principle data for the first effective treatment of CMT2A or other dominantly inherited forms of CMT, representing the preclinical basis to move towards clinical translation.

Disclosure: This work is supported by a grant from "Associazione MFN2" and a grant from "Telethon Foundation"

O1014

Small fiber neuropathy in clinical practice: a diagnostics algorithm

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Background and aims: Small fiber neuropathy (SFN) is a subgroup of painful sensory neuropathies which affects A-delta and C nerve fibers. A diagnostic gold standard is missing for SFN.

Methods: We recruited 92 patients with a pain history indicative of SFN and applied six small fiber tests: complete neurological examination, skin punch biopsy for intraepidermal nerve fiber density (IENFD), quantitative sensory testing (QST), corneal confocal microscopy (CCM), pain-related evoked potentials (PREP), and quantitative sudomotor axon reflex test (QSART). SFN was diagnosed if ≥ 2 tests were abnormal.

Results: Distal IENFD 61/92 (66%) and neurological examination 53/92 (53%) most frequently reflected small fiber impairment in patients followed by CCM 20/57 (53%) and PREP 27/57 (47%). Combining neurological examination, distal IENFD, and CCM and/or PREP resulted in 49/57 (86%) patients diagnosed with SFN, while QST and QSART were of low diagnostic impact.

Conclusion: We show that neurological examination and distal IENFD are key, but additional measures of small fiber abnormality enhance the diagnostic yield in SFN. We further propose a new diagnostic algorithm for SFN in clinical practice, which enables to increase the diagnostic yield when adding CCM and/or PREP to the clinical work-up.

Disclosure: Nothing to disclose

O1015

The role of observing corneal whorl-like nerve plexus in evaluating small fiber neuropathy in transthyretin familial amyloid polyneuropathy

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Background and aims: Small fiber nerve is firstly involved in transthyretin familial amyloid polyneuropathy (TTR-FAP). In vivo corneal confocal microscopy (CCM) is a rapid, noninvasive technique to detect small-fiber polyneuropathy (SFN). The whorl-like pattern of the corneal nerve plexus provides a potential static landmark for observation. We evaluated whether CCM images of the whorl-like patterns can sensitively evaluate SFN and monitor disease progression in FAP patients.

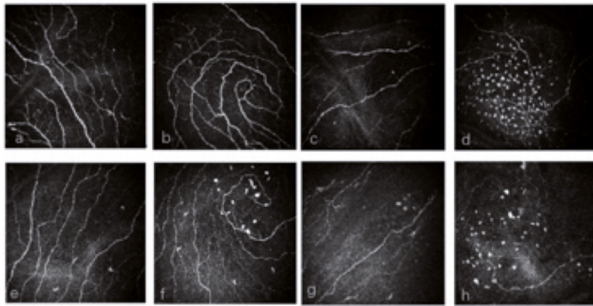
Methods: 15 FAP patients and 15 health controls underwent neurological evaluation and CCM observation. Corneal nerve fiber length (CNFL), density (CNFD), branch density (CNBD) detected by conventional method and inferior whorl length (IWL), branch density (IWBD), fiber density (IWFD) were compared in controls and patients. Langerhans cells (LCs) density in each image was calculated.

Results: CCM parameters were significantly reduced with disease progression (table1). IWL, CNFL, CNBD and CNFD were significantly lower in early phase patients. Only IWL was significantly reduced in preclinical patients ($p=0.008$). LCs density was significantly increased around the whorl area in early phase patients, and was declined in the progressive patients (figure 1). Both IWL and CNFL correlated with severity of neuropathy. IWL was more significantly reduced with disease progression (figure 2). The area under the ROC curve for CNFL and IWL was 88.0% and 89.3%, exceeding other parameters.

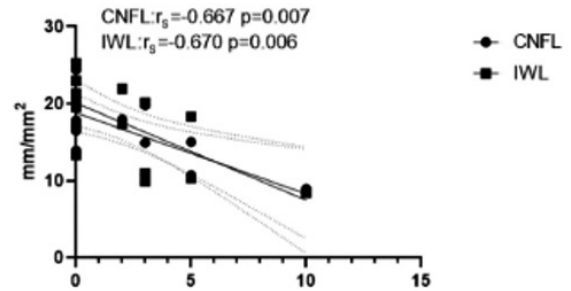
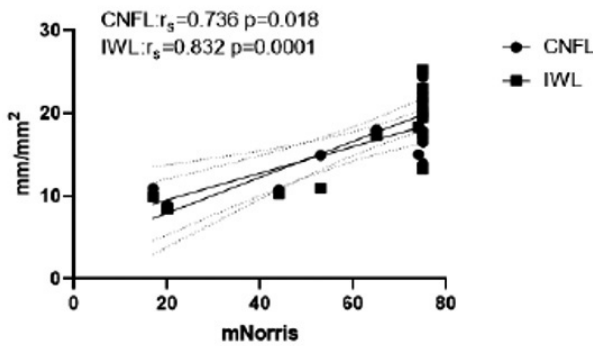
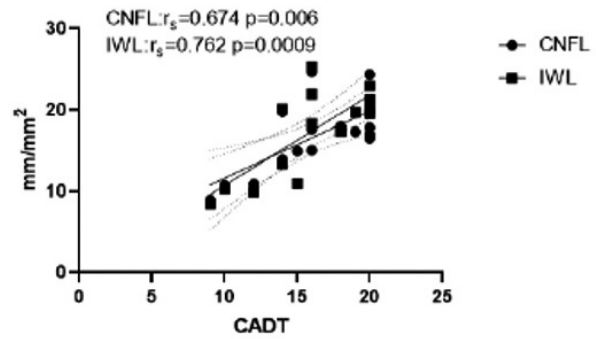
	Control (n=14)	Phase I (n=10)	Phase II (n=5)	P Control vs I	P I vs II
IWL(mm/mm ²)	24.36±3.39	18.26±7.14	11.42±3.47	0.006**	0.001**
IWBD/(mm ²)	87.79±32.71	72.19±14.58	15.42±12.47	0.26	0.001**
IWFD/(mm ²)	39.44±9.61	34.17±11.80	15.83±7.45	0.24	0.008**
CNFL(mm/mm ²)	22.54±3.20	18.42±3.61	11.37±2.53	0.005**	0.04*
CNBD/(mm ²)	68.13±23.36	42.92±14.97	12.08±6.49	0.008**	0.00*
CNFD/(mm ²)	41.13±8.86	32.50±7.62	23.32±11.80	0.014*	0.21
CNFT(°)	141.81±7.02	140.36±6.60	139.20±5.60	0.53	1.00
IW LC(n/mm ²)	86.95±38.93	226.07±175.02	129.20±107.89	0.002*	0.31
LC(conventional)(n/mm ²)	36.83±29.65	35.28±30.58	37.58±17.62	0.68	0.59
IW LC- LC(conventional)	50.05±99.62	190.79 ± 182.19	99.97±96.26		
	(p=0.07)	(p=0.009)	(p=0.19)		

IWL: inferior whorl length; IWBD: inferior whorl branch density; IWFD: inferior whorl fiber density; CNFL: corneal nerve fiber length; CNBD: corneal nerve branch density; CNFD: corneal nerve fiber density; CNFT: corneal nerve fiber tortuosity; LC: Langerhans cells;

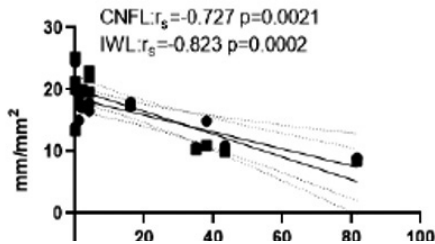
CCM parameters in controls, early phase (phase I) and progressive phase (phase II) of FAP patients.



CCM images of the central cornea and IW in control subject (a and b), preclinical FAP patient (c and d), early phase patient (e and f) and progressive phase patient (g and h). Distinctive whorl-like pattern of the sub-basal nerve plexus could be detected and LC clustered could be noted at preclinical and stage I patient.



Correlation Between Corneal Nerve Length and Neurologic Findings. IWL was more significantly reduced with the progression of disease.



Conclusion: IWL is a more sensitive surrogate to detect SFN in FAP patients and can best discriminate FAP patients from controls. The converge of immature LCs at the whorl area might reflect the inflammation response of small nerve fiber at the very early stage.

Disclosure: Nothing to disclose

Headache and pain

O1016

Cardiovascular safety of erenumab in patients with migraine with or without a history of aura

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Background and aims: Migraine with aura is associated with cardiovascular and cerebrovascular disease. We evaluated cardiovascular safety of erenumab (erenumab-aooe in the US) in patients with migraine with or without a history of aura.

Methods: Safety of erenumab was assessed in a post-hoc analysis of adverse events (AEs) from four double-blind, placebo-controlled studies and their open-label extensions in patients with episodic or chronic migraine with/without a history of aura. Standardised search terms were used to identify cardio/cerebrovascular and hypertension AEs.

Results: Of 2443 patients treated with erenumab (70 mg/140 mg once monthly) or placebo during double-blind treatment phase (DBTP), 1140 (47%) had a history of aura. At baseline, ≥ 2 cardiovascular risk factors were present in more patients with aura than without (35% vs 27%). Vascular disease risk factors were more prominent in the aura subgroup (Table). Cardio/cerebrovascular AE rates were low throughout the erenumab exposure period (up to 256 weeks) with no differences among patients with/without aura (n=6, 0.4/100 patient-years; n=5, 0.3/100 patient-years). Hypertension-related AEs were reported at similar rates in both subgroups (n=30, 2.3/100 patient-years; n=37, 2.2/100 patient-years). Rates of cardio/cerebrovascular and hypertension-related AEs, general AEs, and all serious adverse events were similar between the placebo and erenumab treatment groups during the 12-week DBTP regardless of aura history.

Table. Vascular disease risk factors in the subgroup populations with aura and without aura

Vascular disease risk factors	With aura	Without aura
Diabetes	2.6%	1.0%
History of hypertension	8.2%	6.6%
High blood pressure (systolic ≥ 140 mm Hg or diastolic > 90 mm Hg)	7.5%	6.1%
High lipids (triglyceride > 150 mg/dL)	26.7%	22.5%
BMI > 30 kg/m ²	30.4%	20.6%
Elevated cholesterol (total cholesterol > 200 mg/dL, LDL > 130 mg/dL, or HDL < 40 mg/dL)	47.9%	47.7%

BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein

Conclusion: The vascular safety profile of long-term erenumab treatment was similar in patients both with and without a history of aura and was comparable to that of placebo over 12 weeks, with no increased emergence of events over time.

Disclosure: Novartis Pharma AG, Basel, Switzerland, funded this study. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance outstanding.

O1017

Characteristics of the first head-to-head randomized, double-blind, double-dummy trial of erenumab and topiramate for the prevention of episodic and chronic migraine

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Background and aims: Migraine is one of the most common causes of disability worldwide. In the past, several drug classes with a multitude of mechanisms have been used for prophylactic treatment of migraine, most of which are associated with high treatment discontinuation rates due to poor tolerability or insufficient efficacy. In 2018, the FDA and EMA approved erenumab as the first specifically developed prophylactic migraine treatment. For the first time, erenumab will directly be compared to one of the most commonly prescribed first-line prophylactic drugs.

Methods: HER-MES is the first head-to-head trial comparing the tolerability and efficacy of erenumab to the highest individually tolerated dose of topiramate in a German cohort of 750 episodic and chronic migraine patients who are naive to, not suitable for or have already failed up to three previous prophylactic treatments. HER-MES comprises a 24-week double-blind, double-dummy treatment epoch (DBTE) in which patients receive either 70mg or 140mg erenumab (investigator's choice) and a topiramate-placebo. The control group receives an erenumab-placebo and the maximally tolerated dose of topiramate, titrated within the first six weeks of the DBTE. Patients will complete eDiaries during baseline (4-weeks) and DBTE to evaluate treatment efficacy. As primary endpoint, tolerability will be assessed by the rate of treatment discontinuation due to adverse events.

Results: We will present the detailed study design and an analysis of the population characteristics of the enrolled patients.

Conclusion: This analysis will provide insights into the patient population enrolled in the first head-to-head trial comparing the tolerability and efficacy of erenumab and topiramate.

Disclosure: Nothing to disclose.

O1018

Type of headache at onset and severity of reversible cerebral vasoconstriction syndrome

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Background and aims: In a recent Italian study, 30% of patients with reversible cerebral vasoconstriction syndrome (RCVS) presented without typical thunderclap headache (TCH), and had a tendency to present more severe forms of RCVS than patients with TCH (Caria et al., Cephalalgia 2019). We aimed to analyze the severity of RCVS in patients with and without TCH at onset.

Methods: In a cohort of 173 French patients with RCVS, we compared patients with and without TCH at onset regarding rates of any brain lesions on imaging and any neurological complications (namely persistent focal deficit, seizures, dissections and brain lesions); and severity of RCVS defined as mild (absence of brain lesions, mRS 0 at 3 months) vs. moderate/severe (presence of brain lesions, mRS ≥ 1 at 3 months).

Results: As compared to the 142 patients with TCH at onset, the 31 patients without TCH had significantly more brain lesions (52% versus 30%, $p=0.035$, OR 2.5 [1.1-5.4]), neurological complications (64.5% versus 34%, $p=0.002$, OR 3.6 [CI 1.6-8.0]), and a higher risk of having a moderate/severe form of RCVS (52% versus 30%, $p=0.035$, RR 1.7 [CI 1.1-2.6]).

Conclusion: Absence of TCH at onset might predict a higher risk of severe RCVS. Our results warrant further studies in order to provide better pathophysiological understanding and clinical management of patients with RCVS.

Disclosure: Nothing to disclose

O1019

BRAIN NETWORKS IN MIGRAINE: a pilot study using advanced fMRI techniques in experimentally-induced attacks

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Background and aims: Resting state functional magnetic resonance imaging (rs-fMRI) studies have depicted cyclical functional connectivity changes during the ictal and inter-ictal phase of the migraine attack.

In this pilot study, FC changes during nitroglycerin (NTG) induced migraine attacks versus pain-free state were assessed on 5 subjects with episodic migraine (EM) without aura (3M-2F, 33±6.5 years). NTG-triggered a spontaneous-like migraine attack in all the 5 EM subjects without aura.

Methods: All subjects underwent 4 rs-fMRI repetitions during different phases of the attack (baseline, prodromal, full blown, recovery phase) using a 3T MRI-scanner.

Subjects' rs-fMRI data were processed with a seed-based correlation analysis (SCA), selecting different brain areas as seeds, according to literature in the pain field.

Results: In EM, results showed that the brainstem elements involved in the pain circuits (such as the spinal trigeminal nucleus, periaqueductal grey and dorsal raphe nuclei) and the thalamus exhibit an altered functional coupling within themselves and the hypothalamus, particularly during the prodromal phase. The whole brain activity coupled with the left thalamus instead, showed greater involvement during the full-blown phase.

Conclusion: These findings reveal that during the NTG-induced migraine attack the whole brain FC changes systematically, involving areas well known for their roles in pain modulation and migraine generation. Therefore, this study with the NTG model applied to advanced fMRI approach promotes the idea of migraine as a cyclical functional disorder in which brainstem pain-modulating circuitry and hypothalamus have a leading role in the premonitory phase, while the thalamus plays a more relevant role in the full-blown phase.

Disclosure: Nothing to disclose

O1020

Prevention of post-dural puncture headache – a randomized controlled trial

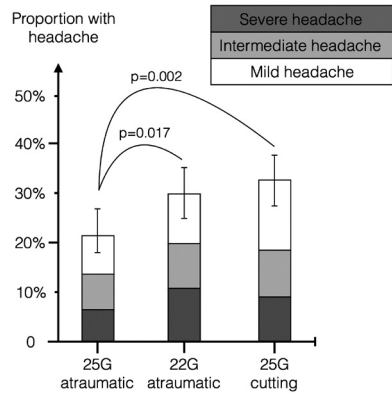
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Background and aims: The objectives were to investigate the effects of needle size, needle design and stylet reinsertion on the risk for post-dural puncture headache (PDPH). To this end, we investigated n=952 subjects undergoing diagnostic LP.

Methods: This randomized double-blind study was performed at Umeå University Hospital in Sweden during 2013–2018. Subjects were randomly assigned one of three needles (22 Gauge (G) atraumatic, 25G atraumatic and 25G cutting); and stylet reinsertion before needle withdrawal or not. The main outcome measure was PDPH assessed by standardized telephone interview(s) 5 days after the LP, repeated until headache cessation. We used logistic regression to calculate odds ratios (ORs) with 95% CIs for PDPH.

Results: Mean (SD) age was 51.1 (16.7) years and 53.6% were females. The smaller bore (25G) atraumatic needle incurred a lower risk for headache, 22.0% (69/314), compared with the larger bore (22G) atraumatic needle, 30.2% (98/324), OR (95% CI) = 0.65 (0.45–0.93); and compared with the cutting needle, 32.8% (103/314), OR (95% CI) = 0.58 (0.40–0.82). Reinserting the stylet before needle withdrawal did not reduce the risk for headache, 26.3% (125/475) vs. 30.4% (145/477), OR (95% CI) = 0.82 (0.62–1.1).



No. of subjects with post lumbar puncture headache	69/314	98/324	103/314
Odds ratio (OR) and 95% confidence interval (CI) for any headache	0.65 (0.45–0.93)	Reference	– (size)
Odds ratio (OR) and 95% confidence interval (CI) for any headache	0.58 (0.40–0.82)	–	Reference (design)

Proportion of subjects within each needle arm reporting post-dural puncture headache (PDPH). The PDPH was graded as mild (not needing intervention), intermediate (exceeding the previous grade but not meeting the criteria for severe headache), and severe (preventing daily activities such as studies, work etc.).

Conclusion: This study provides class 1 evidence that a 25G atraumatic needle is superior to a larger atraumatic needle, and to a same sized cutting needle, to prevent PDPH after diagnostic LP; and that stylet reinsertion does not prevent PDPH.

Disclosure: This study was funded by a research grant from the Department of Clinical Science, Neurosciences at Umeå University.

Movement disorders 1

O1021

Clinical and genetic findings in a multigenerational Austrian family harbouring a SCA40 mutation

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Background and aims: We report clinical features and genetic findings of the first Austrian and third reported family worldwide with Spinocerebellar Ataxia Type 40 (SCA40). SCA40 is an autosomal dominant disease. Clinical symptoms include ataxia, spastic paraparesis, and parkinsonian symptoms. It is caused by mutations in the CCDC88C gene on chromosome 14, which activates the c-Jun terminal kinase (JNK) pathway and triggers apoptosis. To date only two families (China, Poland) with SCA40 have been reported.

Methods: We identified a family with six affected patients from three generations. Clinical follow-up is available in three patients for up to nine years. Genetic workup, repeated neurological examinations, and cerebral imaging were performed in affected family members. Interestingly, two affected patients suffer from haemochromatosis, diabetes mellitus and one of non-Hodgkin lymphoma. We undertook further genetic and functional testing to elaborate the pathogenicity of the mutation and its impact on downstream pathways.

Results: First clinical symptom was gait disturbance in their mid-thirties. All patients subsequently developed a slowly progressive pure cerebellar syndrome. MR imaging displayed cerebellar atrophy. SARA-scores range from 10.5 to 14/40 points. Genetic testing revealed a new missense mutation (c.956G>A;p.Arg319Gln) in the conserved hook domain of the CCDC88C gene. It was classified as Variant of unknown Significance. Functional testing in fibroblasts revealed hyperphosphorylation of JNK.

Conclusion: We hereby present the third reported family with SCA40. Our patients presented with an adult onset slowly progressive cerebellar syndrome. Genetic and functional testing indicated pathogenicity of the mutation. Functional testing on the impact on downstream pathways is under way.

Disclosure: Nothing to disclose

O1022

Disruption of white matter tracts and cognitive decline after deep brain stimulation in Parkinson's disease

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Background and aims: Deep brain stimulation of the subthalamic nucleus (STN-DBS) is a well established treatment with marked motor benefits for patients with Parkinson's disease (PD). However, adverse cognitive effects have been described and their mechanisms are still poorly understood. It has been suggested that it may be related to a microlesion effect due to the electrodes trajectories. We evaluated the lesions of white matter tracts as a possible reason for cognitive side effects of STN-DBS.

Methods: A consecutive group of 51 PD-patients underwent neuropsychological assessment before DBS and 6 months after in on-drug/on-stimulation condition. It included a global cognitive evaluation and selective cognitive investigation comprising attentional-executive functions, verbal memory, phonemic and semantic verbal fluency tasks. Pre-operative brain MRI and post-operative CT were acquired. We segmented the trajectories of the electrodes and after normalization we used a white matter tract atlas (Tractotron Software) to obtain probability and proportion of fibers disconnection.

Results: We found a decline six months after surgery in global cognitive evaluation and in selective cognitive domains including episodic verbal memory, executive functions and phonemic and semantic verbal fluency. The tract atlas analysis revealed that the electrodes intersected with the frontal aslant tract, arcuate tract, superior longitudinal fasciculus, anterior thalamic radiation and fronto-striatal tract. We found a correlation between decline in cued recall in verbal memory and proportion of lesion of superior longitudinal fasciculus.

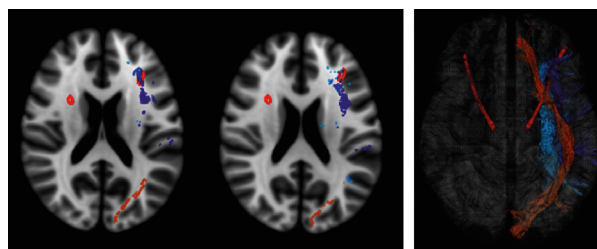


Figure. Axial slices and 3D reconstruction of Superior Longitudinal Fasciculus (blue) and Inferior Longitudinal Fasciculus (orange). In red : electrodes trajectory.

Axial slices and 3D reconstruction of Superior Longitudinal Fasciculus (blue) and Inferior Longitudinal Fasciculus (orange). In red : electrodes trajectory.

Conclusion: The trajectories of electrodes in STN-DBS intersect with tracts involved in different cognitive domains. Our study provides further support for a micro-lesion effect in cognitive decline after surgery.

Disclosure: Nothing to disclose

O1023

A prediction model for functional movement disorders based on associated features

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Background and aims: Functional movement disorders (FMD) pose a diagnostic challenge for clinicians. Over the years several associated features showed to be suggestive for FMD. We examined which of the associated features mentioned in literature are discriminative between functional and organic movement disorders. Secondly, we developed a prediction model for FMD based on these differences.

Methods: We reviewed the medical records of all consecutive patients who visited the hyperkinetic outpatient clinic from 2012 till 2019 and compared 12 different clinical characteristics and associated features in patients with functional versus organic movement disorders. We performed an independent t-test for the continuous variable age of onset and Pearson Chi-square analyses for all other categorical variables. Multivariate logistic regression analysis was applied to develop a model for the prediction of FMD.

Results: A total of 874 patients were eligible for inclusion in the study of which 554 (63%) had an organic and 320 had a functional movement disorder. The features that significantly differed between these groups were sex, age of onset, more than one movement disorder, psychiatric history, family history, pain, fatigue, abrupt onset, waxing and waning over long term, and fluctuations during the day. Based on these we computed a predictive model with a discriminative value of 91%.

Conclusion: The good to excellent discriminatory capacity of the model could be used to assist physicians identify patients with FMD. When there is a high predicted chance of FMD, the physician can be alert for testing positive signs at neurologic examination.

Disclosure: Nothing to disclose

O1024

Patient characteristics, treatment patterns and disease burden in people with Parkinson's disease: insights from the Parkinson's disease real-world impact assessment (PRISM) study

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Background and aims: PRISM was a European survey of the burden of Parkinson's disease (PD), medication use, healthcare resource utilisation and health-related quality of life (HRQoL) in people with PD (PwP) and their care-partners. Data on patient characteristics, treatment patterns and burden of disease in PwP are presented.

Methods: PRISM was a descriptive, exploratory, observational study with cross-sectional design. The survey was designed in collaboration with The Cure Parkinson's Trust (a UK-based advocacy group) and an international scientific committee. Data were collected using an online survey completed by PwP and their care-partners as matched samples. Multivariate analysis was used to explore drivers of Parkinson's Disease Questionnaire-39 (PDQ-39) summary score.

Results: Between April-July 2019, data were collected from 861 PwP (599 complete responses; 262 partial responses) from six European countries (characteristics in Table 1). Levodopa was used by 84% of PwP in the previous 12 months and as monotherapy in 22% of all PwP (Table 2). In 67% of PwP (544/812), levodopa was the first prescribed anti-PD medication. PwP had impaired HRQoL (mean±standard deviation PDQ-39 score, 32.1±18.3), a wide range of non-motor symptoms (mean±standard deviation Non-Motor Symptoms Questionnaire score, 12.8±6.0) and frequent issues with sexual functioning (Table 3). Higher numbers of comorbidities and non-motor symptoms were associated with worse HRQoL (Table 3).

Conclusion: Two-thirds of PRISM respondents have been levodopa users since PD treatment start, in contrast to previous prescription patterns [1], and experienced decreased HRQoL in relation to more comorbidities and non-motor symptoms.

1. Fargel et al. Clin Drug Invest 2007;27(3):207-218.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

Table 1. Patient characteristics of PwP

Characteristic	N=861
Country, n (%)	
France	63 (7.3)
Germany	92 (10.7)
Italy	264 (30.7)
Portugal	80 (9.3)
Spain	149 (17.3)
UK	213 (24.7)
Male gender	
N	851
Male, n (%)	433 (50.9)
Age, years	
N	855
Mean (SD)	65.0 (10.2)
Age at diagnosis, years	
N	827
Mean (SD)	57.7 (11.3)
Disease duration, years	
N	813
Mean (SD)	7.7 (6.3)
Most frequently reported ^a comorbidities	
N	845
Hypertension, n (%)	217 (25.7)
Depression, n (%)	188 (22.2)
Anxiety, n (%)	136 (16.1)
Rheumatic diseases, n (%)	91 (10.8)

^a≥10% of PwP. PwP, people with Parkinson's disease; SD, standard deviation

Table 2. Medication use in PwP

Parameter	
Current use ^a by agent ^b , %	
L-dopa/DDCI, n/N (%)	659/788 (83.6)
DA, n/N (%)	397/779 (51.0)
MAO-Bi, n/N (%)	318/779 (40.8)
COMTi, n/N (%)	114/778 (14.7)
Amantadine, n/N (%)	75/775 (9.7)
Rivastigmine, n/N (%)	33/774 (4.3)
Anticholinergics, n/N (%)	16/773 (2.1)
Current use ^a by therapeutic combinations ^c	
N	800
L-dopa monotherapy, n (%)	175 (21.9)
L-dopa + COMTi, n (%)	21 (2.6)
L-dopa + DA, n (%)	111 (13.9)
L-dopa + MAO-Bi, n (%)	71 (8.9)
L-dopa + COMTi + DA, n (%)	26 (3.3)
L-dopa + DA + MAO-Bi, n (%)	115 (14.4)
L-dopa + COMTi + MAO-Bi + DA, n (%)	30 (3.8)
DA monotherapy, n (%)	31 (3.9)
DA + MAO-Bi, n (%)	28 (3.5)
MAO-Bi monotherapy, n (%)	17 (2.1)
No therapy, n (%)	46 (5.8)

^aWithin previous 12 months; ^bn/N, affected subjects/total number of replies; ^ccombinations with ≥1-2% of use. COMTi, catechol-O-methyltransferase inhibitor; DA, dopamine agonist; DDCl, dopa decarboxylase inhibitor; L-dopa, levodopa; MAO-Bi, monoamine oxidase-B inhibitor; PD, Parkinson's disease; PwP, people with Parkinson's Disease

Table 3. Current health-related quality of life in PwP

Parameter	
PDQ-39 score	
N	859
Mean (SD)	32.1 (18.3)
NMSQuest score	
N	591
Mean (SD)	12.8 (6.0)
Problems with sexual functioning ^{a,b}	
Erection (men), n/N (%)	121/205 (59.0)
Orgasm (women), n/N (%)	51/142 (35.9)
Enjoyment, n/N (%)	117/335 (34.9)
Arousal, n/N (%)	115/343 (33.5)
Interest, n/N (%)	111/348 (31.9)
Current variables associated with worsened PDQ-39 summary score, mean (95% CI) increase in score	
One additional comorbidity	3.1 (1.6-4.6)
One additional non-motor symptom ^c	2.1 (1.7-2.4)

^aPatients reporting 'Very much of a problem' or 'Somewhat of a problem'; ^bn/N, affected subjects/total number of replies; ^cOne unit increase in NMSQuest score. CI, confidence interval; NMSQuest, Non-Motor Symptoms Questionnaire; PD, Parkinson's disease; PDQ-39, Parkinson's Disease Questionnaire-39; PwP, people with Parkinson's Disease; SD, standard deviation

O1025

Cerebellar rTMS theta burst for postural instability in progressive supranuclear palsy: a double blind cross-over sham-controlled study using wearing sensors technology

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Background and aims: There are no medical effective treatments for progressive supranuclear palsy (PSP). Imaging, neurophysiology and pathology studies have been suggesting the cerebellum as a promising target for tbrain stimulation to reduce postural instability. The objective of this pilot study was therefore to test the efficacy of TTS on postural instability in PSP patients using a cross-over design.

Methods: Probable PSP patients with no dementia and able to walk were included. Each patient underwent a single session of sham TBS or cerebellar TBS with a wash out period of ≥14 days. Each participant was evaluated before and after stimulation with the Berg Balance Scale (BBS), Tinetti scale, PSP-rating scale (PSP-RS), and 30-seconds-trials in semitandem and tandem positions with eyes open and closed measured with validated digital mobile technology.

Results: 20 PSP patients (mean age 74.3 years, disease duration 3.8 years, PSP-RS 29.4 + 9.6 points) entered the study. No differences in clinical scales and clinically assessed gait parameters in sham vs real stimulation sessions were detected. In static balance tests with digital technology endpoint, active stimulation was associated with increase in time without falls in tandem/semitandem tasks (p=0.04). Rehgait-extracted parameters revealed significant improvement in volume of perturbation (p=0.007), 3D-acceleration compensatory movements (p=0.005) and anterior-posterior speed (p=0.008) in real vs sham trials.

Conclusion: Repetitive cerebellar TBS showed a significant effect on stability in PSP patients, when assessed with mobile digital technology, in a double-blind design. These results of this pilot study should motivate larger and more intensive trials using TBS for stability improvement in PSP patients.

Disclosure: Nothing to disclose

O1026

The role of LRP10 mutations in Parkinson's disease and dementia with lewy bodies

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Background and aims: Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB) belong to a continuum spectrum of neurodegenerative diseases characterized by alpha-synuclein accumulation in neurons, whose etiopathogenesis remains largely uncovered. Recently, a new candidate gene (LRP10) for alpha-synucleinopathies has been identified by linkage analysis and positional cloning on an Italian family with late-onset PD. After the first characterization of a LRP10 pathogenic variant, other eight mutations have been detected in an international series of 660 PD and DLB patients. The aim of our study was to test LRP10 in an Italian cohort of clinically diagnosed PD patients.

Methods: A cohort of 511 PD patients was analysed by NGS panel approach. LRP10 variants identified were subsequently confirmed by Sanger sequencing. All variants were searched in in-house exomes from 3500 healthy subjects.

Results: 8 variants (MAF<1%) were identified in fifteen patients: one was synonymous (c. 1923G>A) and predicted to generate a potential splice site change; one was detected in an intronic region (c. 80-23G>A); seven (c.334G>A, c.415A>G, c.643T>C, c.1105T>C, c.1646G>A, c.1685G>A and c.1991C>T) led to a missense change at protein level, respectively V112I, M139V, S215P, S369F, R549Q, R562H and R661C. The M139V and R562H were detected also in 3500 Italian controls, respectively 17 and 26.

Conclusion: We reported several rare LRP10 variants in patients with PD and DLB. Considering prediction tools and the low prevalence among general population, some of them are possible pathogenic. Further investigations are warranted to define their precise role in alpha-synucleinopathies.

Disclosure: This work was supported by ADF's funds, from Intesa San Paolo and Fresco Institute.

Cerebrovascular diseases 1

O1027

Decompressive neurosurgery for patients with cerebral venous thrombosis. A prospective multicenter registry (DECOMPRESS2)

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Background and aims: Decompressive neurosurgery (DN) may be life-saving in patients with cerebral venous thrombosis (CVT) with large lesions and impending brain herniation. The ESO-EAN Guidelines made a strong recommendation for this intervention, supported by a low level of evidence (retrospective studies, small sample sizes), which could overestimate the treatment effect. We aimed to report the outcomes of CVT patients treated by DN in a large multicenter cohort.

Methods: We included consecutive CVT patients treated by DN at the participating centres. Outcomes were evaluated at discharge and 6 months. The primary outcome was modified Rankin Scale (mRS) 0-4 vs. 5-6. Secondary outcomes were complete recovery (mRS 0-1), independence (mRS 0-2), severe dependence (mRS 4-5) and death.

Results: 118 patients (80 women, median age 38 years) were included from 14 centers in Europe, Asia, and America. DN (115 craniectomies, 36 hematoma evacuations) was performed a median of 1 day after diagnosis. 71 (60.2%) patients were comatose before surgery. Pupillary reflexes were absent unilaterally in 27 (22.9%) and bilaterally in 9 (7.6%). 65 (55.1%) patients had a mRS 0-4 at discharge and 61.9% at 6 months. Mortality during hospital admission was 24.6% and 31.4% at 6 months. Complete recovery (1.7 to 11.4%) and independence (6.8 to 29.5%) increased between discharge and 6 months, while severe dependence decreased (from 49.1 to 13.3%).

Conclusion: Mortality and functional dependence were higher than those reported in previous studies of DN in CVT. Still, 2/3rd of patients were alive and 1/3rd independent by 6 months.

Disclosure: Nothing to disclose

O1028

The reliability of serum glial fibrillary acidic protein testing in differentiating between ischemic and hemorrhagic strokes: a meta analysis of diagnostic accuracy studies

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Background and aims: The aim of this meta analysis is to assess the reliability of serum glial fibrillary acidic protein (GFAP) testing in differentiating between ischemic and hemorrhagic stroke patients within the first 6 hours of onset of symptoms.

Methods: Data sources were extracted from literature search in MEDLINE, EMBASE, Cochrane library and other sources. QUADAS-2 quality grading tool was used to include the most appropriate studies relevant to our review topic. Due to the absence of heterogeneity, a fixed effect model was applied to calculate the pooled sensitivity (SN), specificity (SP), positive likelihood ratio (PLR), negative likelihood ratio (NLR), summary receiver operating characteristics curve (SROC), and diagnostic odds ratio (DOR) with their 95% confidence intervals (CI).

Results: Four studies were included in the review, all studies were observational and prospectively enrolled the total number of 584 patients (441 ischemic stroke patients and 143 hemorrhagic stroke patients). The pooled SN, SP, PLR, NLR and DOR of serum GFAP testing in diagnosing patients with hemorrhagic stroke were 0.79 (95% CI 0.69-0.86), 0.95 (95% CI 0.093-0.97), 16.56 (95% CI 10.53-26.03), 0.22 (95% CI 0.16-0.33) and 71.75 (95% CI 37.94-135.71), respectively. The area under the curve (AUC of the SROC) was 0.95.

Conclusion: Serum GFAP testing showed a high diagnostic accuracy in confirming the presence of hemorrhagic strokes within the first 6 hours of onset of symptoms.

Disclosure: Nothing to disclose

O1029

Intracranial pulsatility index on transcranial Doppler sonography: a marker of microangiopathic white matter hyperintensities?

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Background and aims: Previous studies suggested an association between increased intracranial arterial pulsatility and the severity of microangiopathic white matter hyperintensities (WMH). However, possible confounders such as age and hypertension were rarely considered and longitudinal data are lacking. We here hypothesize that in community-dwelling stroke-free subjects an increased middle cerebral artery (MCA) pulsatility index (PI) measured by transcranial Doppler sonography (TCD) relates to WMH severity and progression over 5 years follow-up.

Methods: The study population consisted of elderly participants without stroke and dementia from the community-based Austrian Stroke Prevention Study. Baseline and follow-up assessment comprised TCD, brain MRI and clinical/laboratory examination of cerebrovascular risk factors. Individuals TCD PI was averaged from baseline PIs of both MCAs and was correlated with baseline WMH severity and WMH progression over a median follow-up of 5 years. WMH severity was rated by the Fazekas scale and quantified by semi-automated volumetric assessment.

Results: The final study cohort comprised 491 participants (mean age: 60.7±6.9 years; female: 48.5%). TCD PI was related to more severe WMH at baseline ($p<0.001$) and tended to be associated with WMH progression during follow-up ($p=0.099$). However, in multivariable analyses only age ($p<0.001$) and arterial hypertension ($p<0.05$) remained significantly associated with baseline severity and progression of WMH, while TCD PI was not predictive ($p>0.1$, respectively).

Conclusion: In this large community-based cohort, MCA PI on TCD was neither associated with microangiopathic WMH severity at baseline nor predictive of WMH progression during follow-up after adjustment for important co-variables.

Disclosure: Nothing to disclose

O1030

Long-term functional decline in spontaneous intracerebral haemorrhage survivors

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Background and aims: To identify clinical characteristics and cerebral small-vessel disease (SVD) markers associated with long-term functional decline in 6-month survivors of spontaneous intracerebral haemorrhage (ICH).

Methods: We included consecutive spontaneous ICH patients with a modified Rankin scale (mRS) score between 0 and 3 six months after the index event. Long-term functional decline was defined by a transition to a mRS score of 4 or 5 during the follow-up. We evaluated clinical and radiological characteristics associated with long-term functional decline using univariate and multivariable cause-specific Cox' proportional hazard regression models.

Results: Of 560 patients with spontaneous ICH, 174 (31%) were alive and had a mRS score of 0 to 3 at 6 months. During a median follow-up of 9 years (interquartile range [IQR] 8.1-9.5), 49 patients (28%) died and 40 patients (23%) reached a mRS score of 4 or 5. Age (cause specific hazard ratio [CSHR] per 10-year increase: 1.08; 95% confidence interval (95%CI): 1.04-1.11), male sex (CSHR: 0.47; 95%CI: 0.24-0.92), diabetes (CSHR: 2.81, 95%CI: 1.31-6.01), and baseline ICH volume (HR per 1ml increase: 1.03; CI: 1.01-1.06) were independently associated with functional decline. In the subgroup of 144 patients who underwent a magnetic resonance imaging (MRI)-scan, cerebral atrophy (CSHR: 2.31; 95%CI: 1.44-3.69) and presence of strictly-lobar cerebral microbleeds (CMBs; CSHR: 3.55, CI 1.22-10.37) and mixed-CMBs (HR: 4.70; CI 1.77-12.42) were also independently associated with long-term functional decline.

Conclusion: Besides age, male sex, diabetes and baseline ICH volume, MRI markers of SVD are associated with long-term functional decline.

Disclosure: Nothing to disclose

O1031

Prospective observational study of safety of early treatment with Edoxaban in patients with ischemic stroke and atrial fibrillation (SATES STUDY)

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Background and aims: New direct oral anticoagulants are recommended for stroke prevention in patients with non-valvular atrial fibrillation (NVAF). However, no data is available for the optimal timing for starting oral anticoagulation after a stroke or TIA. We conducted this observational perspective study to evaluate the safety of early initiation (within 72 hours) of full dose of edoxaban in patients with acute ischemic stroke.

Methods: The primary objective was to evaluate any major bleeding (MB) in the first 3 months of treatment. The secondary endpoints were to evaluate the incidence of MB, hemorrhagic transformation (HT) and symptomatic hemorrhagic transformation rate, 3±2 days after the start of Edoxaban treatment. We included patients with CT/MRI signs of <1/3 MCA infarction, NVAF, no previous treatment with any other anticoagulant, preserved swallowing function. Patients with eGFR <50ml/min, body weight <60kg, receiving ciclosporin, dronedaron, eritromicine, ketoconazole were excluded.

Results: We enrolled 50 patients, the average age was 77 years and the mean NIHSS 7.8. After 3 months we observed only one MB (gastrointestinal bleeding) which comported a temporally suspension of edoxaban and 8 minor bleeding, without stroke recurrence. Evaluating the secondary objectives, we did not observe any MB or symptomatic hemorrhagic transformation; the incidence of HT was 12% for HI-1 (small petechiae) and 8% for HI-2 (confluent petechiae) without neurological deterioration. After 3 months no patient stopped the treatment.

Conclusion: According to our data the early initiation of Edoxaban seems to be safe in patients after a cardioembolic stroke. However, further studies are needed.

Disclosure: Nothing to disclose

Sunday, May 24 2020
Epilepsy 1

O2001

The connectivity epileptogenicity index: a new method for estimating the seizure onset zone from SEEG signals

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Background and aims: The main diagnostic challenge of drug resistant epilepsies is to find epileptogenic zone, which will be enough to remove to reach seizure freedom. Most of the existing machine methods focus on seizures with fast activity in the onset (FSO). Our aim was to create a new tool that helps recognize epileptogenic zone through all types of seizure onset patterns from stereo-EEG signals.

Methods: We studied seizures from 51 patients, suffering from focal drug-resistant epilepsy associated with malformation of cortical development. We separated seizure onset patterns to slow and fast. We quantified combined epileptogenicity index (cEI), based on a directed connectivity measure in beta-gamma (“out-degree”) and the classical epileptogenicity index (EI). The results were compared with seizure onset zone (SOZ), detected visually. The quality of the detector was quantified by the area under the precision-recall curve. To test differences between measures was used the Friedman test with Bonferroni correction.

Results: cEI showed the best concordance with visual SOZ in both slow (SSO) and fast (FSO) groups (figure 1). Median AUC whatever seizure onset type 0.73; (range 0.4-1, p<0.05). For fast seizure onset difference between out-degree and cEI is significant (p≤0.05). For slow seizure onset difference between EI and cEI is very significant (p≤0.01).

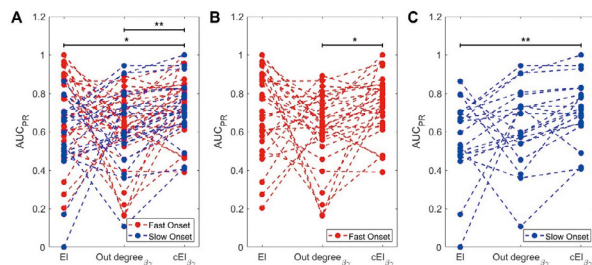


Figure 1. AUC (precision-recall) values according to the fast (FSO) and slow (SSO) seizure-onset patterns. A/ results in the whole population B/ Results in FSO C/ Results in SSO.

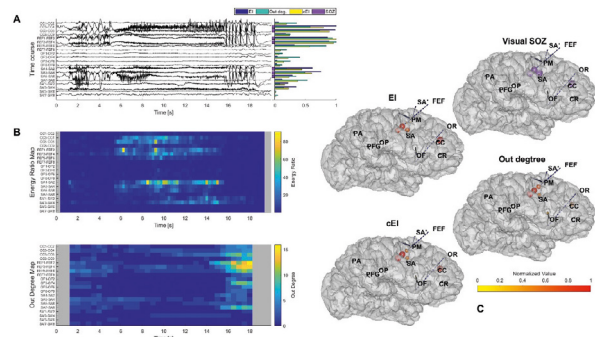


Figure 2. Fast seizure onset example (patient 21). Comparison of EI, Out-degree, cEI in and vSOZ. A/ SEEG time series B/EI energy ratio map and out-degree map. C/3D MRI –electrode map estimation of EI, out-degree, cEI and vSOZ.

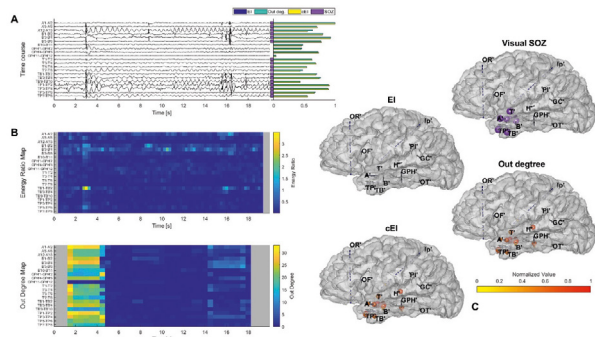


Figure 3. Slow seizure onset (slow waves) example (patient 10). Comparison of out-degree, EI, cEI and vSOZ. A/SEEG time series map. B/EI energy ratio map and out-degree map. C/3D MRI –electrode map estimation of EI, out-degree, cEI and vSOZ.

Conclusion: cEI may help epileptologist to delineate SOZ in a complex epileptogenic network. As cEI include the very beginning of fast activity during seizure onset and ictal changes in the epileptogenic network.

Disclosure: This research has been supported by the European Academy of Neurology MD/PhD fellowship program 2019.

O2002

Long-term safety and efficacy of Cannabidiol (CBD) treatment in Lennox Gastaut syndrome: results overall and for patients completing 1–3 years of an open-label extension (GWPCARE5)

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Background and aims: We assessed the long-term safety and efficacy of add-on CBD in patients with Lennox-Gastaut syndrome (LGS) in the 3rd interim analysis of the open-label extension (OLE; GWPCARE5; NCT0224573) of two randomised controlled trials (RCTs; GWPCARE3, GWPCARE4).

Methods: Patients who completed either RCT could enter this OLE, in which they received plant-derived highly purified CBD medicine (Epidyolex[®]; 100mg/mL oral solution). Primary endpoint: safety (n=366). Secondary endpoints: median percentage change from baseline in drop and total seizure frequency overall (n=364) and patients completing 1, 2, and 3 years (n=299, 236, and 200).

Results: 99% (366/368) of eligible patients with LGS enrolled. Median follow-up was 150 weeks (3 days–179 weeks) overall. Mean age was 16 years; 33% ≥18 years; 54% male. Patients were taking a median of 3 concomitant antiepileptic drugs at baseline; 54% were on clobazam and 39% valproate. Mean modal CBD dose was 24mg/kg/day overall and ranged from 21–25mg/kg/day over follow-up for 3-year completers. 33% (119/366) of patients withdrew. Adverse events (AE) occurred in 96% of patients and serious AEs in 42%; 12% discontinued due to AEs. Aspartate/alanine aminotransferase levels >3× upper-limit-of normal occurred in 13% of patients. There were 11 deaths; none deemed treatment-related by the investigator(s). Median percentage reduction in drop seizure frequency during 12-week visit windows over 156 weeks was 48–71% overall; and 55–61%, 58–71%, and 55–71% for 1-, 2-, and 3-year completers.

Conclusion: Long-term treatment with add-on CBD in patients with LGS produced sustained seizure reductions, with no new safety concerns.

Disclosure: This trial was sponsored by GW Pharmaceuticals.

O2003

Epilepsy phenotype in patients with rare de novo DYNC1H1 variants

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Background and aims: Dynein, cytoplasmic1-heavy-chain1 (DYNC1H1) encodes subunit of the cytoplasmic dynein complex, which traffics cargo along microtubules. Dominant DYNC1H1 mutations are implicated in neural diseases, including spinal muscular atrophy with lower extremity dominance (SMA-LED), intellectual disability with neuronal migration defects, malformations of cortical development, Charcot-Marie-Tooth disease. Epilepsy has been described in sporadic reports. Our purpose was to study the epilepsy features of patients bearing rare de novo DYNC1H1 variants collected through an international collaboration

Methods: Genetic, clinical, neurological and epilepsy features, electroencephalography's (EEG), therapy and brainMRI data have been collected

Results: 14 patients (8M, 6F); median age 19,7 years old (1-37); 13 had a missense variant (11 denovo, one unknown and one inherited) and 1 had a stop-codon denovo variant. Mean age at onset was 5.9 years old (range 5 months-18 years old). 6 patients had infantile spasms (IS) with onset at 5-7 months; 4 had hypsarrhythmia. 7 had a severe epilepsy with polymorphic seizures and multifocal EEG abnormalities (3 of them were consistent with Lennox-Gastaut Syndrome-LGS). 1 patient had a drug-resistant generalized myoclonic epilepsy; interestingly he has no intellectual disability. 3 patients were seizures free at last follow-up. 8 patients had mild brain atrophy; 6 had brain malformations (4 lissencephaly, 1 heterotopia, 1 cortical dysplasia). None had spinal muscular atrophy or Charcot-Marie-Tooth disease.

Conclusion: DYNC1H1 de novo rare variants might manifest with severe drug resistant epilepsy including IS

and LGS. Less than half of these patients have an associated cortical malformation, while none had a motoneuron or a peripheral nerve condition. A broader cohort will help elucidate the genotype-phenotype correlations.

Disclosure: Nothing to disclose

O2004

The maternal effect in epilepsy – findings from a Danish population-based study

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Background and aims: Many previous studies have found a higher risk of epilepsy in offspring of affected mothers than in offspring of affected fathers. We examined whether this maternal effect was present in a large-scale population-based sample.

Methods: We considered all singletons born in Denmark between 1981 and 2016. Using diagnostic information from the Danish registers, we identified diagnoses of epilepsy and other neuropsychiatric disorders in all cohort members and their family members.

Results: We included 1.754.742 individuals contributing with >30 million person-years of follow-up. The incidence rate (IR) of epilepsy in offspring of unaffected parents was 78.8 (95% CI: 77.8-79.8) per 100.000 person-years, while the corresponding rate was 172 (95% CI: 156-187) in offspring with an affected father, and 260 (95% CI: 243-277) in offspring with an affected mother. Thus, having an affected mother was associated with a 1.45-fold (95% CI: 1.30-1.65) higher risk of epilepsy in the offspring, compared to having an affected father. This maternal effect was found both in male (adjusted hazard ratio (aHR) =1.39, 95% CI: 1.19-1.61) and female offspring (aHR=1.53, 95% CI: 1.31-1.79), across various ages at onset in the offspring (0-4, 5-9, 10-14, 15-19, 20-24 and 25-29 years), and in familial epilepsies, where the affected parent had an affected sibling (aHR=1.50, 95% CI: 1.07-2.12). The maternal effect was stronger in epilepsy, than in other neuropsychiatric disorders (e.g. schizophrenia aHR: 1.19, 95% CI: 1.04-1.37).

Conclusion: We found a clear maternal effect on offspring risk of epilepsy in this nationwide cohort study.

Disclosure: This study was supported by Novo Nordisk Foundation grant NNF16OC0019126, the Central Denmark Region, the Danish Epilepsy Association, and NINDS grant NS106104-01A1

MS and related disorders 1

O2005

Assessing the immune cell subtype reconstitution profile using deconvolution algorithms in patients treated with cladribine in the CLARITY study: findings at the 96-week timepoint

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Background and aims: Following treatment with cladribine tablets (CT) there are transient reductions in total lymphocyte cell counts and B-cells and potentially long-lasting reductions in memory B-cells according to flow cytometry findings. The aim was to assess immune cell subtypes in peripheral blood of patients with relapsing-remitting multiple sclerosis (RRMS) in the CLARITY study using advanced computational algorithms.

Methods: In CLARITY, patients received CT 3.5mg/kg (cumulative licensed dose), CT 5.25mg/kg or placebo administered as two short oral courses over 2 years. Gene expression profiling was undertaken using Human Array U133 Plus 2.0 of whole blood collected at week 96 post-baseline from 189 patients (62 on CT 3.5mg/kg, 70 on CT 5.25mg/kg and 57 on placebo). The CIBERSORT5 deconvolution algorithm and xCell6 signature-based method were used to estimate absolute fractions of 22 immune cell subtypes and cell type enrichment analysis for 43 immune cell subtypes in the samples, respectively. A Wilcoxon Rank Sum test was used to compare the arms with a P-value of less than 0.05 considered nominally significant.

Results: At 96 weeks, the relative abundance of naïve B-cells was significantly higher and memory B-cells and plasma cells were significantly lower with CT versus placebo (Figure 1). There were significant reductions in the abundance of naïve and memory CD4+, CD8+ and TH2 T cells (Figure 2) and enhancement of the M2 macrophage signature (Figure 3).

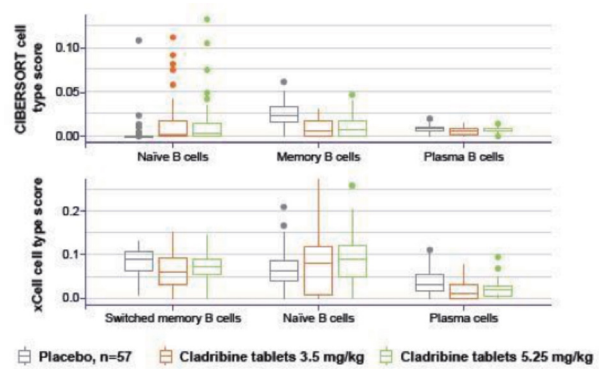


Figure 1: B cell abundance

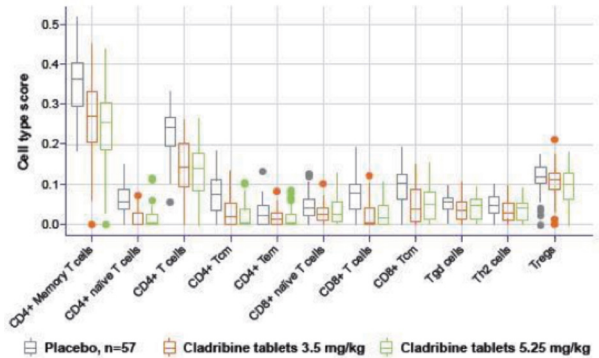


Figure 2: CD4+ and CD8+ T cell abundance

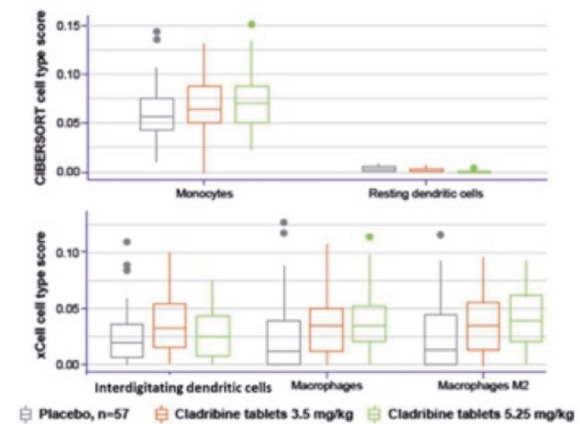


Figure 3: Monocyte and macrophage abundance

Conclusion: These findings suggest that there is a shift towards an anti-inflammatory phenotype at 96 weeks following CT treatment in Year 2.

Disclosure: The trial is sponsored by Merck KGaA, Darmstadt, Germany.

O2006

MEsenchymal StEm cells for Multiple Sclerosis (MESEMS) study: results from a multi-center, randomized, double blind, cross-over phase 2 clinical trial with autologous Mesenchymal Stem Cells (MSC) for the therapy of multiple sclerosis

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Background and aims: Prevention of disability accumulation and protection of the nervous tissue by detrimental effects of inflammation are still unmet needs in the treatment of multiple sclerosis (MS). Bone marrow-derived mesenchymal stromal cells (MSC) are multipotent cells with anti-inflammatory and neuroprotective potential, as demonstrated in EAE.

Methods: MESEMS was an international, multi-center phase II double-blind, randomized, cross-over, placebo-controlled trial lasting 56 weeks. Active relapsing remitting, secondary progressive or primary progressive patients were randomized to receive intravenously either autologous MSC (1-2 x 10.6/Kg) or sham MSC infusion (placebo). At 24 weeks, treatments were switched. Primary endpoints were safety, as measured by the number and severity of adverse events (AE) and efficacy in terms of reduction, as compared to placebo, in the total number of contrast-enhancing lesions (CEL) on MRI over 24 weeks. Secondary efficacy outcomes included evaluation of treatment on other MRI, clinical and neuropsychological measures.

Results: 144 subjects were randomized in the MESEMS trial. Demographic measures and disease characteristics were similar among the 2 randomization arms. The number of AE and serious AE was not higher in subjects treated with MSC compared to control group. Mean number of CEL at 24 weeks did not differ among 2 treatment groups.

Conclusion: Treatment with MSC is safe but did not decrease the number of CEL at 24 weeks compared to placebo. Analysis of secondary and exploratory outcomes is ongoing to reveal whether MSC are effective on other MRI and/or clinical parameters in MS, as well as on any defined metrics suggesting repair.

Disclosure: Funders: Fondazione Italiana Sclerosi Multipla (FISM), European Committee for Multiple Sclerosis, Multiple Sclerosis International Foundation, The Danish Multiple Sclerosis Society, The Toyota Foundation, Danish Blood Donors' Research Foundation, Spinal Cord Injury and Tissue Regeneration Center Salzburg, Paracelsus Medical University, Salzburg, Austria, ARSEP Foundation, AFM (France), UK MS Society, the NIHR Biomedical Research Centre funding scheme to Imperial College, the NIHR Imperial Clinical Research Facility, The Multiple Sclerosis Society of Canada and the Multiple Sclerosis Scientific Research Foundation.

O2007

Patterns of grey matter atrophy in patients with MS: a multivariate analysis using source-based morphometry

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Background and aims: Grey matter (GM) involvement is crucial in multiple sclerosis (MS). Here, we used source-based morphometry (SBM) to characterize GM atrophy and its 1-year follow-up evolution across different MS stages.

Methods: MRI/clinical data were obtained at 8 European sites from 170 healthy controls (HC) and 398 MS patients (34 clinically isolated syndromes [CIS], 226 relapsing-remitting [RR], 95 secondary progressive [SP] and 43 primary progressive [PP] MS). 57 HC and 144 MS underwent 1-year follow-up. Baseline GM loss, GM atrophy progression and correlations with disability and 1-year clinical worsening were assessed.

Results: SBM identified 26 cerebellar, subcortical, sensorimotor, visual, temporal, default-mode, fronto-parietal, hippocampal, executive and salience GM components. GM reduction was found in MS vs HC in almost all components ($p=\text{range}<0.001-0.04$). CIS patients showed circumscribed subcortical, cerebellar, temporal and salience GM loss vs HC, while RRMS patients exhibited widespread GM atrophy. Cerebellar, subcortical, sensorimotor, salience and fronto-parietal GM loss was found in PPMS patients vs HC, and in SPMS vs RRMS. At 1-year, 21 (15%) MS patients had clinically worsened. GM atrophy progressed over time in MS in subcortical, cerebellar, sensorimotor, and fronto-temporo-parietal

regions. Baseline higher disability was associated ($R^2=0.65$) with lower normalised brain volume ($\text{beta}=-0.13$, $p=0.001$), higher sensorimotor GM loss ($\text{beta}=-0.12$, $p=0.002$) and longer disease duration ($\text{beta}=0.09$, $p=0.04$). Normalised GM volume (odds ratio=0.98, $p=0.008$) and cerebellar GM atrophy (odds ratio=0.40, $p=0.01$) independently predicted clinical worsening (area-under-the-curve=0.83).

Conclusion: GM involvement differed across disease stages and progressed at 1-year in MS. Sensorimotor and cerebellar GM atrophy explained baseline disability and clinical worsening.

Disclosure: Nothing to disclose

O2008

Clinical relevance of multiparametric MRI assessment of spinal cord damage in multiple sclerosis

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Background and aims: We aimed to explore the pathophysiology of cervical spinal cord (cSC) damage in multiple sclerosis (MS) patients and to identify MRI predictors of disability and disease course, using a multiparametric MRI approach.

Methods: 111 MS patients, 57 with relapsing-remitting (RR) and 54 with progressive MS (PMS), and 32 age- and sex-matched healthy controls (HC) underwent brain and cSC 3 Tesla MRI with pulse sequences for assessing lesions, atrophy and microstructural damage (with diffusion-tensor metrics), and a complete neurological assessment. Age-, sex- and phenotype-adjusted linear models were built.

Results: MS patients had cSC lesions, higher brain T2-lesion volume (LV), brain and cSC atrophy and microstructural damage, compared to HC. In MS patients, multivariable analysis identified brain grey matter (GM) volume, cSC lateral funiculi fractional anisotropy (FA) and lateral funiculi T2-LV as independent predictors of EDSS score. The independent predictors of EDSS score were cSC lateral funiculi FA, brain T2-LV and cSC lateral funiculi T2-LV in RRMS ($R^2=0.48$); and cSC lateral funiculi FA and cSC GM atrophy in PMS ($R^2=0.52$). Similar results were confirmed for limb function tests. Logistic regression analysis identified cSC GM atrophy and cSC T2-LV as independent predictors of clinical phenotype ($AUC=0.964$).

Conclusion: cSC involvement has a central role in explaining disability in MS. The processes contributing to disability differ according to the stage of the disease. In RRMS, lesions and microstructural damage to cSC tracts have a prominent role, whereas in PMS, cSC GM atrophy becomes clinically meaningful.

Disclosure: Nothing to disclose

Sleep disorders 1

O2009

Skin biopsy: a sensitive and specific biomarker for idiopathic REM sleep behavior disorder versus subtypes of secondary RBD and versus periodic limb movement disorder

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Background and aims: Isolated RBD (iRBD) has been linked to an underlined synucleinopathy. The pathophysiology of secondary RBD (as for example: RBD within narcolepsy, RBD within obstructive sleep apnea syndrome – OSAS) or of periodic limb movement disorder – PLMs- is instead a vexing issue.

We aimed at comparing results of skin biopsy looking for alpha-synuclein (p-alpha-syn) deposits in patients with iRBD, RBD due to narcolepsy and OSAS and in patients with PLMs.

Methods: The population included 50 patients with iRBD, 10 patients with RBD and OSAS, 17 patients with RBD and narcolepsy and 20 patients with PLMs. All groups underwent neurological examinations, neuropsychological investigations, video-polysomnography, neuroimaging, and skin biopsy looking for phosphorylated p-alpha-syn deposits.

Results: Analysis of data shows that skin biopsy can discriminate between iRBD and RBD due to narcolepsy or PLMs. Indeed, skin biopsy was positive in up to 70% of patients with iRBD and in none of RBD due to narcolepsy or of PLMs patients. Few patient with RBD and OSAS have instead positive skin biopsy. Within this group, positive skin biopsy correlated with abnormal muscle tone during REM sleep (i.e. with atonia Index).

Conclusion: Skin biopsy confirms to be a sensitive a specific marker of iRBD.

Disclosure: Nothing to disclose

O2010

Altered resting state functional connectivity of lateral hypothalamus and amygdala in childhood narcolepsy type-1

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Background and aims: Narcolepsy type 1 (NT1) is a chronic sleep disorder characterized by the loss of hypocretinergic neurons in dorsolateral hypothalamus. Functional and structural neuroimaging results are controversial, but compatible with dysfunction of the hypocretinergic system. The aim of the present study was to investigate the functional connectivity of hypothalamus and amygdala in childhood NT1 during rs-fMRI.

Methods: Fifteen drug naïve children with NT1 (9 males; mean age 11.7+3 years) and fifteen healthy children (9 males; mean age 12.4+2.8 years) participated in an EEG-fMRI study. Functional images were acquired on a 3T Philips Achieva system. Seed-based functional connectivity analyses were performed using SPM12. Regions of Interest were lateral hypothalamus (2mm radius spheres, x=+6, y=-10, z=-10) and amygdala (intersection between the healthy controls' hypothalamic functional connectivity map and the AAL Atlas). The BOLD signal time course was extracted by means of MarsBaR toolbox. Second-level group analyses were conducted using 2x2 full-factorial design.

Results: When comparing to controls, NT1 patients showed decreased functional connectivity between lateral hypothalamus and left superior parietal lobule, hippocampus and parahippocampal gyrus. Decreased functional connectivity was detected between amygdala and post-central gyrus and several occipital regions, whereas it was increased between amygdala and right pre- and post-central gyrus, inferior frontal gyrus and claustrum, bilateral insula and putamen.

Conclusion: Alteration of hypothalamus and amygdala functional connectivity in NT1 patients, suggests that the loss of hypocretin containing neurons in NT1 causes abnormal connectivity between the hypothalamus and brain regions involved in arousal and emotional processing.

Disclosure: Nothing to disclose

O2011

CSF and serum ferritin levels in narcolepsy type 1 comorbid with restless legs syndrome

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Background and aims: To investigate whether cerebrospinal fluid (CSF) and serum ferritin levels differ between patients with narcolepsy type 1 (NT1) comorbid with restless legs syndrome (RLS) or periodic leg movements during sleep (PLMS), and patients with NT1 or controls without comorbid RLS or PLMS.

Methods: 66 drug-free patients with NT1 (44 males, age 38.5 years[14-81]) were enrolled, including 20 with RLS, 18 with PLMS index ≥ 15 /hour (6 with both RLS and PLMS). 38 drug-free patients (12 males, age 22.5 years [12-61]) without central hypersomnia, RLS, PLMS were included as controls. Clinical, electrophysiological and biological (CSF ferritin, orexin, and serum ferritin) data were quantified.

Results: NT1 patients with and without RLS did not differ for age, gender and BMI. No between-group differences were found for CSF ferritin, orexin, and serum ferritin levels. No CSF ferritin, orexin, and serum ferritin level differences were found between NT1 patients with and without PLMS, or with RLS or PLMS vs not. CSF-ferritin levels were not different between NT1 and controls in adjusted analyses. CSF-ferritin levels in the whole population correlated positively with age, serum-ferritin, BMI, negatively with orexin, but not with PLMS index. In NT1, CSF-ferritin levels correlated with age and serum-ferritin but not with PLMS.

Conclusion: The absence of CSF ferritin deficiency in NT1 with comorbid RLS or PLMS indicates normal brain iron levels in that condition. This result suggests that the frequent association between RLS, PLMS and NT1 is not based on alterations in brain iron metabolism, a pathophysiological mechanism involved in primary RLS.

Disclosure: Nothing to disclose

O2012

A continuous model of sleep depth to evaluate age-related sleep changes

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Background and aims: In traditional sleep scoring, a 30-s epoch is classified discretely as either wakefulness (W), REM sleep, or a non-REM sleep stage (N1, N2 and N3). With ageing, wakefulness increases and deep sleep decreases. We hypothesized that a continuous model of sleep depth better reflects these changes than traditional scoring of discrete epochs.

Methods: 97 healthy subjects (44.7 \pm 15.2 years, range 19-77 years, 38 males) underwent video-polysomnography. Sleep stages were scored manually. 15 time and frequency features were extracted from non-overlapping 3-s mini-epochs of C4-M1, F4-M1 and O2-M1 electroencephalographic channels. The mini-epochs included in manually scored W and N3 sleep of 15 participants (age $<$ 40 years) were used to train a model of sleep depth, which returned as output the sleep depth probability (Pdepth) for each mini-epoch. A mini-epoch was classified as vigilance (V) if Pdepth \leq tv and as deep sleep (DS) if Pdepth \geq td (the thresholds tv and td were optimized during training). For the remaining 82 participants, the percentages of manually scored W (%W) and N3 sleep (%N3) and of estimated V (%V) and DS (%DS) were obtained. Pearson's correlation coefficients were calculated between age and percentages.

Results: High accuracies were obtained when comparing V to W and DS to N3 (Table 1). The proposed model achieved higher correlation between age and the known ageing-related sleep changes than traditional sleep scoring (Table 2).

	W - V	N3 - DS
Training data	0.93 \pm 0.04	0.90 \pm 0.05
Test data	0.89 \pm 0.08	0.92 \pm 0.04

Table 1: Accuracy values in training and test data when manually scored wakefulness (W) and N3 sleep were compared to the automatic identified vigilance (V) and deep sleep (DS).

	Continuous model of sleep depth		Traditional discrete sleep scoring		
	Coefficient	p-value	Coefficient	p-value	
% _v - age	0.34	0.002	% _w - age	0.22	0.048
% _{ds} - age	-0.37	<0.001	% _{n3} - age	-0.33	0.003

Table 2: Pearson's correlation coefficients and relative p-values between age and the calculated percentages. %V: percentage of estimated vigilance; %W: percentage of manual scored wakefulness; %DS: percentage of estimated deep sleep; %N3: percentage of manually scored N3 sleep.

Conclusion: Our continuous model of sleep depth is better suited for individuating age-related sleep changes than traditional sleep scoring and might be applied to evaluation of neurodegeneration-related sleep changes.

Disclosure: Nothing to disclose

O2013

Sleep-wake disturbances after acute stroke predict a higher risk of subsequent cardio-cerebro-vascular events

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Background and aims: Sleep-wake disturbances (SWD) are frequent in stroke patients and may have a detrimental effect on its outcome. The aim of this study is to assess prospectively and systematically whether the presence of one or multiple SWD's are linked with outcome after acute stroke.

Methods: Stroke characteristics, cardiovascular risk profile and sleep disordered breathing (SDB) were recorded during the acute phase by interview, standardized questionnaires and respirography. After 1, 3, 12 and 24 months, we also assessed the presence of several SWD (insomnia, RLS, excessive daytime sleepiness and fatigue). In addition, neurological outcome (modified Rankin score) and occurrence of new cardio-cerebrovascular events (CCVE) were scored. We calculated a "sleep burden index" from the combined severity of different SWD up to 3 months post-stroke as a predictor for subsequent CCVE in multiple regression models.

Results: We recruited 438 acute stroke patients (85% with ischemic stroke, 15% with TIA, mean age 65 years [21-86], 64 % male). The mean NIHSS-score was 3.5 (SD 4.5, range 0-40) at admission and 1.2 (SD 2.1, range 0-18) at discharge. The Sleep Burden Index shows a twofold higher risk for CCVE (Odds Ratio = 2.07 [95% CI: 1.30-3.29, p = 0.002], adjusted for gender, age and baseline NIHSS). Baseline AHI and the combination of other SWDs demonstrates independent predictivity predictive value.

Conclusion: Preliminary results of this ongoing study suggest that the presence of multiple SWDs after stroke represent an independent risk for new, subsequent CCVE in the first 2 years after stroke.

Disclosure: This project was funded by the Swiss National Science Foundation

O2014

The impact of DBS-STN on restless legs syndrome (RLS) and periodic limb movements of sleep (PLMS) – clinical and polysomnography (PSG) study

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Background and aims: RLS and PLMS are common in Parkinson's disease (PD) and have negative impact on sleep quality, which is one of the key determinants of quality of life. We present results of the study on the impact of subthalamic deep brain stimulation (DBS-STN) on RLS and PLMS in PD.

Methods: 36 patients with advanced PD, who fulfilled the CAPSIT criteria and were qualified for routine DBS-STN, were interviewed for RLS symptoms. Those, who met criteria for the diagnosis of RLS were assessed with International RLS Study Group Rating Scale (IRLS). The evaluations were repeated at 6 and 12 months, additionally 24 patients were assessed with 2-night PSG before and at 6 months after surgery.

Results: DBS-STN resulted in the resolution of RLS symptoms in 40% of patients compared to the baseline, both at 6 and 12 months after surgery. Patients who reported RLS symptoms noted significant improvement (median IRLS score 23.5, 18.0 and 19.5, before, at 6 and at 12 months after surgery, respectively). The leg movement arousal index improved significantly after DBS-STN (median value of 0.9 before and 0.2 at 6 months after surgery), however, the improvement in PLM index was not statistically relevant. There were differences in UPDRS II, however no differences in UPDRS III score, among patients with and without RLS.

Conclusion: DBS-STN significantly improved RLS but not PLM in PD patients. Patient with RLS differed in terms of activities of daily living.

Disclosure: Nothing to disclose

Autonomic nervous system disorders

O2015

Validation of the new index of baroreflex function to identify neurogenic orthostatic hypotension

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Background and aims: Blood pressure (BP) overshoot after Valsalva manoeuvre (VM) is the gold standard to differentiate orthostatic hypotension (OH) due to autonomic failure (neurogenic), from non-neurogenic OH. Recently, an increase in heart rate (Δ HR) <15 or 17 bpm upon standing and Δ HR/ Δ BP ratio at 3rd minute of tilt test ≤ 0.49 were proposed as discriminators of neurogenic OH. Our aim was to evaluate the accuracy of these new HR indexes to differentiate neurogenic from non-neurogenic OH.

Methods: We retrospectively applied the HR indexes to all cardiovascular reflex tests performed at our Institution from 1989 to 2019 who fulfilled the following criteria: (1) presence of classical OH at tilt test, (2) reliable VM, (3) absence of heart disease. We classified OH according to VM, Δ HR/ Δ SBP (≤ 0.49 neurogenic) and Δ HR (≤ 17 and ≤ 15 neurogenic). Lastly, we identified tests with neurogenic OH (defined by VM) belonging to patients with multiple system atrophy (MSA) or pure autonomic failure (PAF).

Results: We identified 370 tests with OH. Based on VM, 349 were neurogenic. The Δ HR/ Δ SBP ≤ 0.49 correctly identified neurogenic OH in 314/349 tests (sensitivity 90%) and non-neurogenic OH in 17/21 tests (specificity 81%). The Δ HR ≤ 15 bpm had 83% sensitivity and 67% specificity. The Δ HR ≤ 17 bpm had 88% sensitivity and 52% specificity. The Δ HR/ Δ SBP had a higher sensitivity in detecting neurogenic OH in PAF than MSA (100% and 88% respectively).

Conclusion: The Δ HR/ Δ SBP was a good index to identify neurogenic OH in our cohort, especially in cases with PAF.

Disclosure: Nothing to disclose

O2016

Transient orthostatic blood pressure changes in Parkinson's disease: impact on falls, syncope and orthostatic intolerance

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Background and aims: Transient orthostatic blood pressure (BP) changes within the first minute upon standing influence morbidity and mortality in the aging population. Their prevalence and impact on major clinical outcomes in Parkinson's disease (PD) is however unknown. Here we assessed the prevalence of transient orthostatic BP changes and their influence on falls, syncope and orthostatic intolerance in PD.

Methods: 167 parkinsonian patients, who underwent cardiovascular autonomic function testing under continuous non-invasive heart rate and BP monitoring at the Medical University of Innsbruck between 2007 and 2016 were retrospectively studied.

Results: Transient orthostatic BP changes (systolic BP fall ≥ 20 mmHg or diastolic ≥ 10 mmHg resolving within the 1st minute upon standing) were detected in 16% of PD patients, classic orthostatic hypotension (OH) in 13% and a combination of both in 4%. Beyond postural instability and gait impairment, falls were associated with syncope (OR: 72.461, $p < 0.001$), which mainly occurred upon standing in PD patients. Under continuous heart rate and BP monitoring patients with history of syncope and orthostatic intolerance had a more severe systolic BP fall, lower systolic BP values and a smaller diastolic BP increase during the first minute upon standing.

Conclusion: Transient orthostatic BP falls are more frequent than OH in PD, cause orthostatic intolerance and increase the risk of falls by increasing the risk of orthostatic syncope. A standing test under continuous BP monitoring may therefore help identifying modifiable risk factors for syncope and falls in PD.

Disclosure: Nothing to disclose

O2017

Small fiber pathology in patients with progressive supranuclear palsy

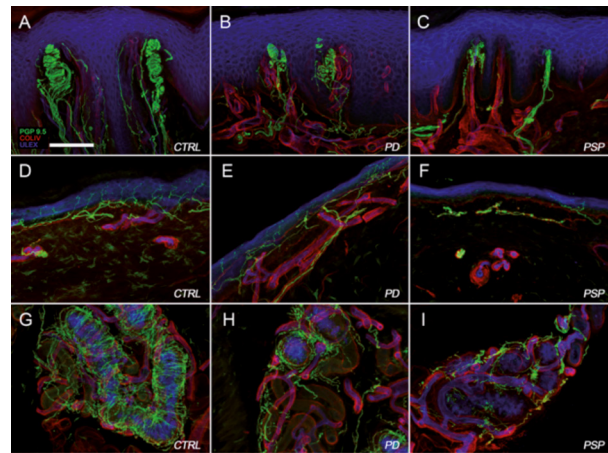
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Background and aims: In the early phase of disease, it can be challenging to differentiate Supranuclear Progressive Palsy (PSP) from idiopathic Parkinson's disease (PD). Small fiber (SF) nerve pathology, involving sensory and autonomic component, is a consistent early feature, that parallels disease progression and sometimes precedes motor impairment in PD. SF involvement is unknown in PSP. Aims of this study were (i) to assess a possible SF involvement in PSP, (ii) to evaluate a possible correlation of SF loss with disease's severity, (iii) to assess possible differences in functional and morphological SF pathology compared to PD.

Methods: We studied 27 PSP and 33 PD patients without electrophysiologic signs of neuropathy, and 33 healthy controls (HC). In addition to motor impairment, assessed by means of UPDRS-III, all patients underwent clinical, functional, and morphologic assessment of sensory-autonomic nerves through dedicated questionnaires, sympathetic skin response, dynamic sweat test, and skin biopsies. Immunohistochemical analysis of cutaneous sensory and autonomic innervation was performed using specific antibodies and confocal microscopy.

Results: PSP patients, compared to HC, displayed a severe length-dependent loss of sensory-autonomic nerve fibers associated to functional impairment (all $p < 0.001$). Motor impairment correlated with autonomic and sensory symptoms and with the loss of intraepidermal nerve fiber density (all $p < 0.01$). Morphological (Figure 1) and functional impairment of SF pathology was more severe in PSP respect to PD (all $p < 0.05$).



Confocal images of immunostained cutaneous nerves. A severe loss of Meissner Corpuscles is evident in PSP patients (C) and a moderate loss in PD patients (B) compared to healthy controls (A). Also in hairy skin of PSP is more evident the epidermal (F) and sudomotor denervation (I) compared to PD (E, H) and healthy controls (D, G).

Conclusion: We demonstrated for the first time a severe length-dependent SF pathology in PSP, paralleling motor severity with peculiar features compared to SF involvement in PD.

Disclosure: Nothing to disclose

O2018

Why does the heart stop? A novel approach to identify the trigger of cardioinhibition in vasovagal syncope.

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Background and aims: Cardioinhibition (CI) is an intriguing phenomenon in vasovagal syncope (VVS). CI causes a decrease in heart rate (HR) including asystole at some point in the process of VVS, but the trigger of CI is still unknown. We developed a novel method for identification of CI and searched for a trigger of CI among haemodynamic variables.

Methods: We included 163 subjects with complete VVS during tilt table testing. All subjects had video and EEG registration and continuous measurements of blood pressure (BP), HR, stroke volume (SV) and total peripheral resistance (TPR). For each subject the start of CI was determined as a downward turn of HR in the minutes before syncope by a 4 person consensus. We evaluated absolute values and variability of BP, HR, SV, TPR three minutes before and at the start of CI.

Results: Our novel approach revealed CI in 149 (91%) of the subjects. The median time from CI to syncope was 58sec (range 12-200 sec). Before the start of CI, BP and SV were already decreasing, HR was increasing and TPR remained stable (fig 1). After the start of CI BP decreased steeply. None of the variables exhibited less variability at the start of CI than before it (fig 2).

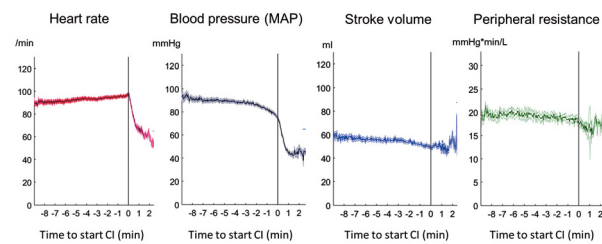


Figure 1. Mean values of heart rate, blood pressure, stroke volume and total peripheral resistance around the start of cardioinhibition

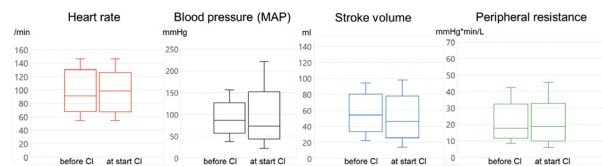


Figure 2. Median values and range of distribution of heart rate, blood pressure, stroke volume and total peripheral resistance at the start of cardioinhibition and 3 minutes before

Conclusion: CI occurred in the majority of subjects with VVS and significantly contributed to the BP lowering in VVS. The start of CI cannot be attributed to a consistent threshold effect of BP, HR, SV or TPR.

Disclosure: Nothing to disclose

O2019

Open-label phase 2 study to explore durability of effect and safety of once-daily oral amprelosetine (TD-9855), a norepinephrine reuptake inhibitor, for symptomatic treatment of neurogenic orthostatic hypotension in subjects with synucleinopathies

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Background and aims: Inadequate norepinephrine (NE) release in neurogenic orthostatic hypotension (nOH) causes fall in standing blood pressure. Amprelosetine, a novel, long-acting NE reuptake inhibitor may improve symptoms of nOH. The objective of this study was to explore durability of effect and safety of once-daily oral amprelosetine for symptomatic treatment of nOH.

Methods: In an open-label, phase 2, exploratory study, subjects received amprelosetine (3-20mg) once-daily for up to 20 weeks, with 4-week follow-up after amprelosetine withdrawal and restarting alternative pressor agents. Assessments included Orthostatic Hypotension Symptom Assessment Item 1 (OHSA#1; dizziness, lightheadedness, feeling faint), OHSA/Orthostatic Hypotension Daily Activities Scale (OHDAS) composite scores, and change in Patient Global Impression of Severity (PGI-S).

Results: Seventeen symptomatic subjects (baseline OHSA#1 score >4) were enrolled (mean age, 65 years). At Weeks 4 and 20, mean (SD) improvement on OHSA#1 was -3.8 (3.1) and -3.1 (3.0) point, and ~77% and ~86% of subjects reported ≥1-point improvement, respectively. Improvement, seen as early as Week 1, was sustained throughout the study. Deterioration to baseline severity was observed after amprelosetine withdrawal. Similar trends were seen in OHSA/OHDAS composite scores, and change in PGI-S. Most common adverse events (AEs) were urinary tract infection (24%), hypertension (19%) and headache (14%), with no study-drug-related serious AEs.

Amprelosetine showed durable symptom improvement over 20 weeks, with return to baseline severity after amprelosetine withdrawal. Amprelosetine was well tolerated.

Conclusion: These encouraging findings of durable symptom improvement with open-label amprelosetine treatment are being evaluated in ongoing Phase 3, double-blind, confirmatory studies in subjects with nOH.

Disclosure: R Vickery is an employee of Theravance Biopharma Ireland Limited and stockholder of Theravance Biopharma, US, Inc.

O2020

Impairment of autonomic cardiovascular modulation is more pronounced in focal epilepsy patients with than without limbic system lesions

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Background and aims: Interictal autonomic dysfunction is common in epilepsy patients. Patients with focal epilepsy (FE) frequently have lesions involving the limbic system which closely interacts with central autonomic modulation. Therefore, autonomic dysfunction might be more prominent in FE-patients with limbic-system lesions (LSL+) than in FE-patients with lesions not involving limbic structures (LSL-). We aimed to assess possible autonomic differences between LSL+ and LSL- patients.

Methods: In 36 FE-patients (20 LSL+, 16 LSL-; mean age 34.8±9.0 years, 15 males) and 30 gender- and age-matched healthy controls, we recorded RR-intervals (RRI), beat-to-beat systolic blood pressure (BPsys), and respiratory frequency during 5 minutes at supine rest. We calculated parameters of total cardiac autonomic modulation [RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), RRI-total-powers (RRI-TP)], sympathetic [low-frequency-powers (LF) of RRI and BPsys] and parasympathetic cardiac modulation [root-mean-square-of-successive-RRI-differences (RMSSD), RRI-high-frequency- (RRI-HF)-powers], and baroreflex sensitivity (BRS). We compared autonomic parameters in LSL+ patients, LSL- patients, and controls (Kruskal-Wallis test and post-hoc Mann-Whitney-U-tests; significance: p<0.05). Data are presented as median and interquartile ranges.

Results: In the patients, all autonomic parameters were significantly lower than in the controls. In LS+ patients, only LF-BPsys (2.5 [1.73-3.38] vs. 5.2 [2.68-6.95] mmHg²; p=0.012) and LF-RRI (234 [172-378] vs. 501 [276-744] msec²; p=0.004) were lower than in LS- patients.

Conclusion: Sympathetic and parasympathetic modulation was reduced interictally in our FE-patients. In FE-patients with limbic system lesions, the decrease in sympathetic heart rate- and blood pressure-modulation was more pronounced than in LSL- patients, probably because limbic lesions more severely compromise the function of the central autonomic network.

Disclosure: Nothing to disclose

O2021

Autonomic response during endotracheal suctioning episodes in subarachnoid hemorrhage patients

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Background and aims: Endotracheal suctioning (ES) provokes a cumulative hemodynamic response by activation of sympathetic and parasympathetic circuits. In this study, we aimed to analyse hemodynamic changes during ES in ventilated subarachnoid hemorrhage (SAH) patients and investigated whether the associated activation relates to the time to arousal and functional outcome.

Methods: For the observational study, 191 SAH patients requiring mechanical ventilation were included. 1080 ES episodes during the first 72 hours of admission were analysed. Baseline median heart rate (HR) was calculated 30-10 minutes before ES and compared to HR during ES (DHR). Multivariable analysis to assess associations between DHR and time to arousal (Richmond Agitation Sedation Scale, RASS≥0) and poor 3-month functional outcome (modified Rankin Scale, mRS>2) was performed using generalized estimating equations.

Results: Patients were 59 (IQR, 50-70) years old and presented with an admission H&H grade of 4 (IQR, 3-5). Median time to arousal was 13 (IQR, 4-21) days. HR increased by 2.2±0.2 beats per minute (bpm) from 75.1±0.5 bpm at baseline. Poor-grade patients (H&H 4-5) showed a significantly lower DHR during suctioning compared to good-grade patients (1.5±0.3 bpm vs 3.3±0.3 bpm, p<0.001). In multivariable analysis, DHR (p<0.001) was significantly lower in patients who aroused later and in patients with poor outcome independently of sedation depth (Table 1).

Table 1: Association between increase of heart rate during suctioning and poor functional 3-month outcome

Variable	Adjusted for midazolam dose		Adjusted for RASS*	
	AdjOR, 95%-CI	p-value	AdjOR, 95%-CI	p-value
ΔHR	0.96; 0.94-0.98	<0.001	0.96; 0.93-0.98	<0.001
Age, years	1.05; 1.04-1.06	<0.001	1.06; 1.04-1.07	<0.001
H&H grade	1.83; 1.64-2.06	<0.001	1.90; 1.68-2.16	<0.001
Absolute HR	1.01; 1.00-1.02	0.01	1.02; 1.01-1.03	0.001
Daily cumulative midazolam dose, mg	1.00; 0.99-1.00	0.475	-	-
RASS	-	-	0.75; 0.54-1.03	0.076

*179 patients were included due to missing RASS recordings
 ΔHR=delta heart rate during suctioning, H&H=Hunt&Hess, RASS= Richmond Agitation Sedation Scale, adjOR=adjusted odds ratio, CI=confidence interval

Conclusion: Augmentation in HR may quantify the hemodynamic response during endotracheal suctioning in brain injured patients. The value as a biomarker to early discriminate the time to arousal and functional outcome needs prospective confirmation.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology; ageing and dementia 1

O2022

Accelerometer speech recording: technical aspects, reliability, clinical and intraoperative utility

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Background and aims: Speech disorders are usually just clinically characterized and in the specific situation of intraoperative mapping with electrostimulation, there is a high risk of seizures. Here, we have investigated the feasibility of accelerometer (ACC) recording of glottis vibration during speech through intraoperative testing of brain tumor patients (BTP) and on dysphonic patients (DP). We aimed to identify technical caveats, to test its reliability and applicability during a picture naming task (PNT).

Methods: A uniaxial ACC was used to record surface infraglottic vibration. We first tested the influence of position and filter bandwidth on recorded parameters such as amplitude, baseline level, burst artefacts and repeatability. Using a scoring scale for artefact contamination, amplitude and reproducibility, 6 evaluators ranked each condition. With the selected settings, we recorded baseline data during PNT in 25 healthy volunteers and compared it with 15 BTP and 7 DP data.

Results: The highest scores were given to the suprasternal notch site and 20-200 Hz filter bandwidth. A intrasubject reliability of 0.92 (range of 0.88-0.95, CI 95%) was found for each parameter. Lower amplitudes and frequencies were identified in DP. We detected mainly a speech arrest with brain stimulation in patients (57% vs 16% in healthy subjects). In intraoperative language testing, 11% of the evoked errors were detected by evaluating parameters' deviation from ACC baseline recordings. In these cases, the brain site was re-stimulated (after increasing 20% of the intensity) and evoked clinical language disturbances.

Conclusion: ACC speech recording was found reliable and allowed to identify language disturbances during PNT.

Disclosure: Nothing to disclose

O2023

Predictive factors for recurrent transient global amnesia

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Background and aims: Transient global amnesia (TGA) is a clinical syndrome characterized by sudden anterograde amnesia of less than 24 hours in duration, in the absence of other neurological symptoms. The risk of recurrence ranges between 2.9-26.9%. The predictive factors for recurrent TGA have not yet been identified.

Methods: Retrospective analysis to identify recurrence predictors in a cohort of 69 TGA patients from a single center in Portugal, diagnosed between January 2012 and June 2019. Clinical features and complementary studies performed during the acute phase were analyzed.

Results: Mean age at presentation was 64.8 years (37-84), 69.1% were female; mean follow-up was 16.5 months (6-36); co-morbidities more frequent: hypertension (50.7%), dyslipidemia (39.1%), diabetes (20.2%), depression (20.2%), migraine (14.5%), and cerebrovascular disease (8.7%). Average episode duration lasting 6 hours and 50.7% had an identifiable trigger – emotional stress (24.6%), physical effort (11.6%), and sexual intercourse (2.9%). In the acute phase, 20 (29.8%) patients performed brain-MRI - 5.8% with hippocampus DWI restriction; 18 patients (26.1%) had TGA recurrence. The following features had a positive association with the risk of recurrence: female sex (p=0.038), depression (p=0.039), shorter duration (p=0.037) and hippocampus signal alteration on brain-MRI (p=0.008). Accompanying symptoms, precipitating events, other coexisting conditions and altered EEG or ultrasound did not show any correlation with recurrent TGA

Conclusion: We present a cohort of TGA patients with a considerable recurrent rate (26%), alerting for the possibility of recurrence of this clinical entity. The following predictive factors were identified: female sex, depression, shorter episode duration, and hippocampal hyperintensity on brain-MRI. Additionally, to its diagnostic value, brain-MRI performed in the acute phase could have prognostic value

Disclosure: Nothing to disclose

O2024

Distinct white matter tract changes associated with apathy in cerebrovascular small vessel disease

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Background and aims: Clinical apathy is a poorly understood neuropsychiatric syndrome characterised by a significant decrease in goal-directed and motivated behaviour 1,2. It occurs in ~30% of patients with cerebrovascular small vessel disease (SVD). With the aim of improving our mechanistic understanding of apathy, we conducted a multimodal investigation combining validated behavioural paradigms and magnetic resonance imaging (MRI) techniques.

Methods: 83 patients with MRI evidence of SVD were recruited from the Oxford Vascular Study (OXVASC) and Oxford neurology clinics. They were investigated using a novel effort-based decision making task³ and the Apathy Evaluation Scale (AES). Structural and diffusion weighted MRI was conducted to measure white matter lesion load (WMLL) and tract integrity, indexed by Fractional anisotropy (FA).

Results: Patients with apathy demonstrated a significant reduction in motivated behaviour and were significantly less incentivised by low levels of reward (Fig 1). Diffusion weighted imaging demonstrated that apathy was characterised by focal changes to limbic association tracts including the uncinate fasciculus and cingulum bundle, as well as fronto-striatal white matter tracts (Fig 2). Importantly, global measures of disease severity did not independently associate with apathy.

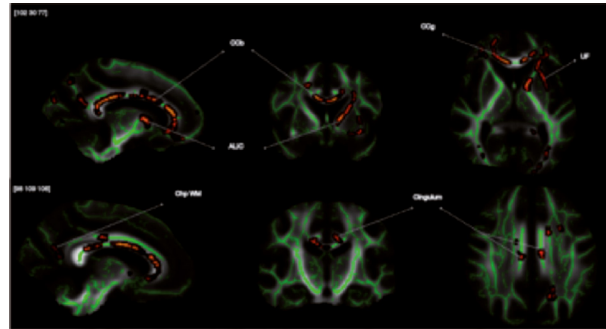
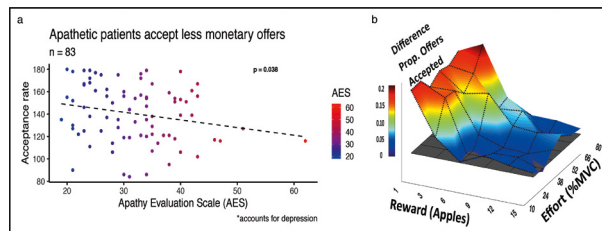


Figure 2. Apathy in SVD characterised by reduced Fractional anisotropy in white matter tracts.

Conclusion: Reduced incentivisation by low reward characterised apathy in SVD, as previously reported in Parkinson’s disease, suggesting a common mechanism underlying apathy across diseases. At the network level, the association of apathy with focal white matter tract changes is consistent with disruption to key frontostriatal circuits (linking medial frontal regions to each other and to the basal ganglia) which previously have been implicated in effort-based decision-making for rewards.

Disclosure: Nothing to disclose



Apathy is related to performance on effort-based decision making task
 a) Severity of apathy predicts motivated behaviour in SVD. b) The greatest differences between motivated and apathetic subjects are shown by the red peaks and occur when the reward levels on offer are low. In other words, apathetic subjects are less incentivised by low reward.

O2025

Linguistic cognitive reserve may influence post-stroke aphasia recovery and rehabilitation: the “QuALiCoMe” study

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Background and aims: Aphasia is a disabling consequence for 30% of ischemic stroke patients. The wide variability of recovery among post-stroke aphasic patients despite similar baseline stroke severity and clinical characteristics could be in part explained by the involvement of a sort of ‘Linguistic Cognitive Reserve’. Therefore, an informant-based questionnaire named “QuALiCoMe”, was developed by an interdisciplinary work based on various branches of linguistics, cognitive psychology, educational research and neurology, with the aim of estimating the pre-morbid linguistic abilities in patients with post-stroke aphasia.

Methods: Validation of QuALiCoMe questionnaire on 182 healthy subjects (HS) and 82 respective caregiver/cohabitant (CC). Pilot study: Frenchay Aphasia Screening Test (FAST) was administered within 48 hours after stroke onset (baseline) and after 6-month follow-up, and QuALiCoMe was administered to aphasic patient’s CC. As explanatory variable for aphasia recovery, we used delta-FAST score (baseline – follow-up).

Results: QuALiCoMe demonstrated a good informativeness and reliability (high concordance between HS and CC), applicability, internal consistency and external validity. Sixty stroke patients (29 female, mean NIHSS±DS=14.30±7.11, mean FAST±DS=10.02±9.61) fulfilled inclusion criteria. In a multivariate analysis, corrected for age, baseline-NIHSS, education, speech and language therapy, and thrombolysis, QuALiCoMe score showed a trend for significance in predicting recovery from aphasia (p=0.062).

Conclusion: This result represents the first clinical evidence of the role of Linguistic Cognitive Reserve as an outcome predictor in post-stroke aphasia. QuALiCoMe demonstrates a valid and promising tool to estimate pre-morbid linguistic reserve in post-stroke aphasic patients. Its potential utility needs to be confirmed in larger cohorts of patients.

Disclosure: This research has been granted by “Ente Cassa di Risparmio di Firenze”.

O2026

The association between cognitive impairment and structural and functional brain organization in amyotrophic lateral sclerosis

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Background and aims: The aim of this study was to evaluate the association between cognitive impairment and structural and functional brain organization in patients with amyotrophic lateral sclerosis (ALS).

Methods: 54 ALS patients with pure motor impairment (ALS-pure), 20 with cognitive and/or behavioural deficits (ALS-plus), and 61 age- and sex-matched controls underwent clinical, cognitive and MRI evaluations. Graph analysis and connectomics assessed structural and functional topological network properties. The relationship between structural/functional brain properties and clinical/neuropsychological data was also investigated.

Results: Both ALS-pure and ALS-plus demonstrated lower structural clustering coefficient within the sensorimotor network relative to controls. In addition, ALS-plus patients showed higher functional mean nodal strength, local efficiency and clustering coefficient in sensorimotor regions. Regarding the connection-wise analysis, ALS-pure showed significant structural changes relative to controls involving connections within and among sensorimotor and basal ganglia regions, whereas ALS-plus patients showed increased functional connectivity within the sensorimotor, anterior frontal, temporal and parieto-occipital areas. Global structural nodal strength positively correlated with verbal fluency in ALS-pure patients. Functional connectivity within the temporal network connections positively correlated with language tests in ALS-plus group, while ALS-pure showed a negative correlation between functional connectivity within the fronto-striatal network connections and scores in verbal fluency test.

Conclusion: Whereas structural disruptions of the sensorimotor network are a common signature of ALS, the occurrence of cognitive impairment is characterized by further functional connectivity changes involving extra-motor brain areas. Graph analysis and connectomics are suitable tools to better characterize ALS phenotypes.

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O2027

Hippocampal atrophy in vascular MCI as biomarker of subclinical memory impairment

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Background and aims: Vascular mild cognitive impairment (VMCI) is a transitional condition that may evolve to vascular dementia (VaD). Deeper understanding of the mechanisms of cognitive impairment in VMCI is crucial to develop biomarkers of disease progression. Studies have suggested hippocampal atrophy as a putative MRI-based biomarker in early VaD. To assess whether hippocampal atrophy occurs in VMCI and to what extent correlates with cognitive impairment and is influenced by vascular risk factors (VRF).

Methods: In this multicentre study, 108 VMCI patients underwent brain MRI and were scored on cognitive tests (Table-1). Hippocampal volume was calculated using FIRST (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki>) and compared with appropriate normative values (cohort of 5139 healthy controls). Linear regression models were used to assess differences in MRI measures and their association with cognitive tests and VRF.

Total n. of patients	108
Sex (male/female)	60/48
Mean (±SD) age, years	74.3 (±6.6)
Mean (±SD) education, years	8.3 (±4.2)
N. patients with vascular risk factors (y/n)	
Hypertension	86/22
Hypercholesterolemia	65/43
Smoking	51/57
History of stroke	33/75
No physical activity	30/78
Diabetes	17/91
Global cognition	
MMSE (range 0-30)*	27.2 ± 2.7
MoCA (range 0-30)*	21.2 ± 4.4
Memory	
RAVL immediate recall (range 0-75)*	32.4 ± 8.6
RAVL delayed recall (range 0-15)*	6.1 ± 2.8
Short Story (range 0-28)*	11.7 ± 4.1
ROCF recall (range 0-36)*	12 ± 5.6
Attention and executive functions	
TMT-A (time to complete, secs)**	67.3 ± 50.1
Visual Search (range 0-50)*	31.8 ± 9
SDMT (correct answers in 90 secs)*	34.4 ± 10.4
Stroop test (time to complete, secs)**	36.6 ± 31.2
TMT-B (time to complete, secs)**	104.4 ± 60
Language	
Phonemic verbal fluency (words in 3 mins)*	28.1 ± 9.6
Semantic verbal fluency (words in 3 mins)*	34.3 ± 7.7
Constructional praxis ROCF copy (range 0-36)*	23.8 ± 9.1
MRI Field strength	
1.5T/3T	90/18

Table 1. Demographic, clinical and MRI characteristics of the VMCI patients

Footnotes: All cognitive tests were corrected by age and education.

* Higher scores correspond to better performance.

** Lower scores correspond to a better performance.

Demographic, clinical and MRI characteristics of the VMCI patients

Results: After comparison with normative values, VMCI were stratified in subjects with no (n=70/108, Group I), mild (n=25/108, II) and moderate (n=13/108, III) hippocampal atrophy (Fig. 1). In patients with hippocampal atrophy there was an association between lower hippocampal volume and worse verbal memory tests scores such Rey-Auditory-Verbal-Learning Test immediate and delayed recall (both $p < 0.001$) and Short-Story ($p = 0.05$). When comparing the groups for each VRF, they differed only for smoking ($p = 0.02$; Fig. 2). There was no association between the number of VRF and hippocampal volume.

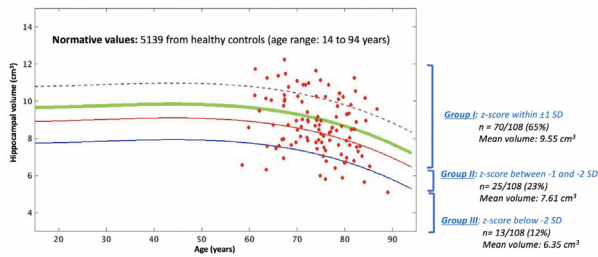


Figure 1: Comparison of hippocampal volumes between patients and normative values. The graph shows the distribution of hippocampal volume in our patients with VMCI (red dots), compared with the average of predictive normative values from a cohort of healthy controls (green line)

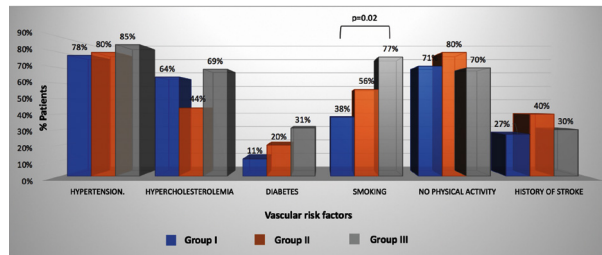


Figure 2: Differences between groups for each vascular risk factor. The graphs show the distribution of patients from the three groups for each vascular risk factor.

Conclusion: Hippocampal atrophy can be detected in patients with VMCI and seems to be closely related to subclinical memory impairment. Presence of hippocampal atrophy may be an unfavourable marker of disease outcome in patients with VMCI.

Disclosure: Nothing to disclose

MS and related disorders 2

O2028

Effectiveness and safety of ocrelizumab in patients with relapsing-remitting multiple sclerosis who had a suboptimal response with prior disease-modifying therapy: 2-year findings from CHORDS

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Background and aims: Ocrelizumab is an anti-CD20-directed monoclonal antibody that showed superior efficacy vs interferon β -1a treatment in pivotal trials of patients with relapsing multiple sclerosis (MS). The Phase IIIb CHORDS study (NCT02637856) examined the effects of ocrelizumab in patients with relapsing-remitting MS (RRMS) who experienced a suboptimal response to previous disease-modifying therapy (DMT).

Methods: The CHORDS study enrolled 608 patients with RRMS who experienced ≥ 1 relapse, ≥ 1 T1 gadolinium-enhancing lesion or ≥ 2 new/enlarging T2 lesions while receiving another DMT for ≥ 6 months. Patients received ocrelizumab 600mg every 24 weeks for ≤ 96 weeks. The primary endpoint was the proportion of patients free of protocol-defined clinical or MRI activity (event), evaluated in a modified ITT population for which patients who terminated early for lack of efficacy or death were imputed as having had an event and patients without an event who discontinued for other reasons were excluded. Secondary endpoints included annualised relapse rate (ARR) and Expanded Disability Status Scale (EDSS) change from baseline.

Results: Among the 555 patients who completed treatment, 48.1% were free of protocol-defined events at Week 96. Most patients did not experience protocol-defined relapse (89.6%), T1 gadolinium-enhancing lesions (95.5%), new/enlarging T2 lesions (59.5%) or 24-week confirmed disability progression (89.6%). 71 relapses were observed (ARR, 0.046). Most patients had stable (61.5%) or improved (22.7%) EDSS. Safety findings were consistent with the overall ocrelizumab safety profile.

Conclusion: This analysis demonstrated the benefits of ocrelizumab over 2 years in patients with RRMS who experienced suboptimal response to another DMT.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Health Interactions, USA.

O2029

MRI-based clustering of multiple sclerosis patients in the perspective of personalized Medicine

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Background and aims: We aimed to find clusters of multiple sclerosis (MS) patients with homogeneous underlying pathophysiology, by using advanced MRI techniques.

Methods: 115 MS (57 relapsing-remitting, 12 primary- and 46 secondary-progressive) patients, and 44 age- and sex-matched healthy controls (HC) underwent brain and cervical cord 3T MRI for assessing lesions, atrophy, and microstructural damage (with diffusion-tensor metrics), and a complete neurological assessment. Clusters of MS patients were identified with hierarchical clustering on age- and sex-adjusted MRI variables.

Results: 5 clusters of MS patients were identified: “early”; “intermediate-cord”, “intermediate-cortical”, “intermediate-late-lesion”; and “late”. “Early” patients showed similar MRI metrics vs HC (except lesions), lower Expanded Disability Status Scale (EDSS) and shorter disease duration (DD) compared to other patients’ groups ($p < 0.01$). Compared to “early” and other “intermediate” groups, “intermediate-cord” patients had higher cord T2-lesion volume (LV) ($p < 0.001$), “intermediate-cortical” had lower cortical thickness ($p < 0.001$), and “intermediate-late-lesion” had higher brain T2-LV, higher deep grey matter (GM) atrophy and longer DD ($p < 0.01$). “Late” patients had higher EDSS and DD, compared to “intermediate” groups ($p < 0.01$), and worst diffusion-tensor metrics and cord/brain atrophy ($p < 0.01$ vs all). “Intermediate-cord” patients could be divided into 2 groups characterized by different cord GM atrophy and cortical thickness ($p < 0.01$), with similar DD; the impaired one including mostly progressive phenotypes and higher EDSS.

Conclusion: MRI-based clustering of MS patients is feasible. It contributes to better characterize disease heterogeneity and in the future it may be useful for personalized medicine. “Intermediate-cord” patients may be the best target to study neuroprotective and regenerative strategies.

Disclosure: Partially supported by Fondazione Italiana Sclerosi Multipla (grant FISM/2018/R/16).

O2030

Challenges of initiating anti-CD20 monoclonal antibodies in RR MS

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Background and aims: Anti-CD20 monoclonal antibodies have demonstrated their efficacy in the treatment of active relapsing-remitting multiple sclerosis (RR-MS). While its drastic efficacy on disease activity has been reported in many studies, none of them have investigated the management of its initiation after another disease modifying therapy (DMT). The aim of this study was to assess the frequency and the predictive factors of disease activity during the wash-out period (WP) between cessation of last DMT and initiation of anti-CD20 monoclonal antibodies in RR-MS.

Methods: All RR-MS patients who initiated a treatment with Rituximab or Ocrelizumab between 2016 and 2019 have been included in this retrospective monocentric study. Univariate and multivariate analysis were conducted to identify predictive factors of disease activity during WP.

Results: 72 RR-MS patients (73.6 % female, mean age 35.4 years) were included, with a mean number of previous DMTs per patient of 3.2 (1-7). The most frequent previous DMT was Fingolimod (Fg, 44.4%). 20 patients experienced disease activity during the WP. The only predictive factor was previous treatment by Fg ($p < 0.001$). After cessation of Fg (32 patients), a WP duration over 1 month was also predictive of disease activity ($p = 0.02$).

Conclusion: Cautious monitoring of disease activity is necessary when switching from another DMT to anti-CD20 monoclonal antibodies, especially after treatment with Fg and according to WP duration. Reduction of WP duration could be enabled by monitoring of immune repertoire reconstitution and the acceptance of a lower threshold of lymphocytes for treatment initiation.

Disclosure: Nothing to disclose

O2031

Serum neurofilament light correlates with reduced grey matter volume in advanced multiple sclerosis

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Background and aims: Grey matter (GM) pathology is associated with physical and cognitive impairment in patients with multiple sclerosis (MS). Increased levels of serum Neurofilament light (sNfL), indicating neuro-axonal damage, have been described in MS and were related to the development of global and regional brain atrophy. However, its relation to MRI-based measures of distinct brain volumes is still poorly investigated.

Methods: We measured sNfL by an ultrasensitive Single Molecule Array (Simoa[®]) in 109 MS patients (mean age 38.1, SD±11.7 years, 63.3% female (16 clinically isolated syndrome (CIS), 72 relapsing-remitting MS (RRMS) and 21 progressive MS (PMS)) and 17 gender- and age-matched non-inflammatory neurological controls (NC). We recorded clinical data and performed 3T MRI to assess global and cortical normalised brain volumes and T2 lesion load.

Results: sNfL correlated with age in the entire cohort (N=126, $r=0.329$, $p<0.001$). We found elevated sNfL levels in RRMS and PMS compared to NC (Figure 1). Decreased total and cortical GM volume was found in MS patients compared to CIS ($p<0.001$). Only in patients with PMS we found sNfL to be correlated with volumes of total GM ($r=-0.475$, $p=0.034$), cortical GM ($r=-0.508$, $p=0.001$) (Figure 2) and lesion load ($r=0.513$, $p=0.017$; data not shown). No such correlation was present when analysing CIS and RRMS patients.

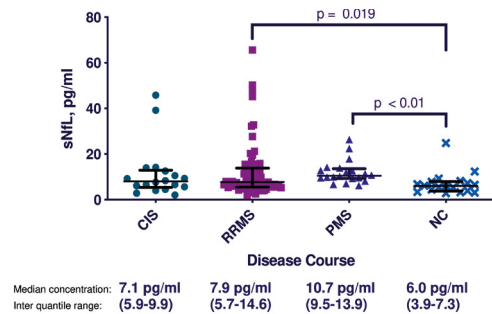


Figure 1 Comparison of sNfL in different stages of MS. sNfL levels are elevated in RRMS and PMS compared to NC (Mann-Whitney-U test, Bonferroni corrected).

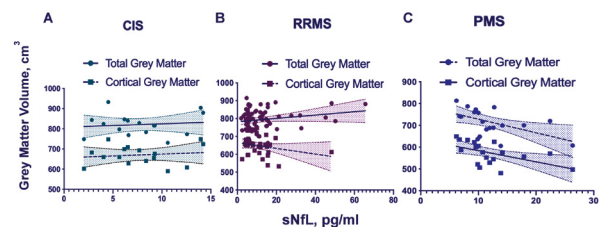


Figure 2 A-C Correlations of sNfL and GM in different stages of MS. 95% confidence bands are shown. Only in PMS we found sNfL to be correlated with volumes of total GM ($r=-0.475$, $p=0.034$) and cortical GM ($r=-0.508$, $p=0.001$) (C). No such correlation was present when analysing CIS (A) and RRMS (B) patients.

Conclusion: Although sNfL is already increased in earlier phases of MS, its relation to brain tissue damage, in particular GM pathology, becomes only apparent in more advanced, progressive forms of the disease. Further analysis of longitudinal data is ongoing to confirm and extend our results.

Disclosure: Nothing to disclose

O2032

TERIKIDS Study: teriflunomide efficacy and safety in paediatric patients with relapsing forms of MS

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Background and aims: Additional therapeutic options are needed for paediatric MS patients. Teriflunomide is approved for adults with relapsing forms of MS (RMS) in >80 countries; the TERIKIDS study (NCT02201108) assessed efficacy and safety in paediatric RMS patients.

Methods: TERIKIDS is a 96-week, randomised, double-blind, placebo-controlled, parallel-group phase 3 study of teriflunomide in paediatric RMS patients, with a 96-week, open-label extension; earlier extension entry is possible for clinical relapse or high MRI activity above protocol-defined thresholds. Patients receive placebo or teriflunomide (based on body weight equivalent to 14mg in adults). Eligible patients had $\geq 1/\geq 2$ relapses within 12/24 months. Primary endpoint is the time to first confirmed relapse, with sensitivity analysis including high MRI activity as relapse equivalent; secondary endpoints include proportion relapse-free, MRI lesion number and volume, brain volume loss, cognition outcomes, and safety/tolerability.

Results: Target enrolment was met (N=166). At baseline, mean age was 14.6 years (67% female). Time since first MS symptoms/diagnosis was 2.3/1.4 years. Mean number of relapses in the past year was 1.5 (42% experienced ≥ 2 relapses); average time since most recent relapse was 5.2 months. Mean (median) EDSS score and gadolinium-enhancing lesion number were 1.3 (1.5) and 3.8 (1.0), respectively. In the previous 2 years, 23% received disease-modifying therapy. Efficacy and safety results will be presented.

Conclusion: At baseline, patients enrolled in TERIKIDS had high relapse and MRI lesion activity, and relatively short disease duration. Results of this study will provide insight into the efficacy, safety, and tolerability of teriflunomide, and may help further understanding RMS in the paediatric population.

Disclosure: STUDY SUPPORT: Sanofi.

O2033

Efficacy and safety results of the phase 3 SPI2 study of MD1003 (high dose Pharmaceutical grade Biotin) in progressive MS

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Background and aims: An unmet need exists for treating progressive forms of multiple sclerosis (MS): primary or secondary progressive (PPMS, SPMS). Biotin is a coenzyme for carboxylases involved in energy metabolism and fatty acid synthesis. MS-SPI, the first study of MD1003 (high dose Pharmaceutical grade Biotin) in progressive MS, demonstrated a significant sustained improvement in disability with treatment vs placebo. SPI2 is a phase 3 study of MD1003 in progressive MS (EudraCT:2016-000700-29).

Objective: Evaluate the efficacy and safety of MD1003 in progressive MS.

Methods: SPI2 inclusion required documented, relapse-free, disability progression in EDSS over the 2 years before entry and an EDSS score between 3.5 and 6.5. Patients were randomized (1:1) to MD1003 100mg tid or placebo. The primary endpoint was the proportion of patients with improvement – decreased EDSS (0.5 or 1.0) or decreased timed 25-foot walk (T25FW) of $\geq 20\%$ – from baseline to month (M) 12, confirmed at M15. Secondary endpoints were time to 12-week confirmed EDSS progression, clinical global impression (CGI/SGI), and T25FW mean change.

Results: Overall, 642 patients were randomized: Europe/North America/Australia (n=338/290/14). At submission, baseline demographics and disease characteristics were: mean age 52.7 years; 53.7% female; 64.6% SPMS; mean time since diagnosis 12.6 years; mean time since SPMS conversion 5.0 years; mean EDSS 5.4; mean T25FW 11.6 seconds. Last patient last visit occurred in November 2019; database lock will be in early 2020.

Conclusion: Efficacy and safety results of the phase 3 SPI2 study of MD1003 in progressive MS will be presented.

Disclosure: This study was sponsored by MedDay Pharmaceuticals. MD1003 is a not approved, investigational product.

O2034

Effect of ofatumumab treatment on disability progression independent of relapse activity in patients with relapsing multiple sclerosis

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Background and aims: Ofatumumab, the first fully human anti-CD20 monoclonal antibody with a monthly 20mg subcutaneous (s.c.) regimen, demonstrated superior efficacy versus teriflunomide in the Phase 3 ASCLEPIOS I/II trials in relapsing multiple sclerosis (RMS) patients. Here, we present data on the treatment effect of ofatumumab versus teriflunomide on progression independent of relapse activity (PIRA).

Methods: In the ASCLEPIOS I/II pooled analysis, the risk of confirmed disability progression at 3/6 months (3mCDP/6mCDP; Expanded Disability Status Scale [EDSS] score increase of ≥ 1.0 if baseline EDSS score < 6.0 , or ≥ 0.5 if baseline EDSS score ≥ 6.0) was evaluated in three subsets of patients: (A) without confirmed relapses during the study, (B) without confirmed relapses during the study or prior to a 3mCDP/6mCDP event, and (C) with secondary progressive multiple sclerosis diagnosis at study-entry and without confirmed relapses during the study. Hazard ratios (HRs) and p-values were calculated by a Cox-regression model adjusted for study as stratum, for treatment, region, and baseline EDSS score as covariates. An inverse probability censoring weighted (IPCW) analysis, censoring patients with confirmed relapses prior to a 3mCDP/6mCDP event, was also performed.

Results: Ofatumumab significantly reduced the risk of 3mCDP and 6mCDP versus teriflunomide in all subsets analysed, except for 6mCDP in the small Subset-C (Table). IPCW estimation of PIRA confirmed a risk reduction of 46.0% for 3mCDP (HR [95%CI]: 0.540 [0.396-0.738], $p < 0.001$) and 42.5% for 6mCDP (0.575 [0.409-0.808], $p = 0.001$) versus teriflunomide.

Disability-related outcomes	Ofatumumab 20 mg n/N	Teriflunomide 14 mg n/N	HR (95% CI)	Risk reduction	p-value
3mCDP					
Subset-A	50/793	67/661	0.587 (0.407–0.848)	41.3%	0.004
Subset-B	53/796	82/676	0.516 (0.365–0.729)	48.4%	<0.001
Subset-C	6/46	11/37	0.312 (0.114–0.859)	68.8%	0.024
6mCDP					
Subset-A	42/793	53/661	0.632 (0.421–0.947)	36.8%	0.026
Subset-B	45/796	66/674	0.551 (0.377–0.805)	44.9%	0.002
Subset-C	6/46	8/37	0.463 (0.158–1.355)	53.7%	0.160

Results of treatment comparison obtained from a Cox-regression model adjusted for study as stratum, for treatment, region, and baseline EDSS score as covariates.

Subset-A: Patients without confirmed relapses during the study; Subset-B: Patients without confirmed relapses during the study or prior to a 3mCDP/6mCDP event; Subset-C: Patients with a SPMS diagnosis at study entry and without confirmed relapses during the study
3mCDP, disability progression confirmed at 3 months; 6mCDP, disability progression confirmed at 6 months; CI, confidence interval; EDSS, Expanded Disability Status Scale; HR, hazard ratio; N, total number of patients included in the analysis; n, number of patients with the specified event; SPMS, secondary progressive multiple sclerosis

Table. Risk of 3mCDP and 6mCDP by patient subsets

Conclusion: Ofatumumab 20mg s.c. monthly dosing regimen markedly reduced disability progression independent of relapses versus teriflunomide in RMS patients.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

Cerebrovascular diseases 2

O2035

Intended bridging therapy or intravenous thrombolysis in minor stroke with large vessel occlusion

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Background and aims: Whether bridging therapy (intravenous thrombolysis [IVT] followed by endovascular treatment) is superior to IVT alone in minor stroke with large vessel occlusion (LVO) is unknown.

Methods: Multicentric retrospective observational study including, in intention-to-treat, consecutive IVT-treated minor strokes (NIHSS \leq 5) with LVO, with or without additional mechanical thrombectomy. Propensity-score (inverse probability of treatment weighting) was used to reduce baseline between-groups differences. The primary outcome was excellent outcome, i.e., modified Rankin score 0-1 at 3 months follow-up.

Results: Overall, 598 patients were included (214 and 384 in the bridging therapy and IVT groups, respectively). Following propensity-score weighting, the distribution of baseline clinical and radiological variables was similar across the 2 patient groups. Compared with IVT alone, bridging therapy was not associated with excellent outcome (OR=0.96; 95%CI=0.75-1.24; p=0.76), but was associated with symptomatic intracranial haemorrhage (OR=3.01; 95%CI=1.77-5.11; p<0.0001). Occlusion site was a strong modifier of the effect of bridging therapy on outcome (Pinteraction<0.0001), with bridging therapy associated with higher odds of excellent outcome in proximal M1 (OR=3.26; 95%CI=1.67-6.35; p=0.0006) and distal M1 (OR=1.69; 95%CI=1.01-2.82; p=0.04) occlusions, but with lower odds of excellent outcome for M2 (OR=0.53; 95%CI=0.38-0.75; p=0.0003) occlusions. Bridging therapy was associated with higher rates of symptomatic intracranial hemorrhage in M2 occlusions only (OR=4.40; 95%CI=2.20-8.83; p<0.0001).

Conclusion: Although overall outcomes were similar in intended bridging therapy as compared to intended IVT alone in minor strokes with LVO, our results suggest that intended bridging therapy may be beneficial in M1 occlusions, while the benefit-risk profile may favor IVT alone in M2 occlusions.

Disclosure: Nothing to disclose

O2036

Post-thrombolysis early neurological deterioration in minor strokes with large vessel occlusion

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Background and aims: Whether endovascular therapy added on intravenous thrombolysis (IVT), as compared to IVT alone, is beneficial in minor strokes with large vessel occlusion (LVO) is unknown. To identify predictors of early neurological deterioration (END) following IVT alone may help to select the best candidates for additional endovascular therapy.

Methods: Multicentric retrospective observational study including IVT-treated minor strokes (NIHSS \leq 5) with LVO intended for IVT alone, i.e., including those who eventually received endovascular therapy because of END. END was defined as a \geq 4 points on NIHSS within 24hrs following admission. Thrombus length was measured centrally either on T2*-MRI or CT/CTA.

Results: 721 patients were included: mean age 70years, median NIHSS 3, occlusion located in internal carotid artery [ICA] -T/L, tandem cervical ICA+MCA, proximal M1, distal M1, M2, and basilar artery, in 3%, 10%, 7%, 21%, 54% and 4%, respectively. The thrombus was visible in 85% of patients. END occurred in 12% of patients and was associated with poor 3-month outcome. In multivariable analysis, a more proximal occlusion site (p<0.001) and a longer thrombus (p=0.002) were independently associated with END. END occurred in 55%, 23%, 19%, 13%, 5% and 27% of patients with ICA-T/L, tandem, proximal M1, distal M1, M2, and basilar artery occlusion, respectively, and in 5%, 7%, 15% and 23% of patients with thrombus length of <6, [6-9[, [9-12[and \geq 12mm, respectively.

Conclusion: Our study suggests that thrombus location and length are strong predictors of END in minor strokes with LVO. This may help to select the best candidates for additional endovascular therapy.

Disclosure: Nothing to disclose

O2037

Net water uptake overestimates cerebral edema volumes in thrombolysed patients at 24-hours compared to anatomical distortion

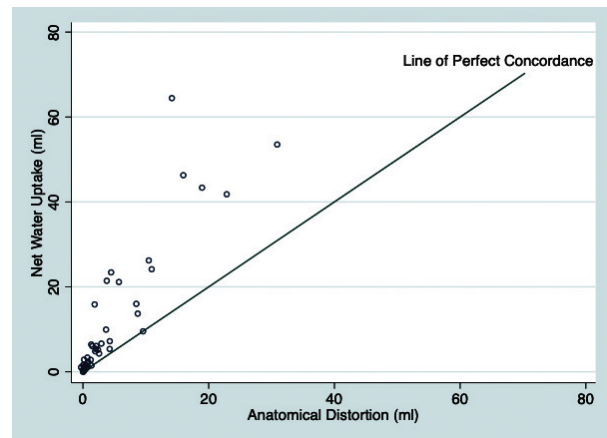
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Background and aims: Following the GAMES-RP trial, there is an increased interest in the measurement of cerebral edema [Net Water Uptake (NWU) Broocks et al. Invest Radiol 2016; Anatomical Distortion (AD): Harston et al. Stroke 2018]. This study uses data from the MAGIC Study [Inzitari et al. Stroke 2013] to explore the agreement between these two methods.

Methods: All patients with a CT Scan available at baseline and at 18-36 hours following symptom onset were included in the analysis. Lesion masks on follow-up imaging were defined and agreed. The volumes of edema (ml) were generated according to the NWU and AD methods. Appropriate statistical tests were used to explore the agreement between these volumes.

Results: On follow-up imaging, 102 patients had scans available for analysis: 28 (27.2%) had no lesion; 23 (22.5%) had evidence of hemorrhage, precluding the use of the NWU method. The mean (SD) volumes of edema were: NWU 10.2ml (15.2); AD 4.0ml (6.5). The Lin Concordance Correlation Coefficient was 0.57 (95% CI 0.47-0.66) with all values above the line of perfect concordance (see figure). The Bland-Altman metrics showed a mean difference in values of 6.2ml (9.8) with 95% CI level of agreement of -13.0ml to 25.4ml. Regression metrics estimated a relationship of $NWU = 1.8 + 2.1 * AD$.



Conclusion: Volumes of cerebral edema generated by NWU and AD methods demonstrated poor concordance and levels of agreement, with NWU volumes typically twice those of those measured by AD. This may influence future trial design where volume is an outcome measure.

Disclosure: Nothing to disclose

O2038

Association between β blocker or statin drug use and hemorrhage from cerebral cavernous malformations

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Background and aims: To determine the association between β blocker or statin drug use and the risk of symptomatic intracranial haemorrhage or persistent/progressive focal neurological deficit in adults with cerebral cavernous malformations.

Methods: The population-based Scottish Intracranial Vascular Malformation Study prospectively identified adults resident in Scotland who were first diagnosed with a cerebral cavernous malformation during 1999-2003 or 2006-2010. We compared the association between β blocker or statin drug use for at least 90 days at any time after first presentation and the occurrence of intracranial hemorrhage or persistent/progressive focal neurological deficit due to the cerebral cavernous malformation for up to 15 years of prospective follow-up.

Results: Of 300 adults in the Scottish Intracranial Vascular Malformation Study, 63 (21%) used β blocker medication (27/63 [43%] used propranolol) and 73 (24%) used statin medication. β blocker medication use was associated with a lower risk of intracranial hemorrhage or persistent/progressive focal neurological deficit (1/63 [1.6%] versus 29/237 [12.2%], adjusted hazard ratio 0.09, 95% confidence interval 0.012-0.68, $p=0.019$) during 15 years of follow-up. Statin medication use was associated with a non-significant reduction of intracranial hemorrhage or persistent/progressive focal neurological deficit (4/73 [5.4%] versus 26/227 [11.5%], adjusted hazard ratio 0.37, 95% confidence interval 0.013-1.07, $p=0.067$) during 15 years of follow-up.

Conclusion: The associations between β blocker and statin drug use and the risk of intracranial hemorrhage or persistent/progressive focal neurological deficit in patients with cerebral cavernous malformations justify the investigation of the effects of these drugs in randomized trials.

Disclosure: Nothing to disclose

O2039

Serum neurofilament light chain levels differentiate spinal cord infarction from inflammatory myelopathies

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Background and aims: To investigate whether serum neurofilament light chain (NfL) levels differentiate spinal cord infarction (SCI) from acute inflammatory myelopathies.

Methods: We retrospectively identified Mayo Clinic patients (January 1, 2000-December 31, 2019) with: 1) SCI; 2) aquaporin-4 (AQP4)-IgG or myelin oligodendrocyte glycoprotein (MOG)-IgG-associated myelitis at disease clinical presentation; or 3) idiopathic transverse myelitis (ITM) from a previously identified population-based cohort seronegative for both AQP4-IgG and MOG-IgG. Serum NfL levels were assessed on available stored samples obtained ≤ 3 months from myelopathy onset at the Verona University Neuropathology laboratory (SIMOA Quanterix) in a blinded fashion. Representative spinal cord MRI T2-lesion areas were manually measured on sagittal images (Figure 1).



Figure 1 - Example of manual measurement of spinal cord lesion area on MRI

Results: 48 patients were included: SCI, 20 (definite, 11; probable, 6; possible, 3); AQP4-IgG-associated myelitis, 17; MOG-IgG-associated myelitis, 5; ITM, 6. Median (range) serum NfL levels (pg/mL) in patients with SCI (188 [14.3-2793.4]) were significantly higher than those of patients with AQP4-IgG-associated myelitis (37 [0.8-6942.9]), MOG-IgG-associated myelitis (45.8 [4-283.8]), and ITM (15.6 [0.9-217.8]); $p=0.01$. The NfL levels to MRI T2-lesion Area Ratio (NAR) showed the highest accuracy for identification of SCI vs inflammatory myelopathies, with values greater than 0.4 yielding 88% specificity and

95% sensitivity, respectively (AUC=0.95; Figure 2). NAR remained independently associated with SCI after adjusting for age, gender, immunotherapy before sampling, and days from myelopathy symptoms onset to sampling ($p < 0.0001$).

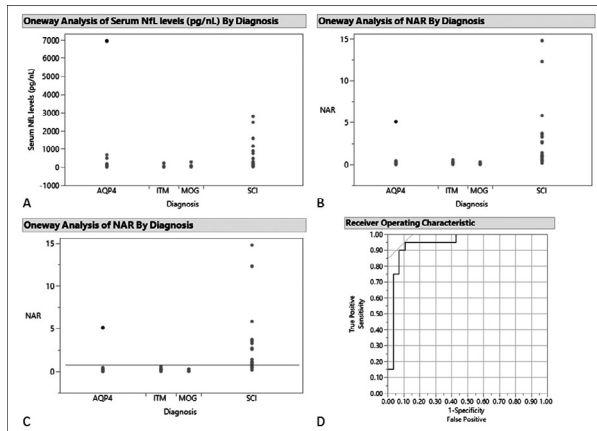


Figure 2 - Scatterplots showing the distribution of NfL levels, spinal cord lesion areas, and NAR in the different groups of myelopathies

Conclusion: In the acute setting, serum NfL and NAR might be a reliable, and easily accessible biomarker to differentiate SCI from acute inflammatory myelopathies.

Disclosure: Nothing to disclose

Clinical neurophysiology

O2040

Interobserver variation of routine EEG vs high value (2000s/mm²) DWI MRI findings in TGA: a prospective study

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Background and aims: Transient global amnesia (TGA) is characterized by the acute inability to form new memories, lasting up to 24 hours. Vascular, epileptic and migrainous events have been proposed as responsible pathophysiologic mechanisms. The value of electroencephalography (EEG) has not been proved, and studies so far have shown EEG to be normal during and after the attack. However, EEG should be performed when transient epileptic amnesia (TEA) is considered likely, as an alternative diagnosis.

Methods: To assess the efficacy of routine EEG at the early phase of TGA, blindly assessed by 2 neurologists, and compare these findings with high-value DWI MRI.

Results: 15 patients were included (male/females:4/11). Mean age was 65 years [SD±4.4]. Mean time from TGA onset to routine EEG (21 electrodes, 10/20 system) was one day [±0.4], mean time to brain MRI was 3 days [SD±2.5]. High-value DWI-MRI was normal in 2 patients, and 2 revealed hippocampal sulcus remnant cysts. Bilateral high 2000-DWI hyperintense hippocampal lesions were noted in 2 patients. In the rest, a unilateral left hippocampal lesion was depicted. Mean PDR was 10c/s [SD±1]. Intermittent slow theta wave activity was recorded in 6/15 EEGs, and was assessed as frequent in 5/6 and occasional in 1 (8-49%). Slow activity was mostly noted in the frontotemporal/anterior-temporal areas. A left predominance of slow activity was noted in the majority of the patients (5/6). Only in 1 patient 2000-DWI MRI findings matched EEG findings, while another had abnormal EEG without concurrent MRI findings.

Conclusion: Routine EEG cannot substitute 2000-DWI MRI in detecting hippocampal involvement in patients with TGA.

Disclosure: Nothing to disclose

O2041

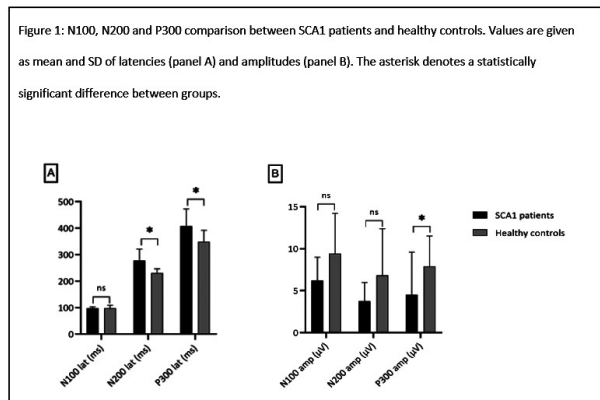
Electrophysiological evaluation of cognition and neuropsychological assessment in Spinocerebellar Ataxia Type 1 patients

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Background and aims: Spinocerebellar Ataxia Type 1 (SCA1) is an autosomal dominant disorder caused by an unstable expansion of CAG repeats. Many studies have provided evidence that cognitive decline is also present along with motor deterioration. In this context, event-related potentials (ERPs) may provide valuable insight into attentive processes

Methods: 10 SCA1 patients (8 females, 2 males) were enrolled in this study. Neuropsychological test battery included: Frontal Assessment Battery, FAS fluency test, Trail Making Test, Raven Progressive Matrices, Stroop Color and Word Test, Rey complex figure, Babcock's short tale, Emotion Attribution Task and VATA-m for anosognosia. Auditory ERPs were assessed through an auditory oddball paradigm by using standard (80% of presenting probability, 2000Hz frequency) and target (20% of presenting probability, 1500Hz frequency) stimuli, presented in a pseudo-randomized manner. EEG signals were recorded from the scalp at the sites of Fz, Cz, Pz with auricular reference. N100, N200 and P300 were detected and analyzed in 9 patients. 11 healthy subjects were chosen to match patients on sex, age and educational level

Results: Neuropsychological tests evaluating frontal, attentive, visuospatial and affective abilities showed significant correlation with SARA score. With regard to ERPs, pathologically longer latencies of N200 and P300 ($p=0.006$; $p=0.012$) and smaller P300 amplitudes ($p=0.02$) were observed in SCA1 patients (Fig.1). Additionally, we found strong correlations between N200 latency and P300 amplitude and scores assessing cerebellar motor symptoms and attentive-affective functions (Fig.2)



Conclusion: This study suggests usefulness of ERPs, providing for the first time electrophysiological evaluation of cognition in SCA1 patients

Disclosure: Nothing to disclose

Figure 2: Spearman's rank correlations between ERP components (N200 latency and P300 amplitude) and clinical and neuropsychological scores. Only significant correlations are reported.

Clinical and neuropsychological features	N200 latency		P300 amplitude	
	r	p	r	p
SARA	0.828	0.006*	-0.765	0.016*
Trail Making Test A	0.820	0.007*	-0.678	0.045*
Emotion Attribution Task	-0.807	0.015*	n.s.	n.s.

O2042

Cortical plasticity after bionic hand prostheses: is the “invasion” hypothesis of deafferented cortex always true?

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Background and aims: Upper limb amputation provokes changes in the cerebral motor and somatosensory cortex that governs the amputated limb and this mechanism is related to Phantom Limb Pain (PLP). Not much is known about the potential reversibility of these changes.

Methods: We tested with TMS motor maps at baseline and after a period of training with a new hand bidirectional prosthesis in three left trans-radial amputees, correlating these changes with the modification of PLP in the same period.

Results: Baseline motor maps showed in all 3 amputees an inter-hemispheric asymmetry of motor cortex with a smaller area of muscles representation of the amputated side compared to contralateral hemisphere. Following training and possibility to re-use again cerebral areas for motor and somatosensory tasks, there was a partial reversal of the asymmetry, with a more symmetrical representation of the forearm muscles on the 2 hemispheres, as in normal subjects. The 2 subjects affected by PLP experienced after training with the prosthesis a statistically significant reduction of pain.

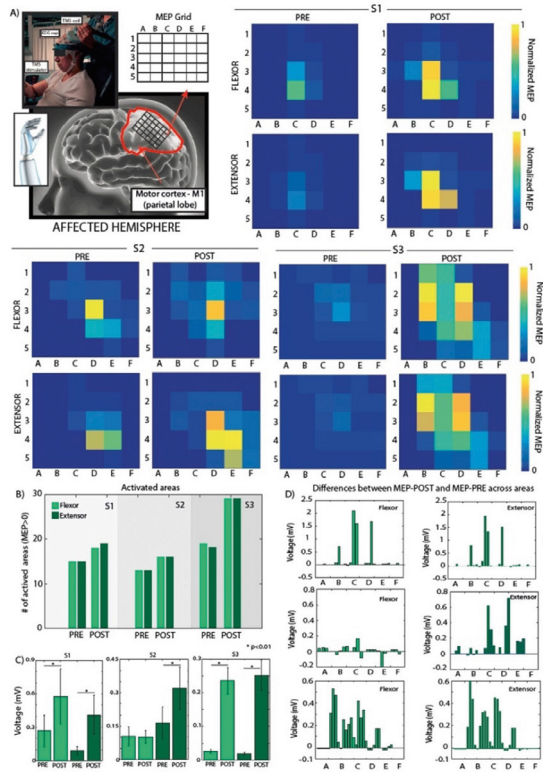


Figure 1: the baseline motor mapping showed that motor area related to the amputee limb was smaller than contralateral

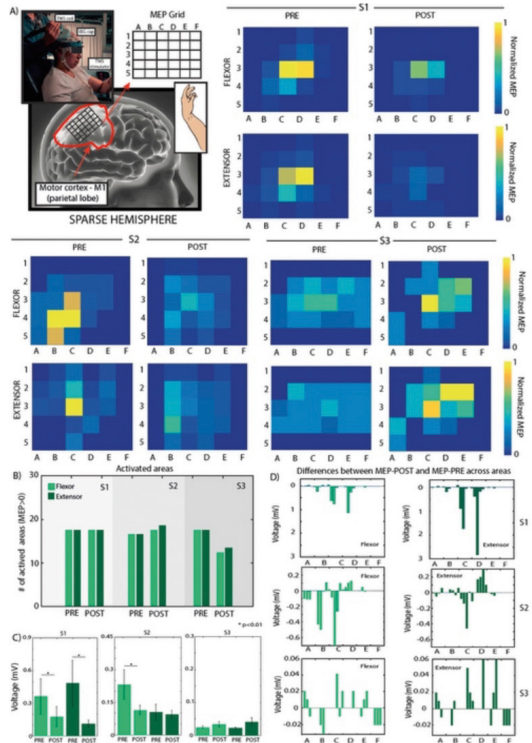


Figure 2: after training with robotic prosthesis able to restore somatosensory feedback, motor area related to stump muscles increased in size

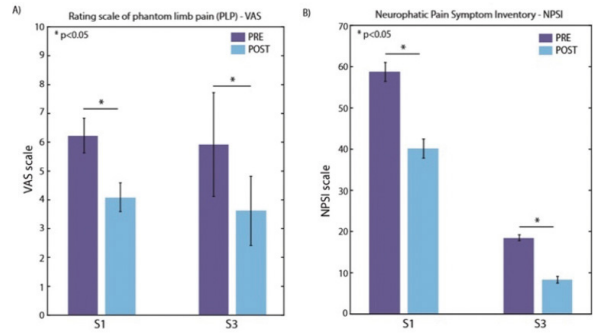


Figure 3: both 2 subjects suffering from Phantom Limb Pain reduced their painful sensations

Conclusion: According to “invasion” hypothesis for plastic brain changes we were supposed to find at baseline a motor cortical area governing the stump increased in size compared with the contralateral, with a rebalancing after the training. Our measurement “in vivo” found opposite results that we can explain as the result of prolonged non-use of the cerebral areas. Motor and somatosensory learning process is partially able to restore symmetry of motor areas and this process correlates with improvement of Phantom Limb Pain.

Disclosure: Nothing to disclose

O2043

Knocking at the brain’s door: a direct measure of brain excitability in alternating hemiplegia of childhood

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Background and aims: Alternating hemiplegia of childhood (AHC) is a rare neurodevelopmental syndrome caused by a mutation in ATP1A3, a Na/K-ATPase pump critical to restore membrane excitability, particularly in fast-spiking interneurons. Both paroxysmal and static clinical features of AHC are typically distributed asymmetrically. Transcranial Magnetic Stimulation (TMS) combined with electromyography (EMG) indirectly shows fluctuations in cortical excitability in AHC, with MEP decreasing during a hemiplegic episode.

Our aim was to obtain a direct, bilateral and longitudinal measure of excitability, using hd-EEG as a readout of TMS response (TMS-EEG).

Methods: 5 AHC adults and 5 healthy controls (HC) were tested with TMS-EEG on 2 separate sessions. Primary motor cortex was targeted using neuronavigation and stimulated bilaterally at subthreshold intensity (98% of resting Motor Threshold). A qualitative analysis of TMS evoked potentials was performed. Pearson correlation test was used to evaluate the interhemispheric symmetry. Differences in interhemispheric symmetry between groups and sessions were calculated using Mann-Whitney test.

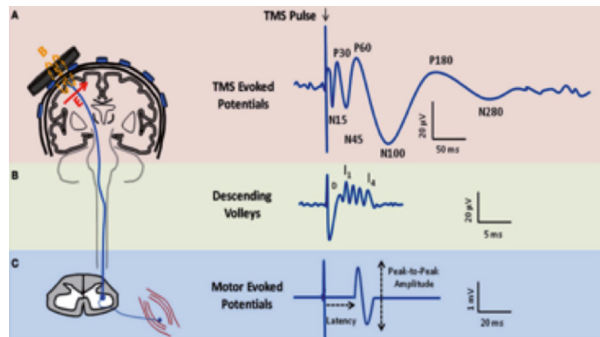


Figure 1: TMS evoked responses at cortical, spinal and muscular level.

Results: In one patient we recorded a baseline condition and a quadriplegic spell, during which the EEG response was abolished. AHC patients exhibited a higher degree of interhemispheric asymmetry compared to HC ($\rho=0.39\pm0.25$ vs. 0.6 ± 0.04 , $p=0.004$). A degree of intersession variability was also observed in patients ($p=0.052$).

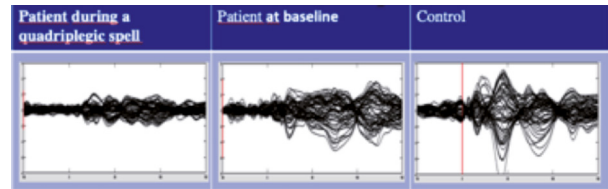


Figure 2: TMS evoked potential during a quadriplegic spell (A), at baseline in AHC patient (B) and in a HC (C)

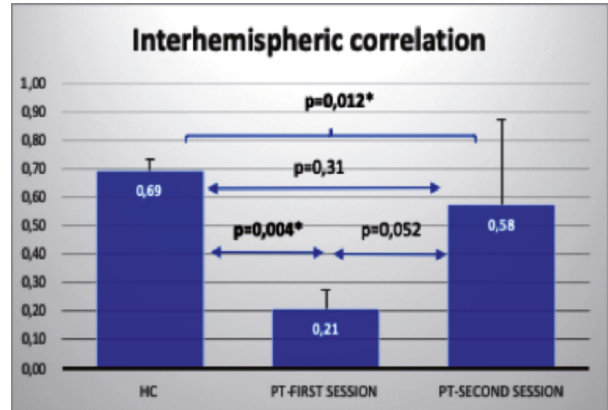


Figure 3: interhemispheric asymmetry in HC and AHC patients

Conclusion: These preliminary data support the central origin of the excitability abnormalities previously described and demonstrate an increased interictal asymmetry in AHC patients. Studies in larger cohorts are needed to further explore the role of TMS as a biomarker and objective outcome measure in interventional trials.

Disclosure: Nothing to disclose

O2044

EEG background patterns correlate with serum neurofilament light after cardiac arrest

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Background and aims: EEG is one of the most commonly used tools for neurological prognostication after cardiac arrest (CA), but the lack of a uniform classification of pathological patterns is a major limitation. A recently proposed classification (Figure 1) based on standardized terminology has high interrater reliability and the proposed patterns predicted 6-month neurological outcome with high specificity but limited sensitivity. Serum neurofilament light (S-NFL) is a novel biochemical marker, potentially superior to other measures of hypoxic brain injury. This study investigated the correlation between S-NFL as a quantitative measure of brain injury and EEG-patterns according to the new classification.

Methods: Retrospective analysis of EEG data and S-NFL from the Targeted Temperature Management (TTM) trial. EEGs were recorded after the temperature intervention was completed (36 hours to 12 days after CA) and classified according to the American Clinical Neurophysiology Society (ACNS) standardized terminology by blinded investigators. The EEG-background and the prevalence of discharges were compared to peak S-NFL-levels at 48 or 72 hours after CA.

Results: We included 262 patients with EEG and S-NFL (Table 1). The classified EEG pattern was significantly related to the peak S-NFL-level (Figure 1). S-NFL-levels increased significantly with increased prevalence of discharges if seen superimposed on a continuous EEG background (Figure 2).

Table 1: Characteristics	
Age, median (IQR), years	65 (58-73)
Male gender, N (%)	214 (81.7)
Time to ROSC, median (IQR), min	27 (20-42)
Peak S-NFL, median (IQR), pg/ml	2316 (158-7673)
Outcome at 6 months, cerebral performance categories scale, N (%)	
1 – Good cerebral performance	56 (21.4)
2 – Moderate cerebral disability	15 (5.7)
3 – Severe cerebral disability	12 (4.6)
4 – Coma or vegetative state	7 (2.7)
5 – Brain death	172 (65.6)
Time to EEG, median (IQR), hours	74 (58-100)
EEG background, N (%)	
Continuous	148 (56.5)
Discontinuous	42 (16.0)
Burst suppression	27 (10.3)
Suppression	45 (17.2)

Table 1 - Patient characteristics

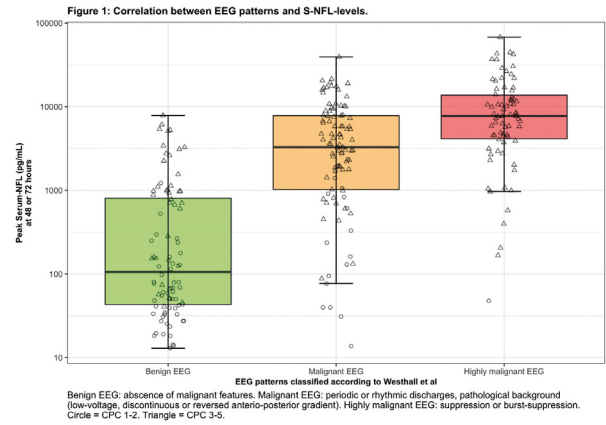


Figure 1 - Correlation between EEG patterns and peak S-NFL-levels

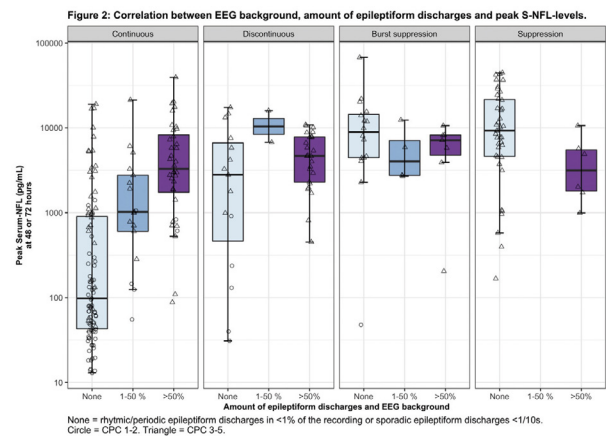


Figure 2 - Correlation between EEG background, amount of epileptiform discharges and peak S-NFL-levels

Conclusion: EEG background is strongly associated with a quantitative biochemical measure of brain injury after cardiac arrest. The amount of epileptiform activity is an additional marker of severity in the subgroup of patients with a more benign EEG background.

Disclosure: This project has received funding from the Swedish National Health System (ALF), the County Council of Skåne and the Skåne University Hospital Foundations.

Monday, May 25 2020

Neuro-ophthalmology/neuro-otology

O3001

Retinal axonal degeneration in Niemann Pick type C disease

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Background and aims: Niemann-Pick disease, type C1 (NPC1) is a heterogeneous autosomal-recessive lysosomal storage disorder, presenting at different ages and progressing at different rates. Optical coherence tomography (OCT) is established to detect retinal degeneration in vivo. We examined NPC1 patients (NPC1-P), clinically asymptomatic NPC1 mutation carriers (NPC1-MC), and healthy controls (HC) using OCT in order to (i) identify retinal degeneration in NPC1-disease and (ii) to investigate possible subclinical retinal degeneration in NPC1-MC.

Methods: 14 NPC1-P, 17 NPC1-MC and 31 age-matched HC were examined using spectral-domain OCT. Neurological examinations, clinical scales and video-oculography (VOG) were correlated with OCT data.

Results: Macular retinal nerve fiber layer and volumes of combined ganglion cell and inner plexiform layer were significantly lower in NPC1-P compared to HC (mRNFL(μ m): 0.13 ± 0.01 vs. 0.14 ± 0.02 ; $p=0.01$; GCIPL(mm³): 0.60 ± 0.05 vs. 0.62 ± 0.04 ; $p=0.04$). No significant differences were found in NPC1-MC in comparison to HC. In NPC1-P the decreased amplitude of upward vertical saccades was associated with thinned peripapillary pRNFL ($\rho=0.645$, $p<0.05$), and thinned GCIP ($\rho=0.609$, $p<0.05$), but not in NPC1-MC. In NPC1-P correlations between combined outer plexiform layer and outer nuclear layer (OPONL) with mDRS ($r=-0.617$, $p<0.05$) and GCIP with SARA ($r=-0.622$, $p<0.05$) were observed. Further, in NPC1-MC motor scores were negatively associated with pRNFL ($\rho=-0.677$, $p<0.01$).

Conclusion: We showed retinal degeneration in NPC1-P and significant correlation between retinal neuro-axonal degeneration with clinical measurements. We observed a non-significant trend of retinal degeneration in NPC1-MC correlating with subclinical motor abnormalities. Based on these preliminary data, OCT may be an important marker of neurodegeneration in NPC1 disease after clinical symptoms' onset.

Disclosure: Nothing to disclose

O3003

Prevalence of visual snow syndrome in the UK

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Background and aims: Visual snow syndrome is a recently described condition of unknown prevalence. We investigated the prevalence in a representative population sample from the UK and tested the hypothesis that visual snow syndrome is associated with young age, headache, tinnitus and mood impairment.

Methods: Using a crowdsourcing platform, we recruited a representative sample of 1015 laypeople from the UK, matched for age, gender and ethnicity according to national census data. Participants were unprimed, i.e. were inquired about the "frequency of certain medical conditions" but not "visual snow syndrome".

Results: 38 of 1015 participants reported symptoms compatible with visual snow (3.7%, 95% CI 2.7-5.2), and 22/1015 met criteria for visual snow syndrome (2.2%, 95% CI 1.4-3.3). Female-to-male ratio for visual snow syndrome was 1.6:1. Subjects with visual snow syndrome were older (50.6 ± 14 years) than the population mean (44.8 ± 15 years), albeit not statistically different ($p=0.06$). Of 22 participants with visual snow syndrome, 16 had mood symptoms (72.7%; $p=0.01$), 13 had headache (54.5%, $p=0.06$), including 5 with visual migraine aura (22.7%, $p=0.15$), and 13 had tinnitus (59.1%, $p=0.0001$). No participant had diabetes or a cleft lip (control questions). Following a multivariable regression analysis to adjust for age and gender, only the association between visual snow syndrome and tinnitus remained significant (OR 3.93, 95% CI 1.63-9.9; $p=0.003$).

Conclusion: The UK prevalence of visual snow syndrome is around 2%. We confirmed an association with tinnitus, but unprimed laypeople with visual snow syndrome are on average older than those seeking medical attention.

Disclosure: Nothing to disclose

O3004

Disrupted functional connectivity within the visual, attentional and salience networks in visual snow syndrome

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Background and aims: Visual snow (VS) is a newly defined neurological condition in which patients describe a continuous static-like disturbance present in the entire visual field, and additional symptoms such as palinopsia, photophobia, entoptic phenomena and nyctalopia. The basic neurobiology of visual snow is still mostly unknown, and treatment is challenging.

We performed a brain resting state functional connectivity in patients with VS to understand more about the underlying pathophysiology of the syndrome.

Methods: Subjects with VS (n = 24) and matched healthy volunteers (n = 24) were scanned on a 3T GE MR750 MRI scanner. Whole-brain maps of functional connectivity were acquired under 2 separate conditions: at rest while watching a blank screen and during a visual paradigm consisting of a visual-snow like stimulus.

Results: Subjects with visual snow had increased and reduced connectivity between key visual areas and the rest of the brain, both in the resting state and during a visual stimulation, compared to healthy controls. In particular, we found altered connectivity between visual areas V1 and V5; between the thalamus and both the basal ganglia and lingual gyrus; between the visual motion network and both the default mode and attentional networks.

Conclusion: The data suggest VS is characterized by a widespread disturbance in the functional connectivity of multiple brain systems, particularly of the pre-cortical and cortical visual pathways, the visual motion network, and the attentional networks.

Disclosure: Nothing to disclose

Epilepsy 2

O3005

GABAergic dysfunction mediates motor impairment in Rett syndrome

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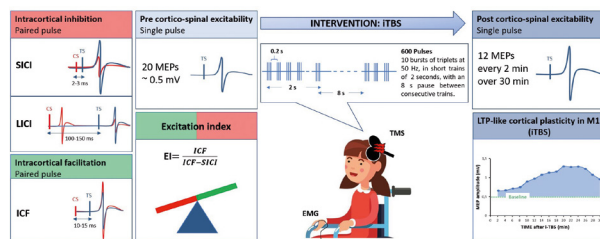
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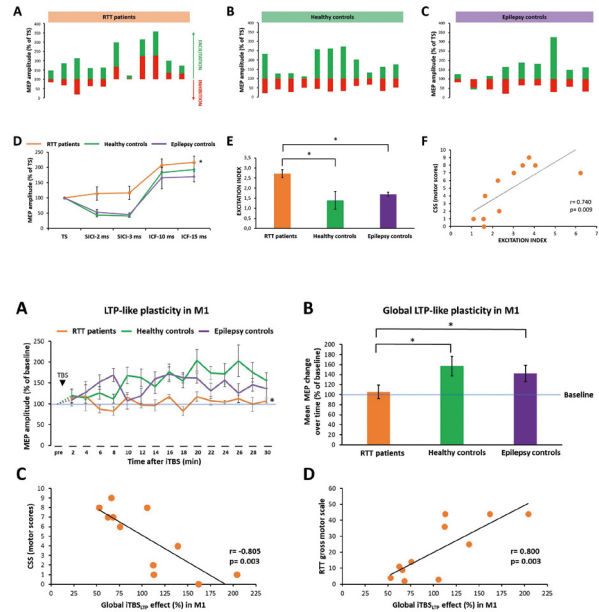
Background and aims: Rett syndrome (RTT) is an X-linked dominant neurodevelopmental disorder due to pathogenic mutations in the MECP2 gene. Motor impairment constitutes the core diagnostic feature of RTT. Preclinical studies have consistently demonstrated alteration of excitation/inhibition (E/I) balance and aberrant synaptic plasticity at cortical level. Herein we aimed at understanding neurobiological mechanisms underlying motor deficit by assessing in "vivo" synaptic plasticity and E/I balance in the primary motor cortex (M1).

Methods: On 14 patients with typical RTT, 9 epilepsy controls patients and 11 healthy controls we applied paired-pulse transcranial magnetic stimulation (TMS) protocols to evaluate the Excitation Index, a biomarker reflecting the contribution of inhibitory and facilitatory circuits in M1. Intermittent TMS-theta burst stimulation was used to probe Long-Term-Potential (LTP)-like plasticity in M1. Motor impairment, assessed by ad hoc clinical scales, was correlated with neurophysiological metrics.



Schematic overview of experiment.

Results: RTT patients displayed a significant increase of the Excitation Index ($p=0.003$), as demonstrated by the reduction of short-interval intracortical inhibition and increase of intra-cortical facilitation, suggesting a shift toward cortical excitation likely due to GABAergic dysfunction. GABAergic impairment was also confirmed by the reduction of long-interval cortical inhibition ($p=0.002$). LTP-like plasticity in M1 was abolished ($p=0.008$) and scaled with motor disability (all $p=0.003$).



Loss of LTP-like plasticity in the primary motor cortex (M1) of RTT patients

Conclusion: TMS is a method that can be used to assess cortical motor function in RTT patients. Our findings support the introduction of TMS measures in clinical and research settings as biomarker to monitor the progression of motor deficit and response to treatment.

Disclosure: Nothing to disclose

O3006

Efficacy and safety of cenobamate as adjunctive therapy in patients with uncontrolled focal seizures: results from two double-blind, placebo-controlled, international studies

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V. Villanueva⁵, C. Brandt⁶

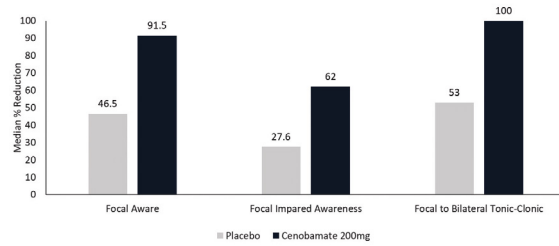
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Background and aims: Cenobamate is a novel antiepileptic drug (AED) recently approved by the Food and Drug Administration. Here we report the safety/efficacy data from 2 international, double-blind, placebo-controlled trials (C013 and C017).

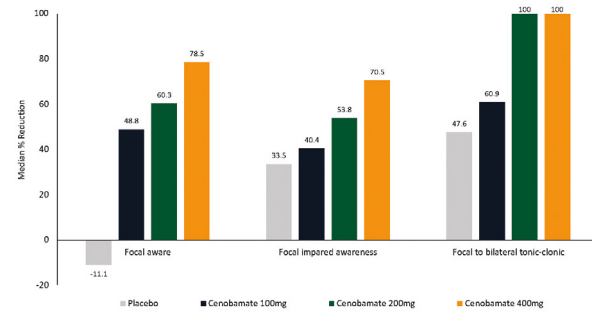
Methods: Adults with uncontrolled focal onset seizures (FOS) with ≥ 3 seizures/month (C013) or ≥ 8 seizures/8 weeks (C017) and treatment with 1-3 concomitant AEDs were enrolled. Patients were randomized to placebo or cenobamate 200mg/day (C013) or placebo vs 100, 200, or 400mg/day cenobamate (C017).

Results: In C013, the responder rate ($\geq 50\%$ reduction in seizure frequency from baseline) in the maintenance phase was significantly greater for cenobamate 200mg vs placebo (62% vs 33%); significantly greater percentages achieved seizure freedom (28% vs placebo 9%). In the C017, $\geq 50\%$ responder rate during maintenance was significantly higher for cenobamate 100, 200, 400mg (40%, 56%, 64%), respectively vs those treated with placebo (26%); significantly greater percentages of patients receiving 200 and 400mg achieved seizure freedom (11% and 21%, respectively vs placebo 1%); In both studies, cenobamate showed a significant reduction across all subtypes of FOS (fig.1, fig.2). Cenobamate was generally well tolerated. Most TEAEs reported in the pivotal studies were mild or moderate in intensity and increased with the dose. The most frequently occurring AEs ($\geq 10\%$) with cenobamate were dizziness, somnolence, headache, fatigue and diplopia.

Conclusion: Consistent, clinically meaningful, and statistically significant response rates ($\geq 50\%$, $\geq 75\%$, $\geq 90\%$, 100%) were observed across the studies.



Percent Reduction in Seizure Frequency by Seizure Type in the maintenance phase (C013 study)



Percent Reduction in Seizure Frequency by Seizure Type in the maintenance phase (C017 study)

Disclosure: Study 017 (NCT01866111) and 013 (NCT01397968) were sponsored by SK Life Science, Inc. and the analyses supported by Arvelle Therapeutics International GmbH.

O3007

Secular trends in adult epilepsy-related and potentially avoidable mortality in Scotland: a nationwide population-based study

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Background and aims: Premature death is common in epilepsy. We aimed to quantify, for the first time, the national burden of avoidable epilepsy-related deaths (EPRDs) in adults (aged ≥ 16 years) in Scotland.

Methods: This retrospective observational study used a sequential cross-sectional design to nationally identify adult EPRDs. We linked death certificates to administrative primary and secondary care datasets. ICD-10 codes (G40-41, R56.8), Read codes (F25.), and antiepileptic drugs (AED) were examined in the linked datasets to identify potential epilepsy patients, using medical records as a diagnostic reference standard to calculate positive predictive values (PPV). EPRDs were determined from death certificates (including post-mortem indicators) and medical records, estimating standardised mortality ratios (SMR) and mortality rates (MR). The Office for National Statistics' Revised Definition of Avoidable Mortality 2016 causes were used to identify potentially avoidable EPRDs.

Results: G40-41-coded causes of death had the highest PPV for epilepsy diagnosis (PPV 93%, 95%CI 89–96%). These codes captured 2,149 epilepsy-related deaths. 1,276 (59%) had ≥ 1 seizure-/epilepsy-related hospital admission during 2009–2016, yet only 516 (24%) were seen in neurology clinic during this period. Age-standardised MR per 100,000 ranged between 6.8 (95%CI 6.0–7.6) in 2009 and 9.1 (95%CI 8.2–9.9) in 2015. SMR was higher in young adults (≤ 55 years), peaking at 6.0 (95%CI 2.3–9.7) between ages 16–24 years. 78% of young adult EPRDs were potentially avoidable. The most common mechanisms of death were SUDEP, aspiration pneumonia, cardiac arrest, alcohol-related, and congenital malformation.

Conclusion: Avoidable epilepsy-related deaths remain common, particularly in young adults, and have not reduced over time despite advances in treatment.

Disclosure: This work was charitably supported by Epilepsy Research UK (R44007) and the Juliet Bergqvist Memorial Fund. The funders played no role in the design or conduct of this review and the authors declare no conflicts of interest.

O3008

Real-world prevalence of autoantibodies in epilepsy

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Background and aims: The prevalence of autoantibodies among people with epilepsy (PWE) is not clear, with widely varying rates of 5–80% reported. Existing studies demonstrate considerable differences regarding participant selection/ascertainment bias, numbers of antibodies tested for (and their clinical relevance), laboratory methods for antibody testing and result interpretation. By determining the prevalence of largely pathogenic antibodies among prospectively recruited outpatients with new-onset focal epilepsy (NOFE), drug-resistant epilepsy (DRE) and seizure-free epilepsy (SFE), we aim to provide a prevalence rate that is generalisable to the broader population of PWE.

Methods: Sera obtained from consecutive adult patients from epilepsy clinics (NOFE patients 2011–2015, DRE and SFE patients 2018–2020) and healthy controls (HC) were screened on live cell-based assays for neuronal-surface antibodies (NSAs) to LGI1, CASPR2, contactin-2, DPPX and the GABAA, GABAB, glycine and NMDA receptors. Radioimmunoprecipitation assays and in-house permeabilised CBAs detected GAD65 antibodies.

Results: Antibodies were detected in 24/232 (10.3%) NOFE, 22/260 (8.5%) DRE, 5/54 (9.3%) SFE and 0/55 HCs. NOFE patients had NSAs only, whereas DRE and SFE cohorts had NSAs and GAD65 antibodies (DRE: 11 NSA, 11 GAD65; SFE: 2 NSA, 3 GAD65).

Conclusion: Overall, 51/546 (9.3%) epilepsy outpatients had autoantibodies detected and the proportion of antibody-positive patients was similar across the three epilepsy groups. Future work should determine any pathophysiological role for antibodies in epilepsy and to explain the striking absence of GAD65 antibodies in NOFE.

Disclosure: Supported by Epilepsy Research UK and Oxford-UCB Alliance.

O3009

Hippocampal epileptogenesis in LGI1, CASPR2 and GABABR antibodies: preliminary findings

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Background and aims: Autoantibody-mediated forms of encephalitis (AE) include neurological disorders characterized by subacute memory loss, movement disorders and, often, frequent, focal epileptic seizures. Yet, the electrophysiological effects of these autoantibodies on neuronal function have received little attention. In this study, we assessed the effects of CSF-containing autoantibodies on intrinsic and extrinsic properties of hippocampal neurons, to define their epileptogenic potential. **Methods:** We compared the effects of CSF containing leucine-rich glioma inactivated 1 (LGI1), contactin associated protein-like 2 (CASPR2) or γ -aminobutyric acid receptor B (GABABR)-antibodies on ex vivo electrophysiological parameters after stereotactic hippocampal inoculation into mice. Whole-cell patch-clamp and extracellular recordings from CA1 pyramidal neurons and CA3-CA1 field recordings in ex vivo murine brain slices were used to study neuronal function.

Results: By comparison to control CSF, AE CSFs increased the probability of glutamate release from CA3 neurons. In addition, LGI1- and CASPR2-antibody containing CSFs induced epileptiform activity at a population level following Schaffer collateral stimulation. CASPR2-antibody containing CSF was also associated with higher spontaneous firing of CA1 pyramidal neurons. On the contrary, GABABR-antibody containing CSF did not elicit changes in intrinsic neuronal activity and field potentials.

Conclusion: Using patient CSF, we have demonstrated that the AE-associated antibodies against LGI1 and CASPR2 are able to increase hippocampal CA1 neuron excitability, facilitating epileptiform activity. These findings provide in vivo pathogenic insights into neuronal dysfunction in these conditions.

Disclosure: Nothing to disclose

Movement disorders 2

O3010

Longitudinal evolution of white matter damage in Parkinson's disease

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Background and aims: No strong MRI biomarkers were identified to define the Parkinson's Disease (PD) progression. We aimed to investigate the longitudinal evolution of cerebral white matter (WM) micro- and macrostructural damage and its relationship with clinical picture.

Methods: 154 PD patients underwent clinical assessment, cognitive evaluation and MRI scan (including T2-weighted and diffusion tensor [DT] MRI sequences) once a year over a follow-up of 36 months. White matter lesions (WML) were manually identified on T2-weighted scans and the total WML volume was calculated and excluded to define normal appearing white matter (NAWM). Applying tract-based spatial statistics, mean fractional anisotropy (FA), mean (MD), axial (axD) and radial (radD) diffusivity values of the total WM and NAWM skeleton were extracted. Regression models and Pearson's correlation between MRI and clinical/cognitive data were performed.

Results: UPDRS-III score ($p < 0.001$) and WML volume ($p < 0.001$) showed significant progression over follow-up. DTI metrics differed significantly between total and NAWM ($p \leq 0.001$). Longitudinal differences of MD, axD, and radD values significantly correlated with UPDRS-III (r ranging 0.24/0.37, p ranging 0.01/0.04) and Addenbrooke Cognitive Examination total score (r ranging -0.27/-0.29, p ranging 0.01/0.02). WML volume did not correlate with longitudinal alterations of clinical variables. Regression analyses showed a significant interaction between axial diffusivity and MMSE and UPDRSIII score both in total WM and in NAWM.

Conclusion: Our study showed that longitudinal evolution of WM microstructural damage is associated with both motor and global cognitive deterioration in PD and it might provide a sensitive biomarker of disease progression.

Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

O3011

First results for the BeyoND study: A phase 2b, international, open-label study evaluating long-term safety of ND0612 in patients with Parkinson's disease experiencing motor complications

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Background and aims: The primary objective of this phase 2b study was to evaluate the long-term safety and tolerability of a 24-hour regimen and a 16-hour 'waking day' regimen of ND0612. ND0612 is a drug-device combination delivering liquid levodopa/carbidopa via continuous subcutaneous (SC) infusion to reduce motor complications in patients with Parkinson's disease (PD).

Methods: This open-label safety study (NCT02726386) was conducted in PD patients (aged >30 y, H&Y ≤ 3 during ON) taking ≥ 4 levodopa doses/day and ≥ 1 other PD medications, and experiencing ≥ 2 hours of OFF time/day with predictable early-morning OFF periods. Patients were assigned to receive ND0612 for a regimen of either 16-hours/day or 24-hours/day.

Results: 214 patients were enrolled (24-hour regimen: $n=90$; 16-hour regimen: $n=124$) at 46 sites in 8 countries. Over the course of the 1-year treatment period, 66% of patients experienced treatment-related TEAE's with 5.6% of subjects experiencing serious treatment-related TEAE's. Systemic safety is typical for PD patients treated with LD/CD. The most frequent AEs were typical for a continuous subcutaneous mode of drug administration and included infusion-site nodules (30.8%), infusion-site hematoma (25.2%), and infusion-site pain (13.1%). Overall, 17.8% patients discontinued due to AEs.

Conclusion: ND0612 infusion was found to be safe with generally mild to moderate local AEs which were reversible and manageable and no unexpected TEAEs for systemic levodopa treatment. Long-term data will continue to be collected in patients enrolled in the study extension, some of whom are now in their fourth year of ND0612 treatment.

Disclosure: This study was sponsored by NeuroDerm.

O3012

Sensory and autonomic assessment in the differential diagnosis of early parkinsonism

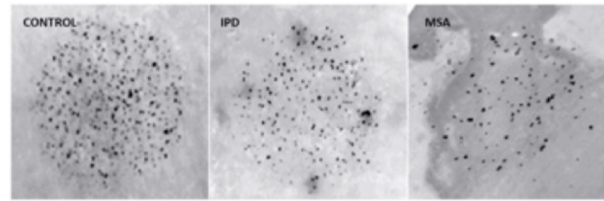
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Background and aims: Parkinsonism such as Parkinson's disease (PD) and multiple system atrophy (MSA) affects 2% of people over 65 years with increased worldwide burden on health system. Diagnosis at early stage of the disease is still challenging in some patients due to the lack of early diagnostic biomarkers. The latter has an implication on effective therapies and to recommend adequate strategies to avoid disease-specific complications.

Aims: To develop biomarkers aiming at improving early diagnosis

Methods: 87 patients with early diagnosis (within 2 years from symptoms onset) of PD or MSA-P (parkinsonian type) (age 62.5±8.7 years; M/F=52/35) and not started on L-dopa treatment, were recruited. Patients underwent a comprehensive functional sensory and autonomic assessment including quantitative sensory testing (QST), the assessment of cardiovascular reflexes (CVR) and sudomotor function (through the dynamic sweat test - DST) and specific questionnaire for sensory and autonomic symptoms at first visit and at 12 months follow up. Patients were recruited from 2 centres (University College London Queen Square, UK and Neurology Division, ICS Maugeri, IRCCS of Telesse Terme, Italy)

Results: Autonomic symptoms scores were greater in MSA compared with IPD patients. In particular, gastrointestinal and genitourinary domains were the ones which better discriminated between the 2 conditions. Also, MSA patients showed a lower density of active sweat glands at distal leg (figure) and a reduced adrenergic cardiovascular response to isometric exercise compared to IPD.



The density of sweat glands activated after pilocarpine by iontophoresis is reduced in patients with parkinsonism compared to controls. In MSA the sweat gland density is significantly lower compared to IPD patients.

Conclusion: Our data support the hypothesis that the functional assessment of sensory and autonomic systems are potential early biomarkers to differentiate MSA versus IPD.

Disclosure: Nothing to disclose

O3013

Disconnected brain in functional movement disorders with anxious & depressive symptoms

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Background and aims: Depression and/or anxiety (DEP/ANX) are common symptoms in functional movement disorders (FMD). However, their neural correlates have not been elucidated.

Methods: Using resting state functional MRI (3T, Siemens, Skyra), we investigated 43 FMD patients (33F, age 45±(SD)9 years, disease duration 8.4±5.6 years) and 44 matched healthy controls (HC). The DEP and ANX symptoms were scored by the Beck depression inventory (BDI-II) and State Trait Anxiety Inventory (STAI). To explore differences in general and selective functional connectivity among FMD-H (n=23; BDI>16, STAI-X2>45), FMD-L (n=17, BDI<16, STAI-X2<45) and HC groups, we used eigenvector centrality (EC) mapping and seed-based connectivity analysis using regions with maximum EC as seeds.

Results: In comparison with the HC group, the FMD-L showed a decrease of general connectivity (EC) in the midcingulate cortex (MCC) (Fig. 1A), while the FMD-H was associated with decreased EC in the inferior occipital gyrus (IOG) (Fig. 1D). Analyzing selective connectivity, the FMD-L<HC comparison revealed decreased connectivity only between the MCC and the motor cortex (Fig. 1B). In contrast, using the FMD-H<HC and FMD-H<FMD-L comparisons, we found that both the MCC and IOG seeds showed decreased connectivity with several cortical and subcortical areas including the frontal, temporal, parietal and occipital cortices, as well the thalamus, the basal ganglia and the cerebellum (Fig. 1C, F-G).

Conclusion: In conclusion, we observed that the brain disconnection pattern differed between the FMD subjects with and without depression and/or anxiety, indicating that these symptoms are in FMD associated with wider disruption of motor and non-motor networks. Supported by the grant AZV 16-29651A.

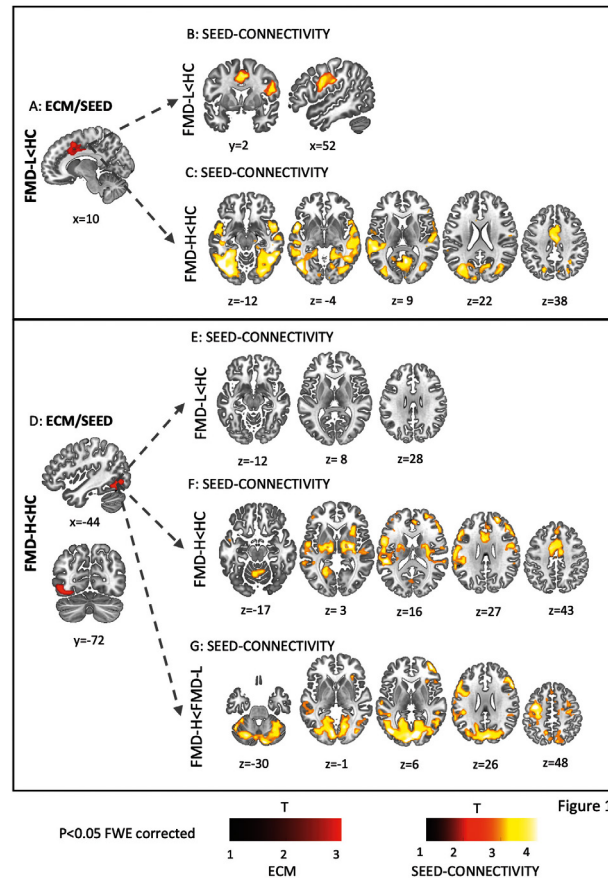


Figure 1

Disclosure: Nothing to disclose

O3014

Directional deep brain stimulation in subthalamic nucleus for Parkinson's disease: results of a multicenter, prospective, blinded, crossover study

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Background and aims: Published reports on directional DBS have been limited to small series from single-center investigations. PROGRESS assessed the safety and clinical efficacy of directional DBS in a large prospective cohort.

Methods: Patients receiving subthalamic nucleus DBS for Parkinson's disease were programmed with omnidirectional stimulation for 3 months, followed by directional stimulation for another 3 months. The primary endpoint was blinded, randomized, off-medication evaluation of TW for directional vs. omnidirectional stimulation at 3 months. Additional endpoints at 3-, 6- and 12-month follow-ups included adverse events, therapeutic current strength (TCS), UPDRS part III motor score, subject and clinician stimulation preference, activity of daily living and quality of life.

Results: A directional DBS system was implanted in 234 subjects. No intracranial hemorrhages or infections occurred. At 3 months, TW was wider using directional stimulation in 90.6% of subjects, satisfying the primary endpoint for superiority. The mean increase in TW with directional stimulation was 41% (2.98±1.38mA, compared to 2.11±1.33mA for omnidirectional). The TCS was decreased by 39% with directional programming. After 6 months, 53% of subjects blinded to stimulation type (102/193) preferred the period with directional stimulation, 26% (50/193) preferred the omnidirectional period and 21% (41/193) had no preference. Additional results including 12-month data will be available.

Conclusion: In this international prospective blinded

crossover study, directional stimulation yielded a wider TW and a lower TCS compared to omnidirectional stimulation and was preferred by subjects blinded to stimulation type.

Disclosure: This study was funded by Abbott

O3015

[18F]FDG-PET imaging of supraspinal locomotor control in Parkinson's disease

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Background and aims: Hypokinetic gait is a clinical hallmark of advanced Parkinson's disease (PD). The aim of this study was to investigate supraspinal locomotor control in PD using a [18F]FDG-PET-based real locomotion paradigm.

Methods: 20 patients with advanced PD and 25 age-matched healthy controls underwent a detailed neurological examination, falls assessment, and quantitative gait analysis (GAITRite®). Patients and controls performed a well-established locomotion PET paradigm, where they had to walk in a hallway for 10min after injection of [18F]FDG. PET scan started 30min p.i. The regional cerebral glucose metabolism (rCGM) was compared between groups and correlated with disease duration, severity and gait parameters using SPM8.

Results: PD patients had a reduced gait velocity, step length and pathological slowing with cognitive dual task compared to controls. Decrease of gait velocity strongly correlated with the Hoehn and Yahr stage and disease duration. [18F]FDG-PET during locomotion revealed a relatively reduced rCGM in the parietal cortex, caudate nucleus and pontomesencephalic brainstem tegmentum and a higher rCGM in the globus pallidus and primary motor cortex in PD ($p < 0.001$). rCGM decrease in the caudate nucleus and rCGM increase in the globus pallidus correlated with a reduced locomotion velocity and longer disease duration. rCGM decrease in the thalamus was associated with a history of falls.

Conclusion: PD patients show characteristic changes in their supraspinal locomotor network. A reduced input to the basal ganglia (via the caudate nucleus) and disinhibition of the direct basal ganglia loop (via the globus pallidus) correlates with hypokinetic gait features. Postural instability is associated with thalamic pathology.

Disclosure: Nothing to disclose

O3016

The epidemiology of progressive supranuclear palsy in the United Kingdom: evidence from the Clinical Practice Research Datalink GP Online Database (CPRD GOLD)

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Background and aims: PSP is a neurodegenerative disorder with a prevalence of ~6/100,000 in the United Kingdom (UK). Prior UK epidemiologic studies have been small in-depth population samples. The study objectives were to estimate the diagnosed prevalence and incidence of PSP in the UK, using a large population base, and to describe PSP patient characteristics.

Methods: PSP cases and age and sex-matched controls were identified 1987-2018 from CPRD GOLD, a national electronic medical record database of ~1.3M patients. PSP was defined as 1 or more codes for PSP and index date (date of first PSP code) age 40 or older. Prevalence and incidence of PSP were age-adjusted to the UK Census Population. Comorbidities and medications were examined in cases and controls.

Results: Among 704 PSP cases, 55.7% were male and mean age at index date was 73.2 years. Crude and age-adjusted prevalence in 2018 was 4.25 and 4.35/100,000. Crude and age-adjusted incidence in 2018 was 0.96 and 0.97/100,000/year. In PSP cases, the most common recorded comorbidities were central nervous system disorders (97.6%), rheumatism (61.2%), acute respiratory infections (58.9%) and hereditary and degenerative diseases of the central nervous system (54.4%). Major comorbidities related to PSP, such as accidental falls, intracranial injury, and fractures were significantly more frequent in cases than controls. Before index date, 31.1% of PSP cases had a Parkinson's disease diagnosis.

Conclusion: We show that epidemiological studies of PSP can be carried out using a large primary care database. Prevalence, incidence, and patient characteristics in this study are comparable to smaller in-depth patient/record review studies.

Disclosure: Research funded by Biogen.

Neurogenetics

O3017

Biodistribution and expression of onasemnogene abeparvovec (AVXS-101) DNA, mRNA, and SMN protein in human tissue

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Background and aims: AVXS-101 is a gene replacement therapy for patients with spinal muscular atrophy type 1 (SMA1) resulting from survival motor neuron 1 (SMN1) deletion/mutation. This study examined the biodistribution and expression of AVXS-101 in human tissues after a single intravenous administration.

Methods: Biodistribution of vector genome, vector mRNA, and SMN protein in the central nervous system (CNS) and peripheral tissues was characterised in 2 infants with SMA1 treated with AVXS-101 in phase 3 studies. Spinal motor neurons were isolated using laser-capture microdissection and vector genome quantified. Both patients died from respiratory illness at 5 weeks and 6 months post-gene therapy. The latter patient demonstrated substantial motor function improvement.

Results: AVXS-101 DNA and mRNA distribution was widespread among peripheral organs, muscles, and all regions of the spinal cord. AVXS-101 vector genomes ranged between 1.5 and 2.7 per diploid genome across spinal segments from both patients. SMN protein expression in motor neurons was detected in all regions of the spinal cord at levels similar to tissue from non-SMA1 controls. Analysis of the motor neuron marker choline acetyltransferase identified motor neurons with morphology similar to non-SMA1 control motor neurons. Expression of SMN protein was detected in cortical and subcortical regions of the motor cortex, medulla, and peripheral tissues, including skeletal muscle.

Conclusion: AVXS-101 traverses the blood-brain barrier following systemic administration with substantial transduction. Expression of SMN protein was detected in the CNS, including motor neurons. AVXS-101 is suited for treating SMA1 by targeting motor neurons and restoring SMN expression in key cellular targets in humans.

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O3018

Spinal cord MRI for early detection of presymptomatic pathology in C9orf72 mutation carriers: a three time-points longitudinal MRI study

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal dementia (FTD) are neurodegenerative conditions with a large portion of familial cases due to c9orf72 gene mutations. Brain imaging studies in asymptomatic carriers demonstrated early white (WM) and grey matter (GM) degeneration.

Aim of this study was to investigate whether longitudinal cervical spinal cord (SC) degeneration can be detected in asymptomatic c9orf72 hexanucleotide carriers using multimodal quantitative imaging.

Methods: 72 asymptomatic individuals were enrolled in a prospective study of first-degree relatives of ALS and FTD patients carrying the c9orf72 mutation. 40 (C9+) were carriers. Each subject underwent a 3T cervical SC MRI. Quantitative measures of GM and WM atrophy and DTI parameters were evaluated at baseline, after 18 and 36 months.

Results: At baseline, significant WM atrophy was detected in C9+ subjects older than 40 years of age (p-value<0.05) without associated changes in GM and DTI parameters. At 18 and 36-month follow-up, WM atrophy in C9+ subjects older than 40 years was accompanied by significant progressive corticospinal tract fractional anisotropy (FA) reduction (p-value=0.031). Intriguingly, C9+ subjects with a family history of ALS exhibited significant CST FA reduction already on their baseline scans.

Conclusion: Cervical SC imaging is able to detect WM atrophy in C9+ subjects older than 40. While WM atrophy remains stable over time, progressive pyramidal tract FA reduction can be detected on follow-up acquisitions. SC MRI in c9orf72 related conditions is a powerful tool to characterise presymptomatic pathological changes and to predict phenotypic conversion to ALS versus FTD.

Disclosure: This study was supported by the Assistance Publique – Hôpitaux de Paris, the ANR (Agence nationale

de la recherche), the Centre d'Investigation Clinique, and the Centre pour l'Acquisition et le Traitement des Images (CATI), Paris, France.

O3019

Extraneurological features in Kennedy's disease: data from the Italian SBMA registry

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Background and aims: Spino-Bulbar Muscular Atrophy (SBMA, Kennedy's disease), is a rare, neurodegenerative, X-linked hereditary neuromuscular disease due to a CAG trinucleotide repeat expansion in the androgen receptor gene. Main neurological manifestations are weakness, atrophy and fasciculations of limb and bulbar muscles. A non-neurological involvement is typical and early, and contributes significantly to quality of life deterioration.

Methods: In a cohort of male patient from the Italian SBMA Registry we assessed non-neurological manifestations by collecting: minimal dataset of clinical information; standard and modified ECG for Brugada-like pattern; questionnaires to evaluate sexual function (International Index of Erectile Function, IIEF), urinary dysfunction (International Prostate Symptoms Scale, IPSS), and laboratory tests.

Results: Patients: n:117; mean age: 61.3±11.2 years, range 31-83; CAG repeats: mean 45.2±3.2, range: 39-57; 101 patients had gynecomastia (92 bilateral, 8 unilateral); 25 diabetes or glucose intolerance; 42 hypertension; only 2 had abnormal ECG with Brugada-like pattern; IPSS mean: 6.94±7, range 0-35; IIEF mean: 15.1±10, range: 0-30. Laboratory test: HbA1c (mmol/mol) mean: 36.4±7.3, range: 26-80 (abnormal 10.6%); total cholesterol (mg/dl) mean: 206.16±33.6 range: 124-305 (abnormal 49.5%); SGOT(U/L) mean: 44.34±18.6, range: 17-121 (abnormal 59%); SGPT(U/L): mean: 49.53±22.8, range: 16-126 (abnormal 57.5%); vitamin D (ng/ml): 20.42±11.7, range: 3.2-60.7 (abnormal: 84%); CK(U/L): mean 954.2±689, range: 53-2997.

Conclusion: SBMA is a multisystem disease: beyond motor neurons and muscle there is evidence of frequent metabolic syndrome and liver dysfunction, while the Brugada-like pattern is very rare and clinically non-relevant.

Disclosure: Funded by Telethon-UILDM grant GUP15009

O3020

Lifetime risk of autosomal recessive mitochondrial disorders calculated from genetic databases

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Background and aims: Mitochondrial disorders are a group of rare diseases, caused by nuclear or mitochondrial DNA mutations. Their marked heterogeneity as well as referral and ascertainment biases render phenotype-based prevalence estimations difficult. We calculated the lifetime risk of all autosomal recessive mitochondrial disorders on basis of genetic data.

Methods: We queried the Genome Aggregation Database (gnomAD) and our in-house exome database for the allele frequency of disease-causing variants in genes associated with recessive mitochondrial disorders. Based on this, we estimated the lifetime risk of 249 mitochondrial disorders. Phenylketonuria served as proof of concept since calculations could be aligned with known birth prevalence data from newborn screening.

Results: The estimated lifetime risk for phenylketonuria (16.0/100,000) correlates well with known birth prevalence data (18.7/100,000), supporting the validity of the approach. The combined estimated lifetime risk of 249 investigated mitochondrial disorders is 31.8 (20.9-50.6)/100,000 in our in-house database, 48.4 (40.3-58.5)/100,000 in the European gnomAD dataset, and 31.1 (26.7-36.3)/100,000 in the global gnomAD dataset. The disorders with the highest lifetime risk (>3/100,000) were, in all datasets, those caused by mutations in the SPG7, ACADM, POLG and SLC22A5 genes.

Conclusion: We provide a population-genetic estimation on the lifetime risk of an entire class of monogenic disorders. Our findings reveal the substantial cumulative prevalence of autosomal recessive mitochondrial disorders, far above previous estimates. These data will be very important for assigning diagnostic a priori probabilities, and for resource allocation in therapy development, public health management and biomedical research.

Disclosure: This work was facilitated by the German Federal Ministry of Education and Research (BMBF, Bonn, Germany) through a grant to the German Network for Mitochondrial Disorders (mitoNET, 01GM1906A to TK and a grant for the E-Rare project GENOMIT (01GM1603 and 01GM1207 to HP and TK).

O3021

The genetic landscape for isolated not-OPA1 autosomal dominant optic atrophy

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Background and aims: Autosomal dominant optic atrophy (DOA) includes a heterogeneous group of inherited diseases in most of the cases due to mitochondrial dysfunction. Besides OPA1 gene, which is responsible of the large majority of DOA, other rare genes are reported in association with DOA.

We aimed at evaluating the presence of mutations in genes other than OPA1 in an Italian cohort of sporadic or familial cases with isolated OA.

Methods: Next generation sequencing (NGS) approaches were used for identifying causative genes in a cohort of 185 Italian cases negative for OPA1 mutations.

Results: Heterozygous mutations with confirmatory in-silico analysis for pathogenicity were identified in ACO2 gene in 12 families, AFG3L2 in 5 families, WFS1 in 4 families, SDHA in 2 families, SSBP1 in 2 families, SPG7 in 2 families and OPA3, DNMI1 and YME1L1 in single cases.

Conclusion: These results highlight the genetic heterogeneity of DOA including SSBP1, ACO2, AFG3L2, SPG7, WFS1, DNMI1, SDHA, OPA3 and YME1L1 as genes responsible for isolated OA. Dominant mutations in SSBP1 gene were already reported in association with nephropathy and retinopathy. Only recessive mutations in ACO2, YME1L1 have been reported in syndromic or isolated OA. AFG3L2, DNMI1 and OPA3 mutations have been already reported in association with isolated or syndromic DOA. WFS1 dominant mutation have been described in association with OA and deafness. Remarkably, the same phenotypic expression can be due to different pathogenic mechanisms including mtDNA maintenance (SSBP1), mitochondrial dynamics (DNMI1 and OPA3), proteolytic control (AFG3L2, SPG7 and YME1L1) and metabolic enzymatic activities (SDHA and ACO2).

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O3022

The MYO-SEQ: beyond the exome. A genotype-phenotype correlation of unsolved LGMD individuals

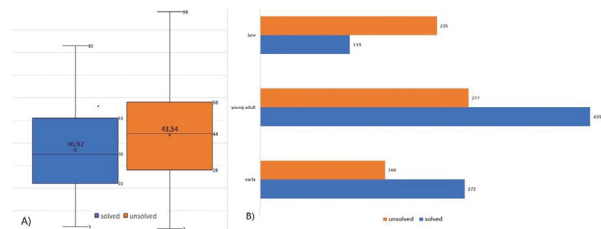
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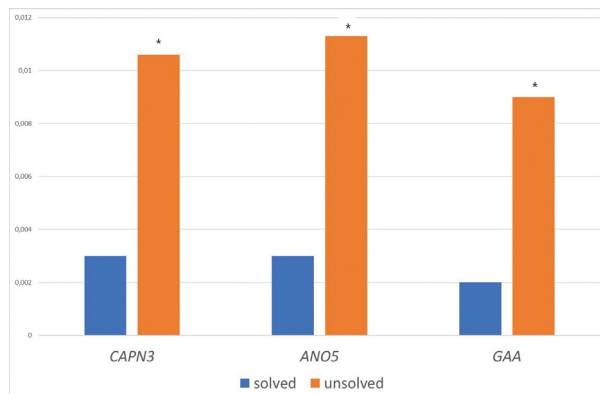
Background and aims: Limb girdle muscular dystrophies (LGMDs) are heterogeneous group of neuromuscular disorders. With whole exome sequencing (WES) diagnostic yield of approximately 25-50% can be reached. Most of the exome sequenced studies concentrate on solved cases analysis. We perform genetic and demographic studies on unsolved LGMD individuals from a large exome sequencing project (the MYO-SEQ).

Methods: We analyzed WES data from 1891 individuals with LGMD. Ethical approval was granted by the NRES Committee North East (reference 08/H0906/28). WES was performed at the Broad Institute of MIT and Harvard's Genomics Platform. Phenotype data collection was performed using the PhenoTips online platform.

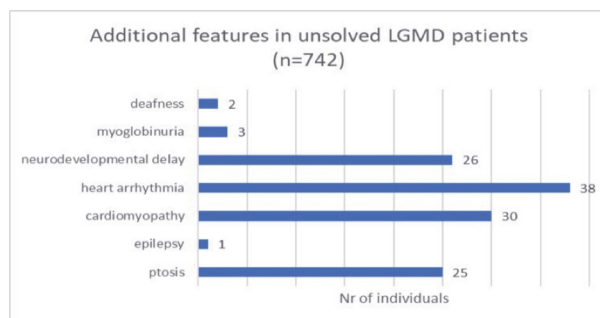
Results: In the MYO-SEQ we reached a diagnostic yield of 52%. The mean age in the unsolved cohort was 43,5 vs. 36,91 yrs in solved (t-test p<0,005). In the unsolved cohort late onset patients represented 36% and early onset 26% of total unsolved vs. 14% and 32% in the solved cohort respectively. Pathogenic variants carrier frequency (solved:unsolved) was for CAPN3 0,003:0,0106; ANO5 0,003:0,0113 and GAA 0,002:0,009. We analyzed WES data for patients sharing a common additional feature (e.g. cardiomyopathy, epilepsy) and identified genetic modifiers (e.g. RYR2 for heart arrhythmia).



A) Age in yrs solved vs. unsolved B) Age structure solved vs. unsolved



Pathogenic single carrier frequency for CAPN3, ANO5 and GAA in solved and unsolved cohort ($p < 0.005$)



Additional features in individuals with unsolved LGMD

Conclusion: Prevalence of late onset LGMD in the unsolved cohort may suggest acquired diseases or polygenic inheritance. Higher pathogenic carrier frequency in unsolved cohort may imply presence of a second deep intronic causative variants. Analysing WES data of individuals sharing an additional feature can identify novel genes or genetic modifiers.

Disclosure: The MYO-SEQ project was funded by Sanofi Genzyme, Ultragenyx, LGMD2I Research Fund, Samantha J Brazzo Foundation, LGMD2D Foundation and Kurt+Peter Foundation, Muscular Dystrophy UK, and Coalition to Cure Calpain 3. Analysis was provided by the Broad Institute of MIT and Harvard Center for Mendelian Genomics (Broad CMG) and was funded by the National Human Genome Research Institute, the National Eye Institute, and the National Heart, Lung and Blood Institute grant UM1 HG008900 and in part by National Human Genome Research Institute grant R01 HG009141.

O3023

Compound heterozygous mutations in ATP10B increase Parkinson's disease risk by compromising lysosomal glucosylceramide export

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Background and aims: Parkinson's disease (PD) causal genes and risk factors provided valuable insights into underlying disease mechanisms and delivered new therapeutic targets.

Methods: We performed whole exome sequencing in 52 unrelated early-onset PD (EOPD) patients (age at onset (AAO) ≤ 50 years) to identify novel genes for PD; targeted resequencing in 617 PD patients (mean AAO 60.0 ± 11.5 years), 226 dementia with Lewy bodies (DLB) patients (mean AAO 70.8 ± 9.8 years) and 597 control individuals (mean age at inclusion (AAI) 70.4 ± 8.0 years); qPCR on mRNA isolated from human brain; and functional assays in in vitro and cellular models.

Results: In 3 EOPD patients with unaffected parents, we identified trans compound heterozygous mutations in ATP10B, compatible with recessive inheritance. Targeted resequencing of ATP10B revealed 3 additional sporadic PD and 1 DLB patient carriers of compound heterozygous mutations. ATP10B mRNA is enriched in the substantia nigra and medulla oblongata, and significantly decreased in patients versus control individuals in these brain regions. We established that ATP10B encodes a late endo-/lysosomal lipid flippase responsible for the export of glucosylceramide and phosphatidylcholine. Mutant ATP10B is catalytically inactive and loss of ATP10B in mouse cortical neurons leads to lysosomal dysfunction and cell death.

Conclusion: We identified recessive loss-of-function mutations in ATP10B increasing risk for PD. Both ATP10B and the PD/DLB risk factor GBA play essential roles in the fate of lysosomal glucosylceramide, and dysfunction of both results in intra-lysosomal accumulation of glucosylceramide.

Disclosure: Nothing to disclose

Neuroimmunology

O3024

Comparison of clinical characterization, risk of relapses and antibody dynamics between children and adults with MOGAD

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Background and aims: Predict the clinical course of myelin oligodendrocyte glycoprotein (MOG)-antibody (Ab)-associated disease (MOGAD) is essential to guide treatment recommendations. We aimed to 1) compare clinical features and disease course, and 2) to evaluate the association of MOG-Ab dynamics and relapses, between children and adults with MOGAD.

Methods: Retrospective study evaluating clinical features of 98 children and 266 adults with MOGAD, between January 2014 and September 2019. To analyse relapses over the whole disease course, Cox regression analysis for recurrent time-to-event data was performed, introducing treatment as time-dependent covariate. To evaluate dynamics, MOG-Ab-delta mean fluorescence intensity ratio signal (MOG-Ab- Δ MFIRatio) was measured in patients with a minimum time elapsed between two samples of 4 months.

Results: Median age at onset of symptoms was 10.9 (interquartile range 5.4-14.3) years in children and 36.2 (27.7-47.6) in adults. Isolated optic neuritis was the most frequent clinical presentation both in children (43.9%) and adults (56.8%). Compared to adults, ADEM-like was more frequent in children (36.7% vs. 5.6%), $p < 0.001$. In multivariate analysis, adults were at higher risk of relapse than children (HR 1.35 CI95%, 1.08-1.67). Among the 124 participants evaluated for MOG-Ab dynamics, 36.3% became seronegative, 60.5% decrease and 3.2% increase the Δ MFIRatio. Relapses occurred in 45/79 patients who

remained persistently seropositive compared to 17/45 who became negative, $p = 0.040$. MOG-Ab- Δ MFIRatio dynamics was similar between age-groups and clinical presentation.

Conclusion: Adults have a higher risk of relapse than children. Although persistent MOG-Ab-positivity is associated with relapses at population level, MOG-Ab dynamics are not useful to predict disease course at individual level.

Disclosure: Nothing to disclose

O3025

Immunological mechanisms for the efficacy of Rituximab in aquaporin-4 autoantibody mediated Neuromyelitis Optica spectrum disorders

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Background and aims: Neuromyelitis Optica Spectrum Disorders (NMOSD) are caused by autoantibodies targeting the astrocyte-expressed water-channel aquaporin-4 (AQP4). Rituximab (RTX), a monoclonal antibody against CD20 expressed on B-cells, is clinically effective despite not reducing overall AQP4-antibody levels. This clinical-serological discrepancy is often attributed to the incomplete depletion of CD20+ B-cells in lymph-nodes. We aimed to investigate the efficacy of RTX on lymph-node resident B-cells with particular reference to AQP4-specific B-cells.

Methods: Cervical lymph-nodes were harvested using ultrasound-guided fine-needle aspirations from NMOSD patients who were RTX-untreated (n=5) or RTX-treated (n=9, including 4 after only 1 RTX infusion). Matched peripheral blood mononuclear cells (PBMCs) were processed in parallel. From 3 patients with detectable lymph-node resident B-cells, CD19+CD3-cells were single-sorted and cultured for 26 days under proliferative conditions with supernatants tested by live cell-based assays for AQP4-antibody reactivity.

Results: We confirmed a significant reduction in the annual relapse rate (ARR) after RTX (p<0.001). Without RTX-treatment, CD19+cells were observed at frequencies of 10% in lymph-nodes, and 5% in PBMCs. Lymph-node aspirates and PBMCs showed AQP4-specific B-cells at frequencies of 0.09% and 0.07%, respectively. CD19+ B-cells in circulation and lymph-node resident B-cells were fully depleted after >1 dose of RTX (p=0.0004).

Conclusion: RTX depletes lymph-node resident B-cells as efficiently as circulating B-cells, suggesting that lymph-nodes do not constitute a RTX-resistant environment in humans. As lymph-nodes contain AQP4-specific B-cells, this depletion may be a mechanism by which RTX shows clinical efficacy without reducing AQP4-antibody levels.

Disclosure: Nothing to disclose

O3026

Cell-based assays for the detection of myelin oligodendrocyte glycoprotein antibodies: a single centre comparative study

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Background and aims: Antibodies against myelin-oligodendrocyte glycoprotein (MOG-Abs) characterize the so-called MOG-Ab-associated disease (MOGAD), in differential diagnosis of multiple sclerosis (MS). Standardization of the cell-based assays (CBAs) for MOG-Ab detection is under progress. Such assays include: a) live-CBA for total IgG with anti-heavy-and-light chain secondary-Ab (LCBA-IgGH+L); b) live-CBA for total IgG with anti-Fc secondary-Ab (LCBA-IgGFc); c) live-CBA for IgG1 (LCBA-IgG1); d) commercial fixed-CBA with anti-Fc secondary-Ab (FCBA-IgGFc). We aimed to define the best strategy for MOG-Ab detection.

Methods: 1557 consecutive sera from patients with demyelinating CNS syndromes were tested by LCBA-IgGH+L. Positive samples (265) were titred and screened by LCBA-IgG1. Seventy-one/265 were also tested with LCBA-IgGFc and FCBA-IgGFc. Patients were classified as “possible MOGAD”, “MS”, or “other neurological disorder” based clinical information, independently of MOG-Ab results.

Results: 204/1557 patients were included. 57/204 samples were MOG-Ab-positive. Sensitivity was 89.1% (confidence interval, CI:77.8-95.9) and specificity 93.3% (CI:88.0-96.7) for LCBA-IgGH+L, and 74.6% (CI:61.0-85.3) and 100% (CI:97.6-100) for LCBA-IgG1. 18/57 samples showed discrepant results, all negative on LCBA-IgG1: 10/18 were low-titre positive for total IgG in non-MOGAD patients, whereas 3/18 medium/high-titre positive, harboring IgG2 subclass, and belonging to the “possible MOGAD” group. In the subgroup analysis, sensitivity was 92.3% (CI:79.1-98.4) and specificity 96.9% (CI:83.8-99.9) for LCBA-IgGFc, and 87.2% (CI:72.6-95.7) and 97.0% (CI:83.8-99.9) for FCBA-IgGFc.

Conclusion: LCBA-IgG1 performed best with regard to specificity. However, MOGAD patients might harbor non-IgG1 high titre MOG-Abs, whose significance warrants further investigations. LCBA-IgGFc yielded the highest accuracy. FCBA-Fc has good specificity, but is at risk of false negative results.

Disclosure: Nothing to disclose

O3027

AMPA autoimmunity: neurological, oncological and serological accompaniments

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Background and aims: Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) autoimmunity is a rare, often paraneoplastic, disorder typically manifesting with encephalitis.

Methods: We retrospectively identified AMPAR-IgG-positive patients (serum and/or cerebrospinal fluid) from the Mayo Clinic Neuroimmunology Laboratory (2004-2019). Clinical information was extracted from records (12) or provided by referring physicians (49).

Results: 61/101 patients (median age 53 years [range 15-81]; 64 female) had available information. Encephalopathy (75%) and seizures (30%) were the most common manifestations. Twelve patients (20%) had - myasthenia gravis and thymoma with AChR (muscle-acetylcholine-receptor) antibodies ; five of them lacked encephalopathy and/or seizures. Brain imaging (9 available) was normal (3) or had T2-hyperintensities (temporal [3], extratemporal [2], both [1]). Neoplasia was detected in 39/61 (64%) patients (46% after symptom onset). The most frequent tumors were thymoma (23, 91% co-existing neural antibodies), small-cell lung carcinoma (3), breast carcinoma (3) and ovarian teratoma (3, 2 co-existing NMDAR [N-methyl-D-aspartate receptor] antibodies). Coexisting neural autoantibodies were detected in 42/61 patients (69%). The most common specificities were muscle AChR, 24; CRMP5 (Collapsin-response-mediator protein-5), 10; voltage-gated calcium channels, 9; striational (titer>7680) 6; NMDAR, 6; and GABABR (γ -aminobutyric acid receptor-B), 5. Other antibody-specificities included: LGI1 (leucine-rich, glioma-inactivated-1 protein), Caspr2 (contactin-associated protein-2), GAD65 (glutamic acid decarboxylase 65-kilodalton-isoform), ANNA1 (antineuronal-nuclear antibody-1), PCA (Purkinje-cell cytoplasmic antibody) 1 and 2.

Conclusion: Encephalopathy is the main manifestation of AMPAR autoimmunity, but some paraneoplastic cases lack CNS manifestations. Thymoma was the most common tumor. Accompanying neural autoantibodies are more frequent than previously reported and the autoantibody profile is a biomarker of the underlying neoplasia.

Disclosure: Nothing to disclose

O3028

Treatment and outcomes in patients with neurosarcoidosis

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Introduction: Neurosarcoidosis is associated with a high degree of morbidity and mortality and its treatments are varied and complex. There is a paucity of information in current literature on patterns of treatment and clinical outcomes in this condition and this is an area of significant unmet need. This study characterises treatment patterns and clinical outcomes in a large cohort of neurosarcoidosis patients.

Methods: We enrolled 85 patients with a diagnosis of neurosarcoidosis based on stringent diagnostic criteria. Prescription patterns were grouped according to first, second and third line regimes. Clinical outcomes before and after treatment were compared using statistical tests.

Results: The most common presentations were cranial neuropathy, pyramidal involvement and headache and the most common treatments were corticosteroids and azathioprine (26.25%), corticosteroids and methotrexate (17.5%), and corticosteroids alone (11.25%). Just over 85% of patients on corticosteroids went on to or started with second or third line treatment. Patients on corticosteroid monotherapy had the worst outcomes and those on a combination of corticosteroids, azathioprine and infliximab showed superior clinical improvements ($p=0.008$).

Conclusions: Patients with cranial mononeuropathy (41.25%) were more likely to be treated with corticosteroids alone than patients with brain parenchymal involvement, hydrocephalus and spinal cord presentations which were more likely to be treated with second and third line treatments. When corticosteroids were given in isolation, patients experienced less favourable outcomes than in all other treatment groups. Patients treated with combination treatments had the best overall outcomes in this study.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology; ageing and dementia 2

O3029

Characterization of mixed primary progressive aphasia: language, functional neuroimaging and pathological features

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Background and aims: Current classification identifies three variants of Primary Progressive Aphasia (PPA): Progressive Non-Fluent Aphasia (nfvPPA), Semantic Dementia (svAPP) and Logopenic Aphasia (lvPPA). 10–41% of patients fulfill diagnostic criteria for more than 1 of the variants (mixed-PPA). We aimed to detail language profiles, neuroimaging characteristics and Alzheimer’s disease biomarkers prevalence of a cohort mixed-PPA (mPPA) compared with defined PPA variants.

Methods: We considered 10 nfvPPA, 16 svPPA, 21 lvPPA and 9 mPPA. mPPA subjects were further classified as 4 nf/lvPPA (showing overlapping linguistic features for nfvPPA and lvPPA) and 5 s/lvPPA (showing overlapping linguistic features for svPPA and lvPPA). All patients underwent language evaluation, 18F-FDG-PET brain scan, and Amyloid-PET (Amy-PET) scan or CSF biomarkers measurement. Patients were rated Aβ+ if at least 1 of Amy-PET, CSF Aβ1-42 or Aβ1-42/40 ratio revealed presence of Aβ positivity.

Results: 100% of nf/lvPPA and 40% of s/lvPPA were Aβ+. None of nf/lvPPA patients showed Speech Apraxia but 100% showed Naming impairment and Grammatical Errors. 100% of s/lvPPA patients were impaired in Naming, 80% in Phrases Repetition and 60% in Single-word Comprehension and in Phrases Comprehension (Tab1, Fig.1). SPM group analysis comparing nf/lvPPA to normal FDG-PET, revealed hypometabolism in left parietotemporal junction and superior temporal gyrus. S/lvPPA had significant hypometabolism in left lateral temporal lobe, temporal pole, medial frontal gyrus, orbitofrontal cortex and parahippocampal gyrus compared to normal subjects (Fig.2)

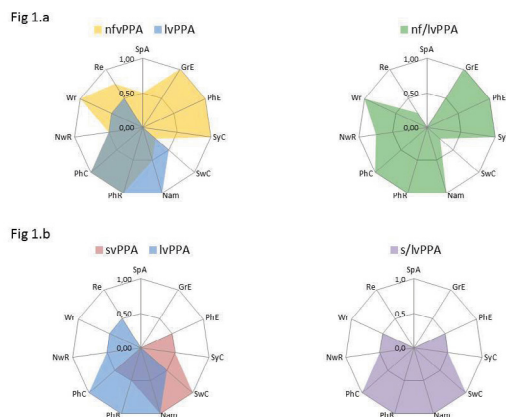


Fig.1. Language profile in each PPA group. SpA=Speech Apraxia; GeE=Grammatical Errors; PhE=Phonologic Errors/Neologism; SyC= Syntactic complexity; SwC=Single-word Comprehension; Nam= Naming; PhR=Phrases Repetition; PhC=Phrases Comprehension; NwR=Non-word Repetition; Wr=Writing; Re=Reading.

	nfvPPA	svPPA	lvPPA	nf/lvPPA	s/lvPPA
Speech Apraxia (SpA)	30%	0%	0%	0%	0%
Grammatical Errors (GeE)	60%	7%	9%	100%	20%
Phonologic Errors/Neologism (PhE)	70%	27%	22%	75%	40%
Syntactic Complexity (SyC)	80%	13%	30%	100%	40%
Single-word Comprehension (SwC)	10%	94%	23%	25%	60%
Naming (Nam)	40%	87%	91%	75%	100%
Phrases Repetition (PhR)	60%	33%	83%	100%	80%
Phrases Comprehension (PhC)	60%	33%	65%	75%	60%
Non-word Repetition (NwR)	30%	14%	10%	50%	40%
Writing (Wr)	60%	47%	48%	75%	40%
Reading (Read)	50%	27%	39%	25%	40%

Tab.1. Prevalence of impaired language domain impairment in each PPA group.

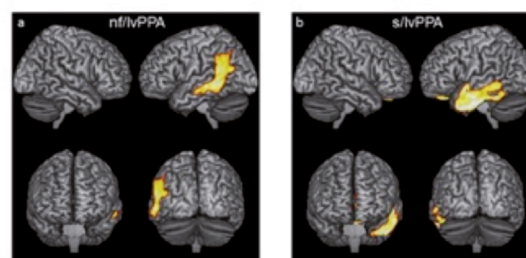


Fig. 2. SPM group analysis comparing nf/lvPPA and s/lvPPA to normal brain FDG-PET.

Conclusion: Even if nf/lvPPA showed grammatical impairment, hypometabolic pattern and pathological biomarkers were consistent with lvPPA. S/lvPPA had lower Aβ prevalence compared to lvPPA and showed typical svPPA hypometabolic pattern.

Disclosure: Nothing to disclose

O3030

Cognitive, neuropsychiatric and quality-of-life sequelae in LGI1-antibody disease demonstrates fatigue as the key determinant of wellbeing

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Background and aims: Despite increasing awareness and early treatment of LGI1-antibody encephalitis, long-term outcomes remain poorly reported. Previous smaller studies have identified multiple deficits in cognitive recovery but few explore psychiatric aspects or quality-of-life (QoL). Here, we delineate long-term follow up of multiple cognitive and neuropsychiatric domains, plus QoL, in a substantial patient cohort.

Methods: 60 patients were recruited at a median of 3.4 years (range 0.3-14.9) post-disease onset. All underwent a detailed interview using validated questionnaires covering several domains our clinical observations had detected to be impaired in this cohort. Clinical, paraclinical and genetic parameters were also collected. Statistical analysis comprised binomial tests, simple and multiple regressions, and a latent variable model, with the LGI1-antibody group's results compared to age-appropriate scores in the literature.

Results: Abnormal scores were observed in 5-52% (median 39%) of patients across disability, cognition, neuropsychiatry, QoL, carer-rated and fatigue measures (Figure). Patients performed significantly worse than controls in episodic and verbal memory, fluency and visuospatial abilities. Significant QoL worsening post-illness was confirmed by 2 separate instruments, which were closely correlated and could be represented by a latent variable model. Multiple regression analysis identified fatigue as an independent predictor of QoL. Fatigue correlated better with QoL than the modified Rankin Scale.

Conclusion: Patients demonstrate widespread difficulties many years after an acute LGI1-antibody episode. Fatigue, independent of depression scores, is the most accurate predictor of long-term QoL. The mechanism by which this occurs and potential treatments need to be further explored in this patient group.

Disclosure: SRI is a co-applicant and receives royalties on patent application WO/2010/046716 (U.K. patent no., PCT/GB2009/051441) entitled 'Neurological Autoimmune Disorders'. The patent has been licensed commercially for the development of assays for LGI1 and other VGKC complex antibodies. SRI and SB are co-applicants on a patent application entitled 'Diagnostic Strategy to improve specificity of CASPR2 antibody detection' (TBA / BB Ref. JA94536P.GBA).

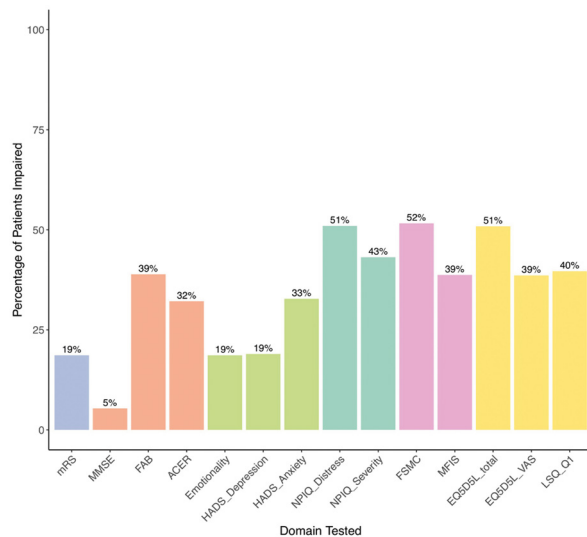


Figure: long-term deficits across multiple domains in LGI1-antibody patients

O3031

Effect of cognitive reserve on structural MR imaging measures in adult healthy subjects

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Background and aims: Early and recurring involvement of cognitive abilities and the exposure to leisure activities during early-life experiences is a requirement to reach a high level of cognitive reserve (CR). However, the impact of this construct on brain measures remains unclear in young-adult population. We investigated the associations between CR and structural MRI measures in young-adult healthy subjects (HS).

Methods: Dual-echo, 3D T1-weighted and diffusion tensor MRI sequences were acquired from 77 HS (40 men; mean age=36 years; range=22-65). A global Cognitive Reserve Index (CRI) and its subdomains (cognitive/social/physical) were assessed including education, leisure activities and IQ. Higher scores reflect higher CR. Regional gray matter (GM) volume was estimated using voxel-based-morphometry (VBM) and white matter (WM) fractional anisotropy (FA) was investigated with tract-based-spatial-statistical (TBSS) analysis. Linear regression analyses were performed.

Results: Higher global-CRI and higher scores in its subdomains were positively associated with higher GM volume of right (R) supplementary motor area. Both higher global and cognitive-CRI were correlated with higher GM volume of left (L) orbital middle frontal gyrus, whereas higher global and physical-CRI were correlated with higher GM volume of L cerebellum. Higher cognitive-CRI was correlated with higher GM volume of L angular gyrus, while higher physical-CRI was correlated with higher GM volume of L medial frontal gyrus and R middle cingulum. TBSS analysis showed no correlations between CRI and WM FA.

Conclusion: These findings suggest that in young adults, higher CRI modulates GM volumes of brain regions involved in motor network, whereas it is likely not to influence WM architecture.

Disclosure: Nothing to disclose

O3032

Defining cognitive phenotypes of multiple sclerosis patients

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Background and aims: Cognitive impairment is one of the most disabling symptoms of multiple sclerosis (MS), affecting about 50% of patients. We aimed to define cognitive phenotypes in a large cohort of MS patients by using a data-driven approach, in order to set the stage for personalized rehabilitative strategies.

Methods: A cohort of 1039 consecutive [925 relapsing-remitting (RR), 40 primary progressive (PP), 74 secondary progressive (SP)] MS patients from 6 Italian MS centers underwent cognitive evaluation with RAO's Brief Repeatable Battery (BRB) and the Stroop Test. Latent profile analysis was used on cognitive domains z-scores (verbal and visuospatial memory, attention, information processing speed, executive functions, language) in order to individuate cognitive profiles.

Results: 5 cognitive phenotypes were identified, characterized by: "preserved cognition" (28%); "mild executive/memory" (13%) impairment with other domains preserved; "mild multi-domain" (36%) impairment with executive function preservation; "severe executive/attention" (19%) impairment with mild impairment of other domains; "severe executive/information-processing" (3%) impairment with preserved memory and mildly impaired attention. "Preserved cognition" patients had shorter disease duration and lower Expanded Disability Status Scale (EDSS) score compared to other groups, but also included PPMS and SPMS patients with high EDSS. Severely-impaired groups had longer disease duration and higher proportion of progressive patients compared to mildly-impaired groups, but were also represented in early MS stages. Interestingly, 47% of PPMS patients had a "mild multi-domain" phenotype.

Conclusion: 5 cognitive profiles of MS patients were identified, pointing at different underlying pathophysiological mechanisms. Future studies will be needed to define personalized rehabilitative strategies for MS patients according to their cognitive phenotype.

Disclosure: Nothing to disclose

O3033

Alzheimer's disease and cerebral amyloid angiopathy were associated with ABCA7 PTC mutation carriers in a large Belgian AD cohort

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Background and aims: We aimed to delineate the clinicopathological Alzheimer's disease (AD) phenotype of carriers with a premature termination codon (PTC) in the ATP-Binding Cassette Subfamily A Member 7 (ABCA7) gene. ABCA7 was initially identified as a risk gene in genome wide association studies of large AD patient cohorts. In an extended Belgian AD patient cohort (n=1580), we identified 15 different ABCA7 PTC mutations in 69 carriers with onset ages varying from early- to late-onset AD.

Methods: Medical records of the ABCA7 mutation carriers were reviewed to obtain clinical and neuropathological data.

Results: Brain autopsy was performed in 10 carriers, revealing AD neuropathology and cerebral amyloid angiopathy (CAA) in all carriers. High levels of CAA were present in both the meningeal and capillary blood vessels, and moderate to high levels of CAA in the parenchymal blood vessels. CAA was not limited to the occipital brain region, but extended to the other neocortices and even to the medial temporal region (n=5). There was no correlation between CAA and levels of AD pathology or APOE genotype. Additionally, 3 carriers showed imaging features compatible with CAA, and 3 patients suffered 1 or more lobar hemorrhages. Chronic microvascular lesions were noticed in 43 patients (78,2%, 43/55).

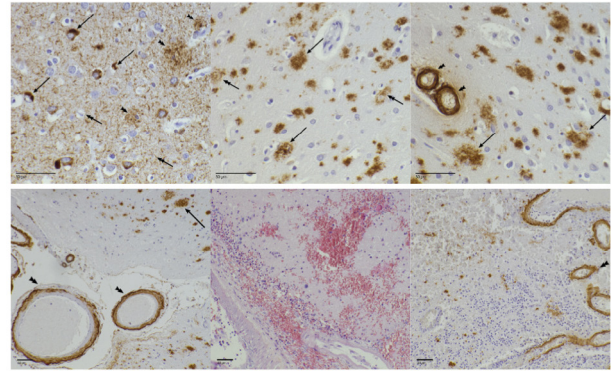


Figure 1 – Neuropathology of ABCA7 PTC mutation carrier DR1317
A. Hippocampus. AT8 stain. Moderate amount of NFTs (arrow) and DN (double arrow head), but many NT (double arrow). **B.** Hippocampus. 4G8 stain showing many SP (classic (arrow) and diffuse (double arrow)). **C.** Frontal cortex. 4G8 stain. There are many SP (arrow) and cerebral amyloid angiopathy (CAA) (double arrow head) is also present. **D.** 4G8 stain. Parietal cortex with many SP (arrow) and severe CAA (double arrow head). **E.** Hematoxylin Eosin stain. Cortical hemorrhage. **F.** 4G8 stain. Cortical hemorrhage with abundant CAA (double arrow head).

Figure 1 – Neuropathology of ABCA7 PTC mutation carrier DR1317

ID	Gender	AAO (y)	AAD (y)	ABCA7 PTC Mutation	gDNA	Protein	APOE	Post-mortem diagnosis	Neuropathology	CAA	Other		
									ABC	Level	Meningeal	Parenchymal	Capillary
DR109	f	90	92	c.2228_2228del	p.E709L	34	Definite AD + CAA	AB3C2-3	Intermediate	2	1	+	Atherosclerosis
DR1211	f	50	55	c.2228_2228del	p.E709L	44	Definite AD + CAA	AB3C2	High	3	2	+	ICH
DR170	f	72	78	c.2228_2228del	p.E709L	33	Definite AD + CAA	AB3C2	High	3	1	+	TDP
DR9	f	83	74	c.2228_2228del	p.E709L	33	Definite AD + CAA	AB3C2	Intermediate	3	3	+	-
DR1229	m	86	88	c.3643G>A	p.W1254*	33	Definite AD + CAA	AB3C2	Intermediate	3	2	+	+
DR1241	f	48	55	c.4080G>A	p.W1288*	34	Definite AD + CAA	AB3C2	High	Moderate CAA	-	-	ICH
DR54	f	61	70	c.4080del	p.L5403fs	34	Definite AD + CAA	AB3C2	High	3	2	+	-
DR51	f	59	73	c.4816A>T>C	p.D	34	Definite AD	AB3C2	High	3	3	+	-
DR156	m	Preclinical	75	c.5370G>C	p.D	33	Definite AD + CAA	AB3C2-3	Intermediate	3	3	+	Cortical necrosis, meningeal hemorrhages, atherosclerosis
DR1317	f	64	68	c.4735G>A	p.D	34	Definite AD + CAA	AB3C2	High	2	2	+	ICH (2x), ICVA, ICVA

Table 1 – Neuropathology of ABCA7 PTC carriers in Belgian AD patients
 Scoring for meningeal and parenchymal CAA: 0 = no CAA, 1 = scant beta amyloid deposition, 2 = some circumferential beta amyloid, 3 = widespread circumferential beta amyloid. Scoring for capillary CAA: + = present (type 1), * = occasional, ** = TDP-43 coloring found 2 neuronal intranuclear inclusions and neuronal cytoplasmic inclusions in limited places (parahippocampal gyrus and near the superior temporal gyrus).
 Abbreviations: AAO= age at onset, AAD= age at death, y= years, AD = Alzheimer's disease, CAA= cerebral amyloid angiopathy, ICH = intracerebral hemorrhage, ICVA = ischemic cerebrovascular accident, ICVA = hemorrhagic cerebrovascular accident.

Table 1 – Neuropathology of ABCA7 PTC carriers in Belgian AD patients

Conclusion: Carriers of ABCA7 PTC mutations present with a classical AD phenotype, but with wide onset-age ranges, even for carriers of the same mutation. Additional to the AD hallmarks in pathology, extensive levels of CAA were present in all autopsied brains. These findings have important implications for future research and clinical practice.

Disclosure: Nothing to disclose

Cerebrovascular diseases 3

O3034

TENecteplase in Central Retinal Artery Occlusion (TEN-CRAOS): a prospective, randomized-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25mg/kg+placebo vs. ASA+placebo (2 arms with 1:1 block randomization)

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Background and aims: Non-arteritic central retinal artery occlusion (CRAO) is an acute neurovascular-ophthalmological emergency that without swift revascularization bears a high risk of permanent blindness. The consequences of a CRAO are severely disabling and yet there is no evidence-based treatment option. Whether revascularization with thrombolytic agents can improve the outcome in CRAO, as proved in ischemic stroke, remains unanswered. Even though a recent meta-analysis of observational data indicates that systemic thrombolysis might improve outcome, no randomized controlled trial of early systemic thrombolysis for CRAO has so far not been performed. The aim of this study is for the first time to assess the effect of intravenous tenecteplase versus placebo administered within 4.5 hours of CRAO onset.

Methods: The study is a prospective, randomized-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25mg/kg+placebo vs. ASA+placebo (2 arms with 1:1 block randomization).

The main endpoint is the proportion of patients with an improvement in visual acuity of at least 15 letters. In addition, we will assess differences in visual field parameters, patient reported outcome measures and adverse events between the groups.

Results: The study is based on a unique collaboration between stroke units and ophthalmologic departments in Norway and selected European centres.

Conclusion: The TEN-CRAO study could be the foundation

for an international change in treatment practice of a sight-threatening disease underrepresented in clinical research by establishing for the first time a novel evidence-based treatment option by means of prompt systemic thrombolysis for these patients.

Disclosure: The study has been funded by the South-Eastern Norway Regional Health Authority, Boehringer Ingelheim and Odd Fellow.

O3035

Association of oral hygiene with occurrence for cerebral aneurysm and subarachnoid hemorrhage: a nationwide population-based cohort study

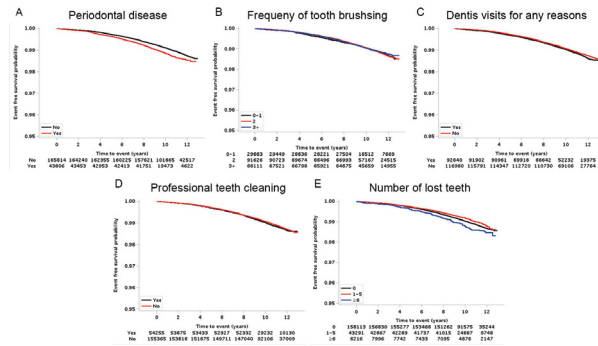
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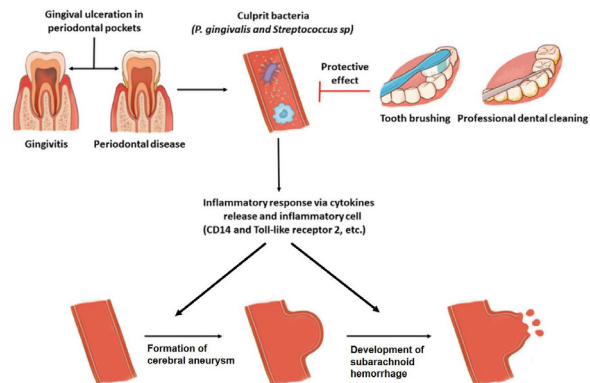
Background and aims: Presence of periodontal disease and poor oral hygiene can provoke systemic inflammatory response, a mediator for the development of cerebral aneurysm and subarachnoid hemorrhage (SAH). Our study hypothesized that presence of periodontal disease and oral hygiene would be associated with occurrence of cerebral aneurysm and SAH.

Methods: Total of 209,620 subjects without missing data including demographic data, medical history, and laboratory findings were analyzed from the Korean National Health Insurance System-Health Screening Cohort. Presence of periodontal disease, frequency of tooth brushing per day, dentist visits for any reason, professional teeth cleaning, and number of lost teeth were investigated as oral hygiene indicators. The occurrence of cerebral aneurysm and SAH were defined as I60 and I67.1, respectively from codes of International Statistical Classification of Diseases Related Health Problems-10.

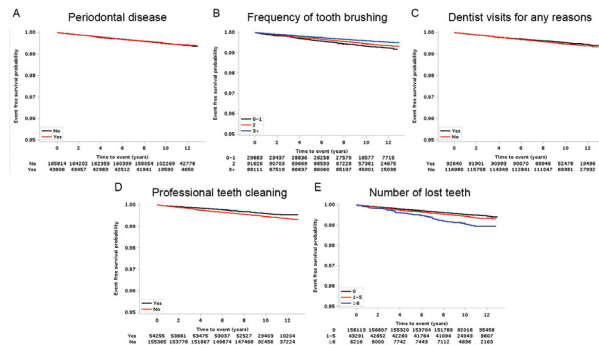
Results: The average age was 53.7±8.7 years, 59.4% were male. Periodontal disease was found in 20.9% of the subjects. During the median follow-up of 10.3 years, 2,160 (1.0%) cases of cerebral aneurysm and 1,097 (0.5%) cases of SAH occurred. Multivariable analysis after adjusting confounding factors showed that the presence of periodontal disease was significantly associated with an increased risk of cerebral aneurysm (hazard ratio [HR]: 1.23, 95% confidence interval [CI] (1.11–1.36), p<0.001). Better oral hygiene behavior was associated with lower occurrence risk of SAH (HR: 0.78, 95% CI: 0.66–0.93, p=0.006).



Conclusion: Poor oral hygiene represented by presence of periodontal disease may be associated with occurrence of cerebral aneurysm.



Disclosure: Nothing to disclose



O3036

Early extubation after stroke thrombectomy is associated with better functional outcome

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Background and aims: We aimed to investigate the clinical impact of the duration of artificial ventilation in stroke patients receiving mechanical thrombectomy (MT) under general anesthesia, which is currently unknown.

Methods: All consecutive ischemic stroke patients who had been treated at our center with MT for anterior circulation large vessel occlusion under general anesthesia were identified over an 8-year period. We analyzed ventilation time as a continuous variable and grouped patients into extubation within 6 hours (“early”), 6–24 hours (“delayed”) and >24 hours (“late”). Favorable outcome was defined as modified Rankin Scale scores of 0–2 at 3-months post-stroke. We also assessed pneumonia rate and reasons for prolonged ventilation.

Results: Among 447 MT patients (mean age 69.1±13.3 years, 50.1% female), median ventilation time was 3 hours. 188 (42.6%) patients had a favorable 3-months outcome, which correlated with shorter ventilation time ($p<0.001$). In patients extubated within 24 hours, early compared to delayed extubation was associated with improved outcome (odds ratio 2.40, 95% CI 1.53–3.76, $p<0.001$). This was confirmed in multivariable analysis ($p=0.007$).

Longer ventilation time was associated with a higher rate of pneumonia during neurointensive care unit/stroke unit stay (early/delayed/late extubation: 9.6%/20.6%/27.7%, $p<0.01$). While stroke-associated complications represented the most common reasons for late extubation, delayed extubation was associated with admission outside of core working hours ($p<0.001$).

Conclusion: Prolonged ventilation time after stroke thrombectomy independently predicts unfavorable outcome at 3 months and is associated with increased pneumonia rates. Therefore, extubation should be performed as early as safely possible.

Disclosure: Nothing to disclose

O3037

Mobile stroke unit for triage of stroke patients: a randomized trial

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Background and aims: Transferring patients with large-vessel occlusion (LVO) or intracranial haemorrhage (ICH) to hospitals not providing interventional treatment options is an unresolved medical problem. Here, we aimed to investigate how management in a Mobile Stroke Unit (MSU) compares with optimized conventional management (OPM) in triaging stroke patients to hospitals providing (comprehensive stroke centre, CSC) or not providing (primary stroke centre, PSC) neurointerventional treatment.

Methods: In this prospective randomized multicentre trial (ClinicalTrials.gov identifier: NCT02465346) with 3-month follow-up, patients were randomly assigned to one of the stroke management pathways. The primary endpoint was the proportion of patients accurately triaged to either CSCs (LVO and ICH) or PSCs (other types of strokes).

Results: A predefined interim analysis was performed after 116 of 232 planned patients had entered the study. The primary endpoint, an accurate triage decision, was reached for 63 (100%) MSU patients and for 37 of 53 (69.8%) patients in OPM (differences, 30.2%; 95% CI, 17.8–42.5; $p<0.0001$). Whereas 7 of 17 (41.2%) optimized conventional group patients with LVO or ICH required secondary transfers from a PSC to a CSC, none of the 11 (0%) MSU patients required such transfers (difference, 41.2%; 95% CI, 17.8–64.6; $p=0.0182$). Stroke management metrics were better in the MSU group, although day 90 outcomes were not different.

Conclusion: Whereas OPM allows correct triage decisions for approximately 70% of patients, MSU-based stroke management enables accurate triage decisions for 100%.

Disclosure: Nothing to disclose

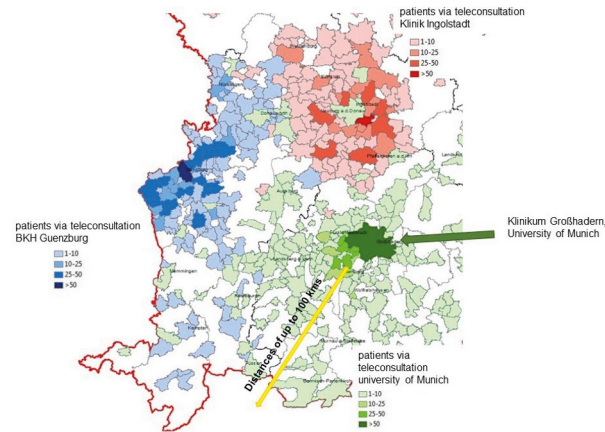
O3038

Inter-hospital transfer for mechanical thrombectomy within the supraregional Neurovascular Network of Southwest Bavaria

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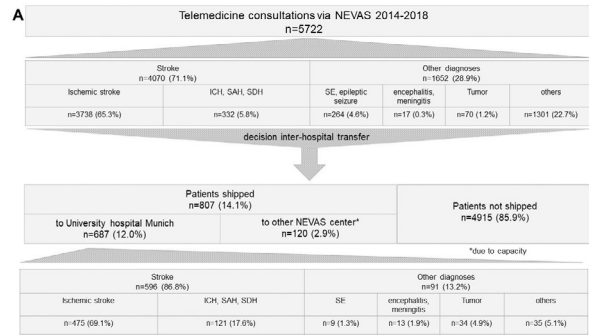
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Background and aims: Telemedicine stroke networks are mandatory to provide inter-hospital transfer for mechanical thrombectomy (MT). We analyzed MT-patients within the supraregional stroke network “Neurovascular Network of Southwest Bavaria” (NEVAS) irrespective of finally MT-treatment.

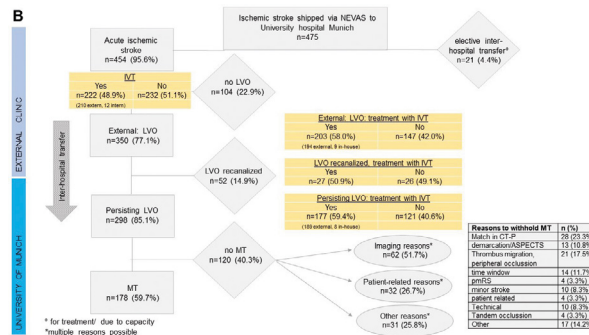


Organization of supraregional stroke network NEVAS

Methods: Consecutive patients from 01/2014-12/2018 who were shipped to our comprehensive stroke center were analyzed. Good outcome at 3 months was defined as modified Rankin Scale of 0-2.



2A: Flow chart of all telemedicine consultations via NEVAS



2B: Flow chart of acute ischemic stroke patients

Results: Out of 5722 telemedicine consultations, n=350 patients presented with large vessel occlusion (LVO). 52 patients (14.9%) spontaneously recanalized before MT (see figure 2). Out of the remaining n=298 patients, n=178 underwent MT and n=120 did not. MT-treated patients had more severe strokes according to the NIHSS (16 vs. 13, p<0.001), higher median ASPECTS (8 vs. 8, p=0.041), were more often treated with intravenous thrombolysis (64.5% vs. 51.7%, p=0.026) and arrived significantly earlier in the comprehensive stroke center (184.5 vs. 228.0, p<0.001). Good outcome (27.5% vs. 30.8%, p=0.35) and mortality (32.6% vs. 23.5%, p=0.79) were comparable in MT-treated vs. no-MT-treated patients at follow-up. In patients with middle cerebral artery occlusion in the M1 segment or carotid artery occlusion good outcome was twice as often in the MT-group (21.8% vs. 12.8%, p=0.184). Independent predictors for performing MT were higher NIHSS (OR 1.096), higher ASPECTS (OR 1.28), and earlier time window (OR 0.99).

Conclusion: Within a telemedicine network stroke care can successfully be organized as only a minority of patients has to be transferred. There are no clear clinical parameters to predict in advance whether MT will be performed or not.

Disclosure: Nothing to disclose

Tuesday, May 26 2020

Neurotraumatology; neurorehabilitation

O4001

IBIA – DoC-SIG multi-centre longitudinal study on clinical and neurophysiological prognostic markers in prolonged disorders of consciousness: a one-year follow-up

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Background and aims: Accurate prognosis in patients with Disorders of Consciousness (DoC) is challenging, but necessary for defining appropriate care pathways 1-3. The present multi-centre, prospective study performed by the Special Interest Group on DoC of the International Brain Injury Association is aimed at identifying predictors for one-year clinical outcome.

Methods: 12 specialized medical institutions enrolled patients in prolonged unresponsive wakefulness syndrome/vegetative state (UWS/Vs) 4 or in minimally conscious state (MCS) 5 with time post-injury (TPI) ≤ 3 months. Demographic, anamnestic, clinical and neurophysiological data were collected at study entry. Clinical follow-up was performed at 12 months post-injury and patients who improved (i.e. recovering from UWS/Vs to MCS, and from

UWS/Vs or MCS to full consciousness) were compared with those who did not (i.e. with unchanged diagnosis or died).

Results: A convenience sample of 147 patients was enrolled (44 women; mean age: 49.4 \pm 19.9 years; mean TPI: 59.6 \pm 25.2 days; UWS/Vs=71, MCS=76; traumatic=55, vascular=56, anoxic=36). At the 12-month evaluation, 71 patients (48%) had improved their diagnosis and 71 (48%) did not (4% dropped out). Logistic and LASSO regression analyses on 134 patients showed that lower age, shorter TPI and presence of EEG reactivity to eye opening and closing at study entry predicted improvement in diagnosis at 12 months post-onset (all $p < .05$).

Conclusion: Multimodal assessment could provide valuable information for prognostication in patients with prolonged DoC. This international project would encourage standardization of diagnostic and prognostic procedures in patients with DoC.

Disclosure: This project was funded by European Union's Horizon 2020 programme (Marie Skłodowska-Curie grant 778234-DoCMA project).

O4002

Pain assessment in non-communicative patients

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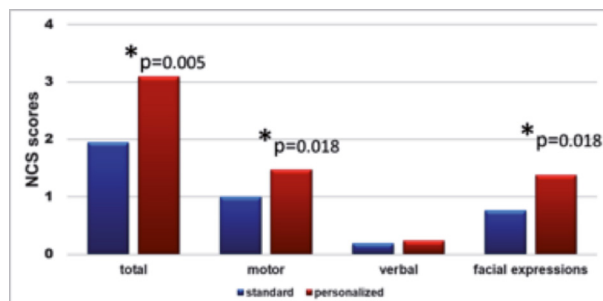
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Background and aims: Recent evidences have shown that covert cognition may be present in around 15% of the patients with DoC. The lack of overt behavioural responsiveness may be due to many clinical confounding factors, including severe spasticity and diffuse pain. Aim of the present study was to compare, in non-communicative patients with DoC, NCS-R scores obtained with the standard pressure on fingernail bed (standard stimulus, SS) versus other personalized painful stimuli (PS), shared with the rehabilitation staff, to verify possible correlation between NCS-R and Coma Recovery Scale-Revised (CRS-R).

Methods: From a population of 66 patients (35 M and 31 F) with a mean age of 42.74 years (range 14-69) diagnosed with DoC, according to the CRS-R enrolled in the study, we selected a subgroup of 22 patients [10 M and 12 F; mean age =40.72 years (range 14-69); etiology: 10 TBI; 3 anoxia; 7 vascular (hemorrhagic or ischemic); 1 encephalitis] were assessed with NCS-R with personalized versus standard painful stimulation.

Results: The personalized painful stimulation (NCS-R-P) reached higher scores as compared to the standard stimulus, both for the total score and for motor and facial expression subscores ($p < 0.05$). Significant correlation with CRS-R were found for both NCS-R-SS ($r = 0.613$, $p = 0.0031$) and NCS-R-PS ($r = 0.539$, $p = 0.0117$).



Bar diagram reporting NCS scores averaged across patients obtained applying both standard (S) and personalized (P) stimuli. We reported the results about the total score and the scores related to the NCS sub-scales. The symbol * highlight a statistically significant difference between S and P painful stimuli (Wilcoxon Matched Pairs Test, $p < 0.05$).

Conclusion: Standard painful stimulation may be affected by sensory deficits (hypoesthesia, anesthesia) of central and peripheral etiology and by the different pain sources. A personalized painful stimulation may be of some support to unveil covert cognition in non-communicative patients, alleviating their possible sufferance and improving their responsiveness and quality of life.

Disclosure: This project was funded by European Union's Horizon 2020 programme (Marie Skłodowska-Curie grant 778234-DoCMA project).

O4003

Coagulopathy and its effect on treatment and mortality in patients with traumatic intracranial haemorrhage

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Background and aims: The role of coagulopathy in patients with traumatic brain injury has remained inconclusively studied. Coagulopathy can be either spontaneous or induced by medication. Our aim was to characterize clinical features of patients presenting with traumatic intracranial haemorrhage and coagulopathy. In addition, we studied the prevalence of coagulopathy and how it affects the treatment and mortality in these patients.

Methods: An observational, retrospective single-centre cohort of 505 consecutive patients with traumatic intracranial haemorrhage treated in Helsinki University Hospital between 01 January and 31 December, 2010 (Figure 1). We compared clinical and radiological parameters in patients with and without coagulopathy – defined as drug- or disease-induced (antiplatelet or anticoagulant medication at a therapeutic dose, thrombocytopenia (platelet count $< 100 \text{ E9/L}$), international normalized ratio (INR) > 1.2 , or thromboplastin time (TT) $< 60\%$). Primary outcome was 30-day all-cause mortality.

Figure 1. Patient selection flowchart

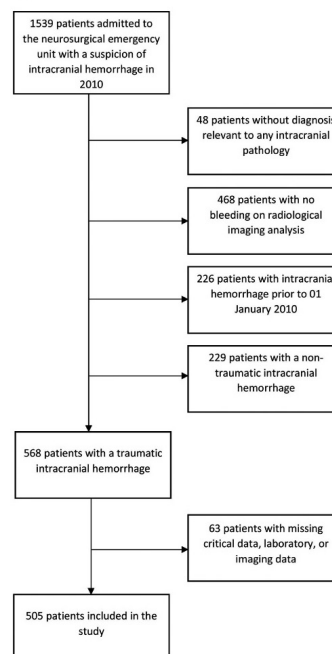


Figure 1

Results: Of our 505 patients, 331 (65.5%) were male and median age was 61 years (IQR 48-75). In total, 206 (40.8%) patients had coagulopathy. Compared to non-coagulopathy patients, coagulopathy patients had larger haemorrhage volumes (121.0ml vs. 82.5ml, $p < 0.001$) (Table 1). Patients with coagulopathy had higher 30-day mortality (18.9% vs.

9.7%, $p=0.002$). In multivariable analysis older age, lower admission GCS, higher haemorrhage volume, and conservative treatment were independently associated with mortality (Table 2).

Variable	Coagulopathy (N=206)	No coagulopathy (N=299)	p
Male gender	137 (66.5%)	194 (64.9%)	0.390
Age, mean (CI)	69.0 (66.8-71.3)	57.5 (55.0-60.0)	<0.001
Age group			<0.001
<50	27 (13.1%)	113 (37.8%)	
50-64	47 (22.8%)	100 (33.4%)	
65-79	82 (39.8%)	53 (17.7%)	
≥80	50 (24.3%)	33 (11.0%)	
Admission GCS, mean (CI)	11.8 (11.2-12.5)	11.3 (10.7-11.9)	0.497
Admission GCS			0.448
13-15	130 (63.1%)	180 (60.2%)	
9-12	26 (12.6%)	32 (10.7%)	
3-8	50 (24.3%)	87 (29.1%)	
Hypertension	90 (43.7%)	73 (24.4%)	<0.001
Atrial fibrillation	64 (31.1%)	6 (2.0%)	<0.001
Coronary heart disease	53 (25.7%)	10 (3.3%)	<0.001
Hematoma evacuation	124 (60.2%)	148 (49.5%)	0.011
Ventriculostomy	6 (2.9%)	8 (2.7%)	0.540
Hemorrhage volume (ml), mean (CI)	140.0 (125.4-154.4)	98.4 (86.4-110.4)	<0.001
Hemorrhage volume (ml)			<0.001
0-50	69 (33.5%)	151 (50.5%)	
51-100	23 (11.2%)	45 (15.1%)	
101-200	67 (32.5%)	60 (20.1%)	
>200	47 (22.8%)	43 (14.4%)	

p = p-value, CI = confidential interval, GCS = Glasgow Coma Scale,

ml = milliliter

Table 1

Variable	Alive	Dead	Multivariate OR (95% CI)	Multivariate p
Male gender	282 (64.5%)	49 (72.1%)	1.712 (0.846-3.467)	0.135
Age group				
<50	128 (29.3%)	12 (17.6%)	Reference	
50-64	128 (29.3%)	19 (27.9%)	1.759 (0.704-4.393)	0.227
65-79	114 (26.1%)	21 (30.9%)	3.213 (1.143-9.028)	0.027
≥80	67 (15.3%)	16 (23.5%)	5.102 (1.566-16.622)	0.007
Admission GCS				
13-15	294 (67.3%)	16 (23.5%)	Reference	
9-12	51 (11.7%)	7 (10.3%)	2.526 (0.873-7.314)	0.087
3-8	92 (21.1%)	45 (66.2%)	14.210 (6.668-30.284)	<0.001
Hypertension	142 (32.5%)	21 (30.9%)	0.798 (0.375-1.699)	0.558
Atrial fibrillation	55 (12.6%)	15 (22.1%)	1.408 (0.567-3.493)	0.461
Coronary heart disease	49 (11.2%)	14 (20.6%)	1.791 (0.711-4.516)	0.217
Coagulopathy	167 (38.2%)	39 (57.4%)	1.534 (0.734-3.206)	0.256
Hematoma evacuation	248 (56.8%)	24 (35.3%)	0.133 (0.059-0.297)	<0.001
Ventriculostomy	11 (2.5%)	3 (4.4%)	2.287 (0.514-10.169)	0.277
Hemorrhage volume (ml)				
0-50	201 (46.0%)	19 (27.9%)	Reference	
51-100	55 (12.6%)	13 (19.1%)	2.782 (1.057-7.323)	0.038
101-200	109 (24.9%)	18 (26.5%)	4.052 (1.526-10.762)	0.005
>200	72 (16.5%)	18 (26.5%)	5.094 (1.807-14.364)	0.002

OR = odds ratio, p = p-value, CI = confidential interval, GCS = Glasgow Coma Scale, ml = milliliter

Table 2

Conclusion: Coagulopathy was frequent in patients with traumatic intracranial haemorrhage and associated with larger haemorrhage volume, but was not associated with higher 30-day mortality. Surgical treatment by hematoma evacuation was associated with lower mortality, regardless of coagulopathy.

Disclosure: The research project has received funding from Maire Tapola Foundation's grant, and from Helsinki and Uusimaa Hospital District's competitive research funding.

O4004

Effect of sex and age on quality-of-life up to ten years after traumatic brain injury

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Background and aims: Traumatic brain injury (TBI) causes lifelong disability and is associated with an increased risk for Alzheimer's or Parkinsonism. Despite its prevalence among the elderly, the influence of age and sex on TBI etiology and health-related quality-of-life (HRQoL) after TBI has not been elucidated. Thus, we conducted a cross-sectional study to assess the effect of age and sex on HRQoL up to ten years after mild, moderate or severe TBI.

Methods: Sex differences (male/ female) were quantified for each TBI severity group (mild, moderate or severe) (%), TBI etiology (traffic accident, fall or others) (%), and the age at TBI (mean±SEM) in 102 male and 33 female TBI patients (18-85 years). The Quality of Life after Brain Injury (QOLIBRI) instrument was used to investigate age- and sex-related HRQoL in this cohort.

Results: TBI etiology differed between males and females in all age groups ($p=0.013$) and in males across ages ($p=0.03$). A shift from traffic accidents to falls was seen between younger (≤ 45 years) and middle-aged males (46-64 years) ($p=0.004$) and between younger and elderly males (≥ 65 years) ($p=0.007$) but was not seen in females. Regarding HRQoL, 69% of males but only 52% of females reported good outcomes with 17% more females than males at risk for one psychiatric disorder ($p=0.01$). This finding was particularly evident in middle-aged females.

Conclusion: Our results show sex- and age-related differences regarding etiology and HRQoL suggesting an increased female brain vulnerability during menopause and emphasizing the need for sex-specific clinical algorithms after TBI.

Disclosure: Nothing to disclose

O4005

Prevalence and prediction of post-concussive symptoms in children and adolescents with mild traumatic brain injury in the CENTER-TBI study

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Background and aims: Mild traumatic brain injury (mTBI) is a frequent injury among children and adolescents from which most fully recover within weeks. However, some patients suffer from persisting post-concussive symptoms. In this study, we aimed to analyze their prevalence, predictive factors, and effects on quality of life using the multi-center, prospectively collected CENTER-TBI database.

Methods: All patients in the CENTER-TBI core study between 5-21 years with available Rivermead Post-Concussion Questionnaire (RPQ) at 6-months were included. Post-concussive syndrome (PCS) was defined according to ICD-10 criteria as having at least 3 of 7 selected symptoms included in the RPQ. Regression analysis using the Lasso method was performed to select a multivariate model with the most important clinical variables predicting PCS. Quality of life was assessed using the Quality of Life after Brain Injury (QOLIBRI) score.

Results: 36% of the 196 included patients reported experiencing at least 1 moderate or severe post-concussive symptom. PCS was present in 13% of patients. Univariate- and multivariate regression analyses identified female gender as significant predictive factor. The final model containing a set of clinical and demographical factors showed reasonable predictive ability but could only explain a small part of the variability in outcome. Pediatric patients with PCS had significantly lower QOLIBRI total scores, indicating a lower quality of life.

Conclusion: Post-concussive symptoms and PCS were present in a considerable proportion of patients and significantly affected patients' quality of life. The developed prediction model displayed reasonable predictive ability, but additional parameters are likely needed for more accurate predictions.

Disclosure: Nothing to disclose

O4006

Therapeutic effects of azithromycin on spinal cord injury in rats: a role for inflammatory pathways

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Background and aims: Inflammatory responses, including macrophages/microglia imbalance, are associated with spinal cord injury (SCI) complications. Accumulating evidence also suggest an anti-inflammatory property for azithromycin (AZM). Thus, we evaluated the therapeutic effects of AZM and its potential anti-inflammatory property on a rat model of SCI.

Methods: Male Wistar rats were subjected to T9 vertebra laminectomy. They were divided into 3 groups: sham-operated group and 2 treatment (normal saline as a vehicle control versus AZM at 180mg/kg/day for 3 days post-surgery) SCI groups. Locomotor scaling and behavioral tests for neuropathic pain were evaluated and compared through a 28-days period. At the end of the study, tissue samples were taken to assess neuroinflammatory changes using the immunohistochemistry, flow cytometry, and ELISA techniques.

Results: Post-SCI AZM (180mg/kg/day for 3 days) treatment significantly improved locomotors ability ($p<0.01$) and decreased sensitivity to mechanical ($p<0.01$) and thermal allodynia ($p<0.001$). Moreover, there was a significant tumor necrosis factor (TNF)- α decline ($p<0.01$) and interleukin (IL)-10 elevation ($p<0.01$) in spinal cord tissue of AZM-treated compared to control groups 28 days post SCI. AZT significantly improved neuroinflammation as evidenced by reduction of expression of M1, elevation of M2 macrophages, and reduction of M1/M2 ratio in both dorsal root ganglion and spinal cord tissue after SCI compared to controls ($p<0.01$).

Conclusion: AZM treatment can be considered as a therapeutic agent for SCI, as it could reduce neuroinflammation as well as SCI sensory/locomotor complications.

Disclosure: The authors declare no conflicts of interest regarding the data presented. This study was funded and supported by a grant (Grant No. 971171, Title: "Evaluation of Azithromycin on Spinal Cord Injury Model in Male Rats") from National Institute for Medical Research Development (NIMAD) in Iran.

MS and related disorders 3

O4007

Development of a circulating microRNA biomarker panel for multiple sclerosis

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Background and aims: Multiple sclerosis (MS) diagnosis is frequently challenging involving clinical examination, imaging and electrophysiological measurements and invasive CSF (cerebrospinal fluid) analysis. Molecules such as antibodies or glycoproteins are used in clinical practice as MS biomarkers with the pitfall of a poor sensitivity and/or specificity. Circulating microRNAs (miRs) are appealing novel disease biomarkers due to the low cost, minimal invasiveness and speed of the analytic process. Several genome-wide studies in both animal models and patients have demonstrated a dysregulation on the miRs profile in MS. Our aim was to analyse the inflammation-associated miR-21, miR-22, miR-146a and miR-155 circulating levels in MS patients and assess its diagnostic performance.

Methods: MiRs serum levels were quantified in 88 patients with definitive MS diagnosis accordingly to McDonald's criteria (87F, 41.8±12.6 years; Mean disease duration: 12.7±9.5years; 75 Relapse Remitting, 9 Progressive MS) and 42 healthy controls. ROC curve, and respective AUC (Area Under the Curve) analysis was performed to assess diagnostic value.

Results: MS patients had lower miR-21 (2 fold, AUC= 0.61) and miR-22 (6 fold, AUC=0.77) and higher miR-146a (2 fold, AUC=0.51) and miR-155 (6 fold, AUC=0.68) circulating levels comparing to controls. The combination of the four studied microRNAs allowed a good diagnostic performance discriminating MS patients from controls, with an AUC of 0.94 (p<0.0001), 90% specificity and 84% sensitivity.

Conclusion: In this study, we report a panel of four circulating microRNAs with promising value as MS biomarker. Our results may contribute to an earlier MS diagnosis and ultimately lead in new directions in MS therapy.

Disclosure: Financial support: BIEM

O4008

Tailoring B-cells depleting therapy in MS according to memory B-cells monitoring: a pilot study

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Background and aims: Phase II and III clinical trials revealed the potent suppressive activity of CD20 directed antibodies in MS. In this study we wanted to evaluate efficacy on inflammatory parameter of rituximab (RTX) personalized reinfusion scheme, using a memory B-cell based reinfusion regimen

Methods: This is an prospective, uncontrolled, open-label, bicentric study including patients with MS treated with RTX in 2 Italian MS units. All patients were treated with rituximab induction, followed by maintenance infusion at the dosage of 375mg/m², according to memory B-cells repopulation (0.05% of PBMC for the first two years, 0.1% for the third year). MS activity was assessed as clinical or MRI activity.

Results: 102 patients were included in the analysis. Mean FU was 2.40 years (range 0.57-7.15 years). ARR was 0.67 in the year before RTX start and decreased to 0.01 in the 3 years after RTX initiation (global ARR). Proportion of patient with MS activity (i.e.: relapse or MRI activity) was 63.16% in the year before RTX start and decreased to 8.7% (0-6 months), 1.3% (6-12), 0% (12-24), and 0% (24-36). Annualized RTX infusion rate was 1.67, 0.76, and 0.78 for the first 3 years after RTX initiation, respectively. Patients were reinfused with a mean infusion interval of 367 days (range 181-839 days).

Conclusion: Results of this study show that memory B-cells based RTX reinfusion protocol is able to reduce mean number of RTX reinfusion with persistent reduction of disease activity.

Disclosure: Nothing to disclose

O4009

Regional outcomes of eculizumab treatment in patients with aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder: findings from the phase 3 PREVENT study

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Background and aims: The standard of care in treating aquaporin-4 immunoglobulin G-positive (AQP4-IgG+) neuromyelitis optica spectrum disorder (NMOSD) varies globally. Eculizumab was EMA-approved in August 2019 for this indication. The phase 3, randomized, double-blind PREVENT study (NCT01892345) assessed the efficacy/safety of eculizumab in patient populations of three pre-specified regions: Americas, Asia-Pacific and Europe. We evaluated use of immunosuppressive therapies (ISTs) and impact of eculizumab on rates of relapse-related hospitalization and acute treatment across geographical subpopulations.

Methods: Adult patients with AQP4-IgG+ NMOSD were randomized to eculizumab 900mg/week for 4 weeks, followed by 1200mg/2 weeks (maintenance dose) or placebo. Stable doses of concomitant ISTs were allowed, excluding rituximab and mitoxantrone. Post hoc analysis examined data from patients by region. Annualized rates were defined as total number of events divided by total patient-years in the study.

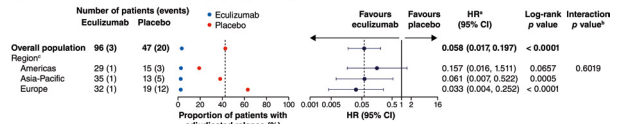
Results: At baseline patient characteristics were similar across all regions, except for IST use (Table 1). Compared with placebo, eculizumab significantly reduced relapse risk, and relapse-related hospitalization and acute relapse treatment rates across all regions (Figure 1, Table 2). In Europe, adjudicated relapses occurred in 1/32 and 12/19 of patients treated with eculizumab and placebo, respectively (p<0.0001); the annualized relapse-related hospitalization rates were 0.05 and 0.43, respectively (p=0.0002), and the annualized relapse-related acute intravenous methylprednisolone (IVMP) treatment rates were 0.11 and 0.47, respectively (p=0.0027).

Table 1. Baseline characteristics and use of ISTs according to pre-specified regional subgroups

Patient characteristic at baseline	Americas (N = 44)		Asia-Pacific (N = 48)		Europe (N = 51)		Overall (N = 143)	
	Eculizumab (n = 29)	Placebo (n = 15)	Eculizumab (n = 35)	Placebo (n = 13)	Eculizumab (n = 32)	Placebo (n = 19)	Eculizumab (n = 96)	Placebo (n = 47)
Female, n (%)	23 (79.3)	14 (93.3)	33 (94.3)	11 (84.6)	32 (100.0)	17 (89.5)	88 (91.7)	42 (89.4)
Age at NMOSD initial clinical presentation, years, mean (SD)	35.8 (17.3)	40.2 (15.6)	35.8 (13.0)	40.8 (15.0)	35.7 (12.2)	35.5 (14.8)	35.8 (14.0)	38.5 (15.0)
Historical annualized relapse rate, mean (SD)*	2.30 (1.04)	1.71 (0.58)	1.84 (0.72)	2.35 (1.48)	1.73 (0.86)	2.17 (0.92)	1.94 (0.90)	2.07 (1.04)
Prior use of rituximab, n (%)†	17 (58.6)	10 (66.7)	3 (8.6)	2 (15.4)	6 (18.8)	8 (42.1)	26 (27.1)	20 (42.6)
No IST	5 (17.2)	5 (33.3)	3 (8.6)	1 (7.7)	13 (40.6)	7 (36.8)	21 (21.9)	13 (27.7)
Corticosteroids only	4 (13.8)	3 (20.0)	8 (22.9)	5 (38.5)	4 (12.5)	3 (15.8)	16 (16.7)	11 (23.4)
Azathioprine ± corticosteroids	6 (20.7)	2 (13.3)	20 (57.1)	4 (30.8)	11 (34.4)	7 (36.8)	37 (38.5)	13 (27.7)
Mycophenolate mofetil ± corticosteroids	13 (44.8)	5 (33.3)	1 (2.9)	2 (15.4)	3 (9.4)	1 (5.3)	17 (17.7)	8 (17.0)
Other ISTs ± corticosteroids	1 (3.4)	0 (0.0)	3 (8.6)	1 (7.7)	1 (3.1)	1 (5.3)	5 (5.2)	2 (4.3)

The Americas: Argentina and the USA; the Asia-Pacific region: Australia, Hong Kong, Japan, Korea, Malaysia, Taiwan and Thailand; Europe: Croatia, Czech Republic, Denmark, Germany, Italy, Russia, Spain, Turkey and the UK.
 *In the 24 months prior to screening.
 †Use of rituximab was not permitted within 3 months of PREVENT start, nor during the trial.
 CI, confidence interval; IST, immunosuppressive therapy; NMOSD, neuromyelitis optica spectrum disorder; SD, standard deviation.

Figure 1. Risk of adjudicated relapse according to pre-specified regional subgroups



Dotted vertical lines show the proportion of patients receiving placebo in the overall population who experienced a relapse (R) and the HR for the overall population (right). The statistical test for interaction assesses whether the treatment effect varies by the different levels of the subgroup variable.
 *Based on a Cox proportional hazards model, with treatment covariate, and Wald CIs.
 †Based on a Cox proportional hazards model, with interaction term.
 The Americas: Argentina and the USA; the Asia-Pacific region: Australia, Hong Kong, Japan, Korea, Malaysia, Taiwan and Thailand; Europe: Croatia, Czech Republic, Denmark, Germany, Italy, Russia, Spain, Turkey and the UK.
 CI, confidence interval; HR, hazard ratio; IST, immunosuppressive therapy.

Table 2. Relapse-related hospitalization and acute treatment rates according to pre-specified regional subgroups

Patient population	Americas (N = 44)		Asia-Pacific (N = 48)		Europe (N = 51)		Overall (N = 143)	
	Eculizumab (n = 29)	Placebo (n = 15)	Eculizumab (n = 35)	Placebo (n = 13)	Eculizumab (n = 32)	Placebo (n = 19)	Eculizumab (n = 96)	Placebo (n = 47)
Patients with relapse-related hospitalization, n (%)	0 (0.0)	2 (13.3)	3 (8.6)	5 (38.5)	3 (9.4)	8 (42.1)	6 (6.3)	15 (31.9)
Annualized relapse-related hospitalization rate* (95% CI)	0.00 (NA, NA)	0.12 (0.03, 0.47)	0.05 (0.02, 0.15)	0.35 (0.14, 0.83)	0.05 (0.01, 0.14)	0.43 (0.22, 0.82)	0.04 (0.02, 0.08)	0.31 (0.19, 0.50)
Patients with a relapse requiring acute treatment, n (%)	2 (6.9)	1 (6.7)	2 (5.7)	2 (15.4)	3 (9.4)	3 (15.8)	7 (7.3)	6 (12.8)
High-dose oral steroids	1 (3.4)	6 (40.0)	4 (11.4)	6 (46.2)	7 (21.9)	10 (52.6)	12 (12.5)	22 (46.8)
IV methylprednisolone	0 (0.0)	1 (6.7)	1 (2.9)	3 (23.1)	3 (9.4)	5 (26.3)	4 (4.2)	9 (19.1)
Plasma exchange	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Annualized relapse-related rate (95% CI) of acute treatment	0.05 (0.01, 0.18)	0.06 (0.01, 0.42)	0.03 (0.01, 0.13)	0.14 (0.03, 0.55)	0.05 (0.01, 0.14)	0.14 (0.05, 0.44)	0.04 (0.02, 0.09)	0.11 (0.05, 0.25)
High-dose oral steroids	0.02 (0.00, 0.16)	0.36 (0.16, 0.79)	0.06 (0.02, 0.17)	0.42 (0.19, 0.93)	0.11 (0.05, 0.23)	0.47 (0.25, 0.88)	0.07 (0.04, 0.12)	0.42 (0.28, 0.64)
IV methylprednisolone	0.00 (NA, NA)	0.06 (0.01, 0.42)	0.02 (0.00, 0.11)	0.21 (0.07, 0.65)	0.05 (0.01, 0.14)	0.28 (0.13, 0.63)	0.02 (0.01, 0.06)	0.19 (0.10, 0.35)
Plasma exchange	0.00 (NA, NA)	0.06 (0.01, 0.42)	0.02 (0.00, 0.11)	0.21 (0.07, 0.65)	0.05 (0.01, 0.14)	0.28 (0.13, 0.63)	0.02 (0.01, 0.06)	0.19 (0.10, 0.35)

CI, confidence interval; IST, immunosuppressive therapy; IV, intravenous; Ig, immunoglobulin; NA, not applicable; NMOSD, neuromyelitis optica spectrum disorder.

Conclusion: Eculizumab significantly reduced relapse rates, relapse-related hospitalizations and acute treatment with IVMPs versus placebo in European patient populations, with potential benefits for healthcare resource utilization in these patients experiencing substantial disease burden.

Disclosure: Research funding for this study was provided by Alexion Pharmaceuticals.

O4010

Efficacy and safety outcomes in patients with relapsing forms of MS treated with the CNS-Penetrating BTK inhibitor SAR442168: results from the phase 2b trial

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Background and aims: SAR442168, a central nervous system (CNS)-penetrating Bruton's tyrosine kinase (BTK) inhibitor, has multiple putative modes of action in MS, targeting antigen-induced B-cell activation and CNS microglia-driven neuroinflammation. We evaluated efficacy and safety of SAR442168 in relapsing MS (RMS).

Methods: The DRI15928 phase 2b study (NCT03889639) is a 16-week, dose-finding, double-blind, randomised, placebo-controlled crossover trial testing 4 SAR442168 doses (5, 15, 30, or 60mg daily, administered orally) in patients with RMS. Patients were randomised 1:1 to receive placebo for 4 weeks before or after receiving one of 4 doses of SAR442168 for 12 weeks, enabling all participants to be treated. Primary/secondary endpoints included radiographic outcomes (new gadolinium [Gd] and new/enlarging T2 lesion activity). Exploratory endpoints included additional MRI outcomes, relapse and disability assessments, and evaluation of plasma-based biomarkers. Safety was assessed throughout the study.

Results: 130 patients were enrolled. At baseline, mean age was 37 years, 70% of patients were women, mean time since MS diagnosis was 5.6 years, mean number of relapses in the previous year was 1.2, and median EDSS score was 2.5. Of 79 patients with available MRI data, 52% had active Gd-enhancing lesions at screening.

Conclusion: Baseline characteristics of patients enrolled in the DRI15928 phase 2b study were consistent with those in the general RMS population. Primary and secondary endpoints, including MRI outcomes and safety and tolerability of SAR442168, will be presented. Exploratory relapse and disability endpoints, and the effect of SAR442168 treatment on levels of plasma-based biomarkers will be shown.

Disclosure: STUDY SUPPORT: Sanofi.

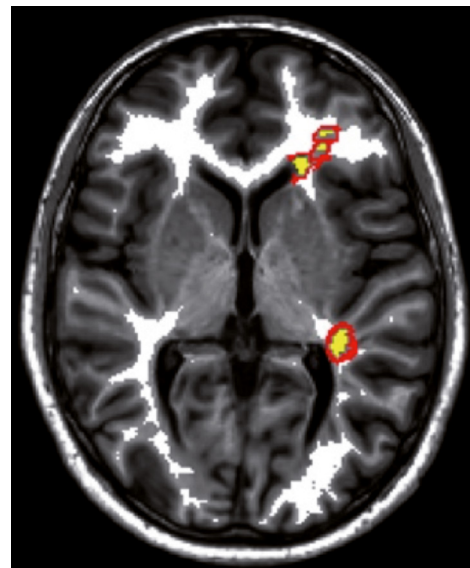
O4011

Exploring the impact of lesional myelin content changes measured with positron emission tomography on perilesional microstructure in multiple sclerosis

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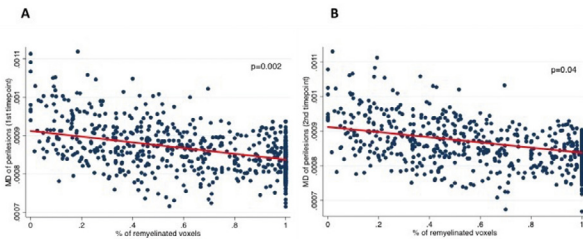
Background and aims: Positron emission tomography (PET) with [11C]PiB allows to explore myelin dynamics in multiple sclerosis (MS). We investigated whether myelin content changes in white matter lesions (WML), measured with [11C]PiB-PET, affect the microstructural integrity in the surrounding normal appearing white matter, as reflected by diffusion tensor imaging (DTI)-derived metrics.

Methods: 19 patients with MS underwent a longitudinal PET/MRI study. Voxel-wise maps of [11C]PiB distribution volume ratio, reflecting myelin content, were employed to calculate for each patient in each non-enhancing WML the percentage of demyelinated voxels at baseline, and the percentage of demyelinating/remyelinating voxels over the follow-up (dynamic indices). After 1mm external lesion erosion to minimize partial volume effects, from each 2mm-thick perilesional area surrounding eroded lesions, mean fractional anisotropy (FA) and mean diffusivity (MD), reflecting microstructural damage, were extracted at both time-points (Fig1). Associations between the 3 PET-derived lesional indices and the DTI-derived perilesional metrics at each time-point were assessed using linear regressions adjusted for age, gender and, for dynamic indices only, baseline demyelination.



Example of 2mm-thick perilesional areas (red) surrounding lesions (yellow) in the white matter of a MS patient on an axial T1-weighted image.

Results: A higher percentage of demyelinated voxels inside lesions at baseline was associated with a more severe tissue damage in perilesions, as reflected by increased MD, at both time-points ($p < 0.0001$). A higher percentage of remyelinating voxels inside lesions correlated with a lower perilesional MD at both time-points, reflecting less severe tissue changes ($p = 0.002$ and $p = 0.04$ at first and second time-point, respectively; adjusted for baseline demyelination, Fig2).



A. Correlation between the normalized percentage of remyelinated voxels inside the lesions and the mean diffusivity (MD) in perilesions at the first (A) and second (B) timepoints. Results were corrected for age, gender and baseline demyelination.

Conclusion: Lesional demyelination, if not compensated by an efficient process of spontaneous myelin repair, results in microstructural damage of perilesional areas.

Disclosure: Nothing to disclose

O4012

Artificial intelligence applied on conventional magnetic resonance images improves the correct diagnosis of CNS diseases mimicking multiple sclerosis

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Background and aims: The diagnostic work-up of patients with suspected multiple sclerosis (MS) may be challenging due to the frequency of brain white matter (WM) hyperintensities on MRI in several neurological conditions. We applied a deep-learning approach for the automated classification of different CNS diseases mimicking MS, comparing the model performance with that of two expert neuroradiologists blinded to diagnosis.

Methods: 268 brain T1-weighted and T2-weighted MRI scans, acquired on 1.5T and 3T MR scanners, were collected from patients with migraine (n=56), MS (n=70), neuromyelitis optica spectrum disorders (NMOSD) (n=91) and CNS vasculitis (n=51). The model architecture, trained on 178 images (Figure 1), was based on a cascade of four 3D convolutional neural network layers followed by a fully dense layer after features extraction. The ability of the final algorithm to correctly classify the diseases in an independent set of 90 MRI was compared with that of 2 expert neuroradiologists.

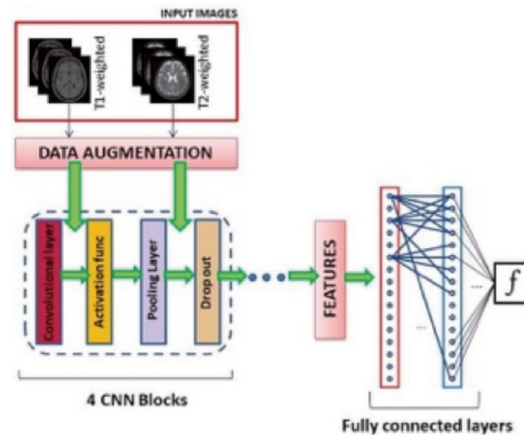


Figure 1. The proposed training architecture for CNS diseases classification. The proposed 4-layer CNN model was trained using multi-sequence 3D images sampled from a subset of training images, where each channel was created from each of the image sequences available and a final model to validate was obtained.

Results: In the test set, the deep-learning algorithm showed higher classification accuracy (92.2% vs 59% for migraine, 98.8% vs 78% for MS, 88.6% vs 4.4% for NMOSD, 92.1% vs 51% for vasculitis) and higher specificity (97.1% vs 88.4% for migraine, 98.4% vs 75.5% for MS, 92.9% vs 92% for NMOSD, 93.2% vs 72.6% for vasculitis) compared with the 2 neuroradiologists ($p=0.01$). The inter-rater agreement was 84.9% (Cohen's kappa=0.78, $p<0.001$, Figure 2).

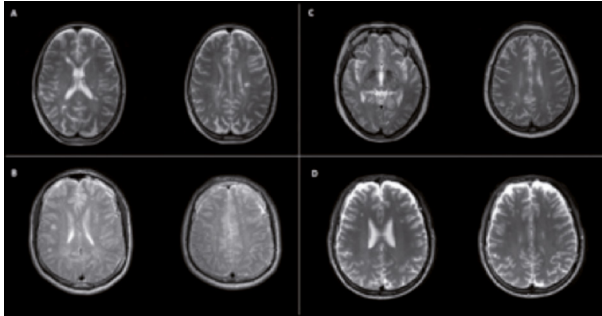


Figure 2. Incorrect diagnoses by human raters. Patients misclassified in agreement by 2 neuroradiologists: A, patient with NMOSD classified as MS; B, patient with migraine classified as CNS vasculitis. Disagreement between the 2 raters: C, patient with NMOSD diagnosed as MS; D, patient with migraine classified as CNS vasculitis.

Conclusion: The classification performance of the deep-learning algorithm exceeded that of 2 expert neuroradiologists, suggesting that artificial intelligence may be a powerful paraclinical tool in the diagnostic work-up of diseases mimicking MS.

Disclosure: Nothing to disclose

Neuro-oncology; neurological manifestations of systemic disease

O4013

Real world clinical features and management of neurotoxicity in CD19 targeted chimeric antigen receptor (CAR) T-cell therapy for high grade lymphoma with off-label use of anakinra

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Background and aims: Immune effector cell-associated neurotoxicity syndrome (ICANS) is a major toxicity complicating CAR T-cell therapy. Presentations and severity are variable, and there remains a clinical need for patients refractory to first line steroid treatment.

Animal models support the use of cytokine targeting therapies such as IL-1 receptor antagonist anakinra. We report our experience of ICANS in a cohort receiving CD19 CAR T-cells, including the first series treated with anakinra.

Methods: Patients with relapsed/refractory B-cell non-Hodgkin lymphoma received axicabtagene ciloleucel (axicel) and tisagenlecleucel (tisagen) between January 2019 and September 2019. Eligibility was determined independently by experts from NHS England and data collected prospectively.

Results: 14 from 43 patients (33%) experienced neurotoxicity, with 7 (16%) having grade 3 or 4. The most common clinical features were dysphasia, delirium, and dyspraxia, while only one patient suffered a self-terminating seizure.

13 patients had neuroimaging, no specific changes were identified. Lumbar puncture performed in 6 patients demonstrated a mild rise in CSF protein (mean 0.96g/L). EEG was performed in 12 patients, almost all (92%) displayed encephalopathic features (generalised rhythmic delta activity) and 2 (17%) had epileptiform foci over the left fronto-temporal region.

Dexamethasone was started for 11 patients, and anakinra administered to 5 patients concurrently for high grade/unresponsive ICANS.

ICANS resolved in all patients surviving to day 30 (n=13), with persistent neurological features in one patient (the sequelae of viral encephalitis) and one sepsis related death.

Conclusion: We describe the clinical features of ICANS in our real-world cohort, and demonstrate feasibility of unresponsive/severe ICANS treatment with anakinra.

Disclosure: Nothing to disclose

O4014

Effects of lentiviral (LV) hematopoietic stem and progenitor cell gene therapy (HSPC-GT) on central and peripheral demyelination and brain atrophy in late-infantile metachromatic leukodystrophy (LI-MLD)

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Background and aims: MLD is a fatal lysosomal disease caused by arylsulfatase A (ARSA) deficiency, leading to accumulation of sulfatides and progressive neurodegeneration, demyelination, and deterioration of motor and cognitive function.

Methods: We have previously reported primary outcomes of 16 LI-MLD patients treated with LV HSPC-GT ("OTL-200", follow-up: 1-7.5 years) compared to a natural history

cohort (NHC) of 19 untreated LI-MLD patients, demonstrating sustained, clinically meaningful benefits in motor function and cognition. Here, we present OTL-200 treatment effects on central and peripheral demyelination and brain atrophy in these 16 LI-MLD patients using brain MRI and nerve conduction velocity (NCV).

Results: ANCOVA modeling showed statistically significant differences in brain MRI total severity scores between OTL-200-treated patients and age-matched NHC patients at year 2 ($p < 0.001$) and year 3 ($p < 0.001$) post-treatment (Figure 1). The score stabilized at lower levels for OTL-200 vs. NHC throughout follow-up ($p < 0.001$, non-linear longitudinal model), suggesting clinically relevant treatment effects on brain demyelination and atrophy. Furthermore, statistically significant differences in NCV Index between OTL-200 vs. NHC at year 2 ($p = 0.004$) and year 3 ($p = 0.010$; Figure 2) were recorded, particularly relevant considering most patients already had signs of PNS impairment at time of treatment. Stabilization or improvement of NCV suggests OTL-200-treated patients may benefit from higher ARSA levels and improved enzyme delivery to the PNS compared to hematopoietic stem cell transplantation (Beerepoot et al. 2019).

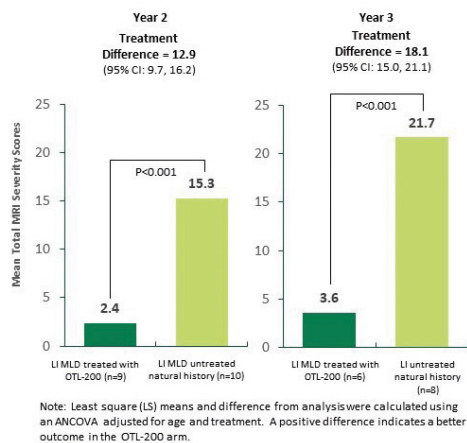


Figure 1: Brain MRI Total Scores at year 2 and year 3, LI-MLD, OTL-200 treated patients with Comparison to Natural History Data (Matched Analysis Set)

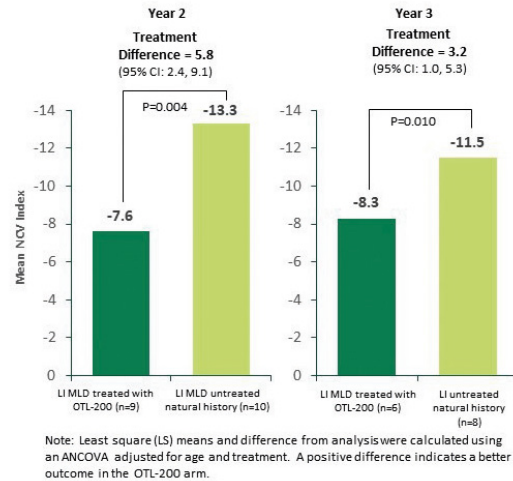


Figure 2: Nerve Conduction Velocity Index at year 2 and year 3, LI-MLD, OTL-200 treated patients with Comparison to Natural History Data (Matched Analysis Set)

Conclusion: Collectively, these results suggest that OTL-200 may prevent, stabilize, or delay the hallmark progressive CNS and PNS damage of LI-MLD, consistent with treatment effects observed on motor function and cognition.

Disclosure: The San Raffaele Telethon Institute for Gene Therapy (SR-TIGET) is a joint venture between Telethon and Ospedale San Raffaele (OSR); MLD gene therapy was licensed to GlaxoSmithKline (GSK) in 2014 and GSK became the clinical trial sponsor; in 2018 MLD development rights were transferred to Orchard Therapeutics (OTL) and OTL became the clinical trial sponsor.

O4015

Reduction in pain during and between attacks in patients with acute hepatic porphyria treated with givosiran: a post-hoc analysis of the phase 3 ENVISION study

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Background and aims: Acute hepatic porphyria (AHP) is a family of rare genetic diseases resulting from enzyme deficiencies in heme biosynthesis. Clinical manifestations include potentially life-threatening neurovisceral attacks and chronic symptoms, with neuropathic pain being the cardinal symptom during and between attacks. In the ENVISION Phase 3 study, givosiran, an RNA interference therapeutic, reduced annualized attack rate ($p < 0.001$), improved daily worse pain (secondary), decreased proportion of days with analgesics use (exploratory) and demonstrated a favorable benefit:risk profile. A post-hoc analysis was conducted to assess reduction in pain and analgesic use during and between attacks.

Methods: ENVISION (NCT03338816), a randomized, double-blind placebo-controlled trial evaluated the efficacy and safety of subcutaneous givosiran in AHP patients (N=94). Daily worst pain, analgesic use (opioid and non-opioid), and the SF-12 health survey were obtained. Analyses are descriptive.

Results: In patients with at least 1 attack, a lower proportion on givosiran (41.7%) compared to placebo (63.2%) had severe pain (median pain score ³7) (Table 1). During attack-free periods, givosiran treatment resulted in reduced daily worst pain scores compared to placebo (Figure 1). This pain reduction was also accompanied by lower analgesic use (Figure 2). The SF-12 Bodily Pain domain demonstrated a greater improvement for givosiran (7.3) versus placebo (2.2) at month 6, suggesting that the reduced pain had a functional impact in patients.

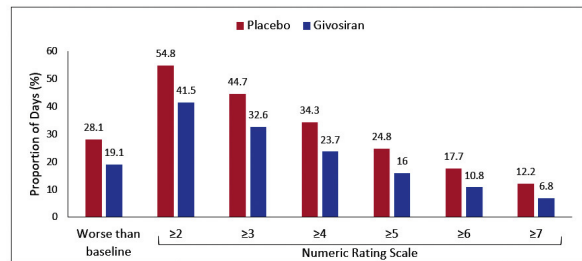
Table 1: Attacks with Median Pain Score ≥ 7 During the 6-Month Double-Blind period in AHP Patients

	Placebo (N=46)	Givosiran (N=48)
Total number of attacks	297	90
Total number of attacks with median pain scores ≥ 7 , n (%)	95 (32.0)	19 (21.1)
Number of patients with at least 1 attack, n (%)	38 (82.6)	24 (50.0)
Number of patients with at least 1 attack with median pain score ≥ 7 , n(%)	24/38 (63.2)	10/24 (41.7)

Attacks included are those requiring hospitalization, urgent care or at home hemin use. Median pain scores of these attacks were calculated based on scores collected during each attack.

Table 1: Attacks with Median Pain Score ≥ 7 During the 6-Month Double-Blind period in AHP Patients

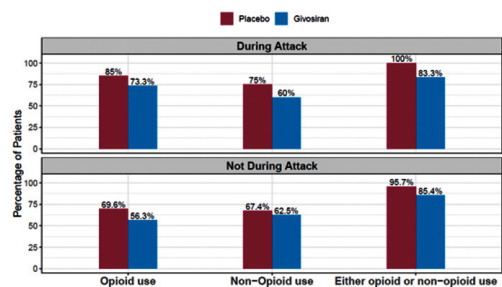
Figure 1. Daily Worst Pain by Numeric Rating Scale on Days Between Attacks During the 6-Month Double-Blind period in AHP Patients



Baseline pain score is the mean score from 4 to 7 days prior to first dose of study drug, when patient not experiencing an attack.

Figure 1. Daily Worst Pain by Numeric Rating Scale on Days Between Attacks During the 6-Month Double-Blind period in AHP Patients

Figure 2. Summary of Analgesic Usage by Attack Status During the 6-Month Double-Blind Period in AHP Patients



All investigator- adjudicated attacks are included.

Figure 2. Summary of Analgesic Usage by Attack Status During the 6-Month Double-Blind Period in AHP Patients

Conclusion: AHP patients on givosiran showed reductions in pain during and between attacks compared to placebo along with decreased analgesic use supporting the potential benefit of givosiran as a disease modifying drug.

Disclosure: This research was funded by Alnylam Pharmaceuticals.

O4016

Neurotoxicity after CAR-T-cell therapy in lymphoma patients: A French neurological multi-center survey

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Background and aims: CAR-T-cell therapy is a promising treatment for haematological malignancies but is frequently associated with cytokine-release syndrome (CRS) and neurotoxicity. The aims of this study are: to follow-up longitudinally patients treated with CAR-T-cell, to exhaustively identify neurological signs, and to describe their occurrence over time.

Methods: During 1 year (July 2018 – June 2019), all patients treated with CD19-targeted CAR-T-cell therapy for relapsing lymphoma were followed-up and monitored for neurotoxicity signs by a neurologist in 4 centres (Paris-Saint-Louis, Lyon, Montpellier, Nantes).

Results: 85 patients, (19-74 years, median 58 years), 28 females/57 males, treated for lymphoma, were included.

Neurotoxicity (presence of at least one neurological sign appearing after treatment infusion) was present in 41% of patients. The median time to onset was 7.7 days after infusion with a median duration of 8.6 days: encephalopathy (43%), cerebellar syndrome (17%), aphasia (23%), headaches (17%), executive syndrome (11%), myoclonus (11%), tremor (11%), agrapahia (9%); meningismus, transverse myelitis, seizure, neglect, dysarthria, neuralgia, dysesthesia: 3%. The severity grade was Grade 1-2: 25 patients, Grade 3-4: 10 patients. CRS was observed in 82% of patients. All patients who developed neurological disorders also had CRS (Grade 1-2: 89%, Grade 3-4: 11%) that preceded neurotoxicity.

Conclusion: The high frequency of neurotoxicity associated with CAR-T therapies underlines the need:

- 1) to neurologically assess all patients before and repeatedly after therapy infusions
- 2) to provide guidelines to improve early recognition of neurotoxicity and its management

Disclosure: Nothing to disclose

O4017

Long-term follow-up of adult neurofibromatosis type 1 patients using whole-body MRI demonstrates dynamic changes in internal neurofibroma size

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Background and aims: Internal neurofibromas (iNFs) affect 40-60% of neurofibromatosis type 1 (NF1) patients and can cause significant morbidity and mortality. They grow more rapidly during childhood and adolescence but adult studies are limited by their retrospective nature and follow-up time <3 years. The long-term natural history of iNFs in adults remains unknown. No guidelines exist on the need and frequency of surveillance imaging. Whole-body MRI (WBMRI) can detect whole-body iNF burden.

Methods: 26 adult NF1 patients who underwent a baseline WBMRI between 2007-2010 underwent follow-up WBMRI between 2018-2019. iNFs were segmented on short tau inversion recovery (STIR) sequences. Tumor volume was calculated using a 3-dimensional tumor quantification software (3DQI). Tumor growth and shrinkage were defined as volume change $\geq 20\%$ over the entire study period.

Results: Median patient age was 42 (baseline) and 52 (follow-up) years. Median time between scans was 9 years. 186 iNFs were assessed (Table 1, Figure 1). 17.7% of tumors grew by a median 68%. 59.1% of tumors spontaneously shrank by a median 59% without treatment. 12 new tumors developed in 10 patients. 18 tumors resolved entirely without intervention. On multivariate analysis, female gender and younger age at baseline were associated with tumor growth ($p < 0.005$).

Number of tumors analysed	186
Median % change in tumor volume	-40.7%
Number of growing tumors (%)	33 (17.7%)
• Median growth (%)	+68%
Number of shrinking tumors (%)	110 (59.1%)
• Median shrinkage (%)	-59%
Number of new tumors (%)	12 (6.5%)
Number of resolved tumors (%)	18 (9.7%)

Table 1. Summary of internal neurofibroma growth behavior in adult NF1 patients

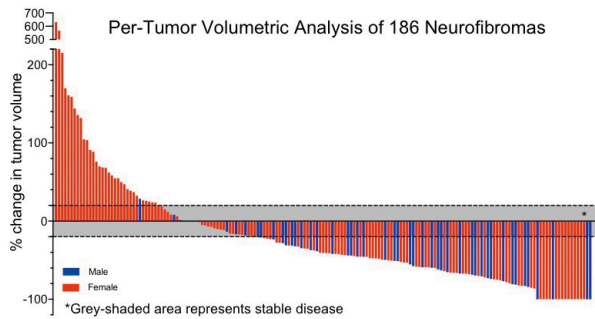


Figure 1. Per-tumor volumetric analysis of 186 neurofibromas summarized as a waterfall plot

Conclusion: A subset of iNFs in adult NF1 patients grow significantly over a long-term period, particularly in female and young adults, suggesting that continued monitoring of high-risk populations is warranted. Surprisingly, more than half of neurofibromas shrink spontaneously without intervention. Continued patient enrollment and correlation of imaging findings with functional outcomes and hormone exposure history are underway.

Disclosure: This research was supported by philanthropic funds to Dr. Scott Plotkin.

O4018

Mechanisms and therapeutic implications of hypermutation in gliomas

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Background and aims: High tumor mutational burden (hypermutation) has been observed in some gliomas; however, its mechanisms of development and whether it predicts immunotherapy response remain poorly understood.

Methods: We comprehensively analyze the molecular determinants of mutational burden and signatures in 10,294 gliomas. We assessed the interactions between DNA damage, repair and the development of hypermutation in patient-derived glioma in vitro and in vivo models. We performed immunohistochemistry, targeted sequencing and single-cell whole genome sequencing to characterize the microenvironment and molecular specificities of hypermutated gliomas. We report the relationship between hypermutation and clinical response to cancer immunotherapy in a pilot cohort.

Results: 2 main pathways to hypermutation were delineated: a de novo pathway associated with constitutional defects in DNA polymerase and mismatch repair (MMR) genes, and a more common post-treatment pathway associated with acquired resistance driven by MMR defects in chemotherapy-sensitive gliomas that recur after temozolomide treatment. Experimentally, the mutational signature of post-treatment hypermutated gliomas was recapitulated by temozolomide-induced damage in cells harboring MMR deficiency. Surprisingly, MMR-deficient gliomas exhibited unique features including the lack of prominent T-cell infiltrates, extensive intratumoral heterogeneity, poor survival and low response rate to PD-1 blockade. Moreover, while microsatellite instability in MMR-deficient gliomas was not detected by bulk analyses, single-cell whole-genome sequencing of post-treatment hypermutated glioma cells demonstrated microsatellite mutations.

Conclusion: This study shows that chemotherapy can drive acquisition of hypermutated populations without promoting response to PD-1 blockade and supports diagnostic use of mutational burden and signatures in cancer.

Disclosure: Nothing to disclose

Sleep disorders 2

O4019

Circadian activity rhythm in isolated REM sleep behavior disorder

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Background and aims: Isolated REM sleep behavior disorder (iRBD) is characterized by abnormal behaviours during REM sleep. Several studies showed that iRBD is a prodromal stage of synucleinopathies. Therefore identifying iRBD in the general population is of utmost importance. In this study we explore whether the assessment of circadian rest-activity rhythm features can distinguish iRBD patients from patients suffering from disorders characterized by other pathological motor activity during sleep and healthy controls.

Methods: 19 subjects with video-polysomnographic (v-PSG) diagnosis of iRBD, 39 subjects with other disorders with motor activity during sleep (19 restless leg syndrome –RLS– and 20 untreated sleep apnea syndrome patients –SAS) and 16 healthy controls underwent 2-week actigraphy, v-PSG, and completed RBD screening questionnaires. Nonparametric analyses were applied to assess rest-activity rhythm features, in addition we computed the I<O index a 24-hours measure that expresses the relationship between nocturnal and diurnal motor activity intensity.

Results: iRBD patients showed lower sleep efficiency, increased WASO and increased frequency of prolonged activity bouts compared to RLS and controls, while no difference emerged with SAS patients. Moreover, iRBD patients presented increased occurrence of estimated nap in comparison to RLS, SAS and controls. The I<O index distinguished iRBD patients from RLS, SAS and controls with an area under the curve greater than that of RBD screening questionnaires.

Conclusion: The I<O index is able to distinguish iRBD patients from patients with other pathological motor activity during sleep and controls, confirming its potential use as an objective measure suitable to screen large at-risk populations.

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O4020

Paroxysmal arousals in Sleep-Related Hypermotor Epilepsy (SHE): the key features to differentiate them from disorders of arousal.

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Background and aims: Sleep-Related Hypermotor Epilepsy (SHE) is a form of focal epilepsy characterized by seizures occurring mostly during sleep ranging from brief paroxysmal arousals (PA) to complex hypermotor seizures and, rarely, ambulatory behaviors. It is difficult to distinguish PA from Disorders of Arousal (DoA), especially from their simplest and shortest episodes called Simple Arousal Movements (SAMs).

Methods: 15 SHE and 30 DoA adult patients and 15 healthy subjects underwent a full-night Video-polysomnography (VPSG). All the sleep-related movements and episodes were analysed by 2 neurologists expert in sleep disorders and epilepsy. For each PA and SAM sleep stage at onset, duration, limbs involvement, progression and semeiology have been identified.

Results: We recorded 121 PA mostly emerging during stage 1-2 NREM sleep, with a median duration of 5 seconds. PA motor pattern at onset was hyperkinetic in 78 episodes (64%), often involving ≥ 3 non-contiguous body parts. A constant progression of movements during PA without any motor arrests was the rule. In DoA patients we recorded 140 SAMs mostly emerging during stage 3 NREM sleep. Their median duration was 12 seconds. In SAMs neither tonic/dystonic nor hypermotor patterns or stereotypy were observed; motor arrest was present in the course of about half of the episodes.

Conclusion: PA in SHE and SAMs in DoA show different semeiological and clinical features. Their recognition could be useful to guide the diagnosis in particular when major episodes are not recorded during VPSG in patients with a clear clinical history of SHE or DoA.

Disclosure: Nothing to disclose

O4021

REM sleep behaviour disorder (RBD) and REM sleep without atonia (RWA): a progression marker for Parkinson's disease?

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Background and aims: RBD is associated with neurodegeneration as a diagnostic marker, but there is not enough data about the long-term development of REM Sleep behaviour disorder (RBD) and REM sleep without atonia (RWA) in PD patients. The aim of this study was to investigate the evolution of RWA and RBD in de novo Parkinson's disease (PD) patients prospectively in the DeNoPa cohort Kassel up to 6 years and to detect potential factors influencing this evolution.

Methods: RBD and RWA were analyzed using video-supported polysomnography (vPSG) in a cohort of de novo PD patients (DeNoPa) Kassel. The influence of time, age, gender, levodopa equivalent daily dose (LEDD), MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) ratings and the intake of benzodiazepines on RWA was investigated using mixed-effect models to account for intra-individual correlations.

Results: RBD prevalence increased from 25% at baseline to 56% after 6 years. For 31 PD patients with RBD at 6 years- follow up, vPSG data were available at every visit. In this PD+RBD group, RWA increased from baseline to 6-years follow-up with 0.26 points per 2 years on a logarithmic scale ($p < 0.001$), time was identified as an independent factor ($p < 0.001$) for RWA increase. Age was shown to be an independent factor influencing RWA increase ($p = 0.04$). Gender, LEDD, MDS-UPDRS, and benzodiazepines did not have any statistical significant influence.

Conclusion: RBD and RWA increase significantly over time in PD, so that RBD and RWA may be regarded as progression markers in PD.

Disclosure: This study was supported by unrestricted grants from the University Medical Centre Goettingen, the Paracelsus-Elena-Klinik, Kassel, Germany, the Michael J Fox Foundation for Parkinson's Research (MJFF), ParkinsonFonds Deutschland and from TEVA Pharma.

O4022

Dopaminergic treatment modulates functional brain connectivity in restless legs syndrome

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Background and aims: Functional brain connectivity studies revealed alterations within thalamic, the salience, and default mode network in patients with restless legs syndrome (RLS). Aim of this study was to characterize functional connectivity and network topology in a large cohort of RLS patients compared to healthy controls, and to investigate the modulatory effect of dopaminergic treatment upon connectivity.

Methods: 82 patients with RLS (untreated, $n = 30$; on dopaminergic medication, $n = 42$; on alpha-2-delta ligands as mono- or polytherapy combined with dopaminergic medication, $n = 10$) and 82 age and gender matched healthy controls were studied with resting state functional MRI. We compared connectivity of 12 resting-state networks with independent component analysis, and among 410 brain regions with graph theoretical modeling.

Results: Patients with RLS showed higher connectivity within salience ($p = 0.029$), executive ($p = 0.001$), somatomotor ($p = 0.050$), and cerebellar ($p = 0.041$) networks, as well as lower ($p < 0.05$) cerebello-frontal communication compared to healthy controls. Untreated patients had lower ($p < 0.05$) cerebello-parietal communication compared to healthy controls. Patients on dopaminergic medication showed no significant intra-network connectivity changes, whereas pronounced ($p < 0.05$) between region connectivity was noted between the thalamus and frontal regions compared to untreated patients and healthy controls.

Conclusion: The networks that showed higher intra-network connectivity (i.e. salience, executive, somatomotor, cerebellar) and lower between regions connectivity (i.e. cerebello-frontal, cerebello-parietal) in RLS correspond to regions associated with attention, response inhibitory control, and processing of sensory information. Dopaminergic medication enhances thalamic connectivity to prefrontal brain regions, and hence, might serve as the functional network correlate that mitigates the occurrence of RLS symptoms.

Disclosure: This study was supported by a grant from Translational Research Fund of the government of Tirol, Austria to Dr. Birgit Högl.

O4023

Automated 3D video analysis of lower limb movements during REM sleep: a new diagnostic tool for isolated REM sleep behavior disorder

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Background and aims: The differentiation of isolated REM sleep behavior disorder (iRBD) or its prodromal phase (prodromal RBD) from other disorders with motor activity during sleep is critical for identifying α synucleinopathy in an early stage. Currently, definite RBD diagnosis requires video-polysomnography (vPSG). Aim of this study was to evaluate automated 3D video analysis of leg movements during REM sleep as objective diagnostic tool for iRBD.

Methods: A total of 122 participants (40 iRBD, 18 prodromal RBD, 64 other disorders with motor activity during sleep) were recruited among patients undergoing vPSG at the Sleep Disorders Unit, Department of Neurology, Medical University of Innsbruck. 3D videos synchronous to vPSG were recorded. Lower limb movements rate, duration, extent and intensity were computed using a newly developed software.

Results: The analyzed 3D movement features were significantly increased in subjects with iRBD compared to prodromal RBD and other disorders with motor activity during sleep. Minor leg jerks with a duration <2 seconds discriminated with the highest accuracy (90.4%) iRBD from other motor activity during sleep. Automatic 3D analysis did not differentiate between prodromal RBD and other disorders with motor activity during sleep.

Conclusion: Automated 3D video analysis of leg movements during REM sleep is a promising diagnostic tool for identifying subjects with iRBD in a sleep laboratory population and is able to distinguish iRBD from subjects with other motor activities during sleep. For future application as a screening, further studies should investigate usefulness of this tool when no information about sleep stages from vPSG is available.

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O4024

A new incidence peak of childhood narcolepsy type 1 in 2013: a new perspective on the role of influenza virus?

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Background and aims: Increased incidence rates of narcolepsy type 1 (NT1) after the 2009-2010 H1N1 influenza pandemic (pH1N1) have been reported worldwide. While some European countries found an association between the NT1 increase and H1N1 vaccination with Pandemrix, reports from Asian countries suggested the H1N1 virus rather than Pandemrix to be linked with the increase of new NT1 cases. Thus, Pandemrix or the virus itself as potential environmental factor induces NT1, is still not completely understood.

Methods: Using a robust data-driven modelling approach (i.e., locally estimated scatterplot smoothing methods), we analyzed the number of de-novo NT1 cases in the last 2 decades until 2016 using the European Narcolepsy Network (EU-NN) database.

Results: We found the peak of NT1 incidence in both childhood and adulthood NT1 during 2009-2010 pH1N1 in more European countries than we have known before, and identified a new peak in 2013 that is age-specific for

children/adolescents. Most of these de-novo cases showed a subacute disease onset consistent with an immune-mediated type of narcolepsy, which is most likely not related to Pandemrix vaccination that was used in 2009-2010, but may have been triggered by some new epidemiological event in Europe.

Conclusion: Our finding of an unexpected peak in de-novo children narcolepsy in 2013 provides a unique opportunity to develop new hypotheses, such as considering other (influenza) viruses to further investigate the pathophysiology of immune-mediated narcolepsy.

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Ageing and dementia 1

EPR1001

A combined RS-EEG/RS-fMRI characterization of the prodromal phase of Alzheimer's disease

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Background and aims: The aim of this study was to evaluate electroencephalogram (EEG) performances alone or combined with resting state functional MRI (rs-fMRI) in order to characterize mild cognitive impairment (MCI) subjects with an Alzheimer's disease (AD)-like cerebrospinal fluid (CSF) biomarkers profile.

Methods: 39 AD, 86 MCI and 86 healthy subjects underwent EEG and/or rs-fMRI. MCI subjects were divided according to their CSF profile: those with phosphorylated tau/β-amyloid-42 ≥ 0.13 (MCI-ATpos) and those with the ratio < 0.13 (MCI-ATneg). Current source density (CSD) analysis was applied to EEG data at a lobar level. To combine the 2 techniques, networks mostly affected by AD pathology were identified using Independent Component Analysis applied to rs-fMRI data. Afterwards, EEG CSD and graph analyses were focused on these networks.

Results: AD showed an increase of delta and theta densities and a decrease of alpha2 and beta1 densities. MCI-ATpos showed higher theta density than MCI-ATneg patients. After the application of rs-fMRI networks to CSD analysis, alpha2 band distinguished MCI-ATpos patients from MCI-ATneg, AD and healthy subjects. Furthermore, at network level, graph analysis from EEG data did not show significant differences between MCI patients groups.

Conclusion: Theta frequency is the most sensitive to AD-like CSF biomarker profile. Furthermore, EEG/rs-fMRI integration highlighted the role of alpha2 band as neurodegeneration biomarker, correlating with disease progression.

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EPR1002

Deep grey matter and hippocampal involvement in genetic cases of frontotemporal lobar degeneration

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Background and aims: This study aimed to assess atrophy of deep grey matter (GM) and hippocampal structures using magnetic resonance imaging (MRI) in patients affected by disorders of the frontotemporal lobar degeneration (FTLD) spectrum with known genetic mutations.

Methods: 3D T1-weighted MRI sequences were obtained from 55 patients carrying mutations in the C9ORF72, GRN, TARDBP or SOD1 genes, including 38 with pure motor neuron disease (MND) and 17 with frontotemporal dementia (FTD). 57 age- and sex-matched healthy controls (HC) were also enrolled. GM volumes of the basal ganglia, thalami and hippocampi were obtained. MRI measures were compared between groups using ANOVA tests applying Bonferroni correction.

Results: The 32 patients carrying a C9ORF72 expansion were divided into two groups of 21 C9-MND and 11 C9-FTD. All 6 GRN-positive patients had an FTD clinical presentation, whereas patients showing TARDBP (n=10) and SOD1 (n=7) mutations had pure MND. Compared with HC, C9-MND patients showed atrophy of the bilateral pallidum, left caudate, and right hippocampus; C9-FTD patients showed atrophy in the same structures, as well as in the right caudate, right putamen, left thalamus and left hippocampus; GRN-FTD patients showed a severe involvement of all basal ganglia and bilateral hippocampi. TARDBP-MND and SOD1-MND patients showed GM volume values that overlapped with those of HC.

Conclusion: Our data suggest that measures of deep GM and hippocampal involvement might be useful markers of C9ORF72-related disorders, regardless of the clinical presentation within the FTL spectrum.

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EPR1003

Longitudinal dynamics of mutant huntingtin and neurofilament light in Huntington's disease: the prospective HD-CSF study

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Background and aims: Mutant huntingtin (mHTT) and neurofilament light (NfL) have emerged as leading biofluid biomarker candidates for Huntington's disease (HD). However, we lack robust data from repeated sampling of individual HD mutation carriers to define the longitudinal dynamics of these markers.

Methods: We quantified mHTT in CSF and NfL in CSF and blood at baseline and 24-months in the prospective HD-CSF study (20 controls, 20 premanifest HD, 40 manifest HD). We characterised longitudinal trajectories of each analyte using mixed effects models and their relationships with disease progression with partial correlations and linear regression. We computed clinical trial simulations to inform clinical trial design.

Results: mHTT in CSF and NfL in CSF and plasma all increased over time, had distinct patterns in HD mutation carriers compared with controls and increased in a manner dependent on HTT CAG count. We defined the age where each measure departed from normality for a given CAG count. The baseline value of each analyte predicted subsequent clinical progression and brain atrophy, better than rate of change in the analytes. Unlike baseline concentrations, rate of change in all analytes did not predict disease status. NfL would require fewer participants per arm than mHTT to run clinical trials as an outcome measure.

Conclusion: NfL is a stronger progression biomarker for HD than mHTT and could be used to inform clinical trial design. CSF mHTT nonetheless possesses prognostic value, and will remain an intrinsically valuable pharmacodynamic marker for huntingtin-lowering trials.

Disclosure: This work was funded by the Medical Research Council, CHDI Foundation, and F. Hoffman-La Roche AG

EPR1004

Biomarker counseling, disclosure of diagnosis and follow-up in patients with mild cognitive impairment: a European survey of EADC centers

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Background and aims: The concept of mild cognitive impairment (MCI) was developed for research to identify patients with objective cognitive impairment but not dementia. It has since diffused into clinical practice. The objective of the study was to assess practices regarding diagnostic procedure and disclosure including biomarker counselling in MCI.

Methods: The present study was designed as an online survey of medical doctors working in European Alzheimer Disease Centers.

Results: 34 center coordinating doctors out of 41 (80.9 %) and 110 out of 213 (50.6 %) individual doctors responded

to the survey. Almost all respondents had access to MRI (98.2%; n=108) and CSF (91.8%; n=101), whereas fewer had access to 18F-FDG-PET (74.5%; n=82) and amyloid PET (50.9%; n=56). Most respondents, always or usually discussed the decision to order biomarkers with patients with MCI (85.7%; n=90) and dementia (81.1 %; n=86). Nearly half (49.5 % n=54) of respondents found that the diagnosis of MCI was meaningful to a great extent, whereas this was 75.5 % (n=84) for dementia ($z=3.77$; $p=0.0002$). Almost all respondents reported always or usually following up MCI (95.2%; n=100) and dementia patients (90.48%; n=95). Half (50.5%; n=53) reported a follow-up period for MCI patients for 5 or more years and 45.3% (n=48) and reported following dementia for a similar amount of time.

Conclusion: Biomarkers are widely available, but that not all patients receive adequate biomarker counselling. For a considerable proportion of practices, we found considerable variability across centers. This may indicate that clinicians lack guidance on issues related to diagnostic disclosure including biomarker sampling.

Disclosure: Nothing to disclose

EPR1005

MAPT p.R406W carriers present with a nonconforming FTD phenotype in the Belgian Flemish population

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Background and aims: The missense mutation, p.R406W in the MAPT gene, is a known causal mutation that was associated with frontotemporal lobar degeneration (FTLD) pathology and an atypical, Alzheimer’s disease (AD)-like clinical phenotype. In our Flemish-Belgian patient cohort, we identified 10 p.R406W carriers. Of 3 index carriers we sampled family members carrying the mutation, resulting in a cohort of 55 p.R406W carriers, to our knowledge the largest number. Our main aim was to analyse in detail their phenotypical and genetic characteristics.

Methods: From longitudinal follow-up over 19 years, we obtained data on clinical characteristics and neuropathology. We investigated the potential genetic modifying effect of the MAPT H1/H2 and the APOE genotypes on the phenotype.

Results: Of the 55 carriers 39 were patients. Allele and haplotype sharing analysis confirmed genetic kinship for all patients, suggesting the presence of a common ancestor. Average onset age and disease duration were 59.8 and 12.7 years (ranges 40-75 and 5-25). The most frequent diagnoses were dementia (unspecified) (43.6%), AD (28.2%) and behavioral variant frontotemporal dementia (bvFTD) (25.6%). FTLT-tau was diagnosed on neuropathology (n=1). A significantly shorter disease duration was found in carriers of at least one APOE ε4 allele (n=7) compared to carriers without (n=3).

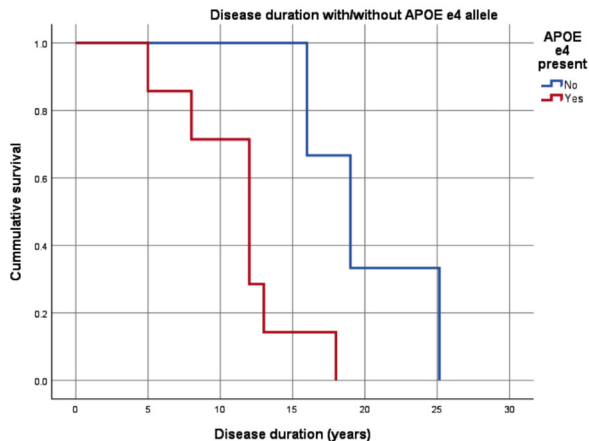


Figure 2. Disease duration with/without APOE ε4 allele.

	Neuropsychiatric symptoms					Cognitive symptoms				Other	
	Disinhibition/ aggression	Apathy/ inertia	Compulsive behavior/ perseveration	Hyperorality/ substance abuse	Depression	Hallucinations/ delusions	Diminished executive functions	Memory problems	Disorientation		Pronounced language deficits
bvFTD (n=10)	100%	40%	50%	50%	30%	40%	20%	80%	30%	20%	20%
AD (n=14)	44%	22%	11%	11%	44%	22%	32%	100%	33%	11%	44%
D (n=1)	100%	0%	0%	0%	0%	0%	50%	50%	0%	0%	0%
MCI (n=1)	0%	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%
All (n=22)	73%	32%	27%	32%	27%	18%	66%	32%	14%	27%	27%

Table 1. Most frequent early symptoms present in 22 affected MAPT R406W carriers with sufficient clinical data. Behavioral variant frontotemporal dementia (bvFTD), Alzheimer’s disease (AD), unspecified dementia (D), mild cognitive impairment (MCI), not available (NA).

Table 1. Most frequent early symptoms present in 22 affected MAPT R406W carriers with sufficient clinical data. Behavioral variant frontotemporal dementia (bvFTD), Alzheimer’s disease (AD), unspecified dementia (D), mild cognitive impairment (MCI), not available (NA).

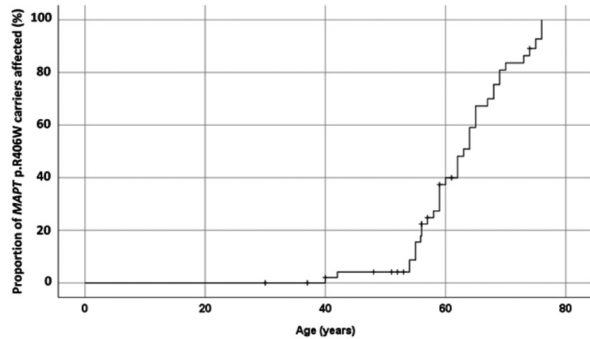


Figure 1. Risk liability curve for MAPT p.R406W mutation carriers.

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Conclusion: A nonconforming clinical phenotype of MAPT p.R406W carriers in the Flemish-Belgian cohort was observed with 25.6 % presenting with a clinical bvFTD phenotype. Prominent behavioral symptoms were highly frequent in the entire cohort (73%). The presence of an APOE ε4 allele shortened disease duration significantly.

Disclosure: Nothing to disclose

EPR1006

Long-term prognosis of cerebral amyloid angiopathy-related inflammation versus the typical type: worse or not?

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Background and aims: Cerebral amyloid angiopathy-related inflammation (CAA-ri) is a rare entity of CAA, thought to be of poor outcome. To date, no study has assessed the long-term prognosis of CAA-ri compared to typical CAA

Methods: In a multicenter study, we retrospectively included all probable CAA-ri patients, according to Chung criteria from 13 French hospitals and a matched control cohort of typical CAA regarding gender and age at diagnosis (± 2 years). The clinical outcome was based on survival, disabilities and cognitive scales. Microbleeds (MBs), intra cerebral hemorrhage (ICH) and cortical superficial siderosis (CSS) were quantified on initial MRI as the Alzheimer CSF biomarkers when available.

Results: 48 CAA-ri patients (52% of males, mean age at diagnosis 73.3 years old) were compared to 48 typical CAA. The mean follow-up duration was 25 months in both groups. CCA-ri patients were more likely to present with worse MMSE (21.2 vs 24.2, $p=0.05$) and modified Rankin scale (2.9 vs 1.8, $p=0.008$) but the rate of death was similar. Mean MBs count was higher in CAA-ri patients (262.0 vs 60.1, $p=0.02$), but we observed less presence of ICH (14.5% vs 90.4%, $p<0.001$) and less CSS (14.5% vs 41.6%, $p=0.01$). In CSF, Tau protein was higher ($p=0.03$) in CAA-ri patients whereas A β 1-42 peptide was lower ($p=0.04$).

Conclusion: This largest CAA-ri study is the 1st showing worse long-term prognosis compared to typical CAA, with higher MBs on initial MRI and specific CSF biomarkers profile

Disclosure: Nothing to disclose

EPR1007

A long-term, retrospective diagnostic comparison of the amyloid, tau and neurodegeneration (A/T/N) classification with a clinical material of early Alzheimer's disease.

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Background and aims: The unbiased A/T/N classification is designed to characterize individuals in the Alzheimer continuum, and is currently little explored in clinical cohorts.

Aims: A retrospective comparison of the A/T/N classification system with the results of a 2-year clinical study, with extended follow-up up to 10 years after inclusion.

Methods: Patients (n=102) clinically diagnosed as AD with dementia or amnesic mild cognitive impairment (MCI), and 61 cognitively healthy control individuals were included. Baseline CSF core biomarkers for AD (A)

Results: A+T+N+ was a strong predictor for AD dementia, even among cognitively healthy individuals. Amnesic MCI was heterogenous, considering both clinical outcome and distribution within A/T/N. Some individuals with amnesic MCI progressed to clinical AD dementia within all 4 major A/T/N groups. The highest proportion of progression was among triple positive cases, but progression was also common in individuals with suspected non-Alzheimer pathophysiology (A-T+N+), and those with triple negative status. A-T-N- individuals who were cognitively healthy overwhelmingly remained cognitively intact over time, but in amnesic MCI the clinical outcome was heterogenous, including AD dementia, other dementias, and recovery.

Conclusion: The A/T/N framework accentuates biomarkers over clinical status. However, when selecting individuals for research, a combination of the 2 may be necessary since the prognostic value of the A/T/N framework depends on clinical status.

Disclosure: Nothing to disclose

EPR1008

Can routine gastrointestinal biopsies be used to assess eventual “preclinical” Parkinson’s disease.

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Background and aims: Parkinson’s disease (PD) is initiated years before the onset of characteristic motor symptoms. As the preclinical stage is difficult to identify, it is of great interest to develop biomarkers that would enable early diagnosis. The definite diagnosis is obtained post-mortem applying immunohistochemistry (IHC) to demonstrate α -synuclein (α Syn) pathology in the brain tissue. It is however known that α Syn pathology can be detected in peripheral nervous system, particularly in the gastrointestinal (GI) system, probably prior to brain involvement. The objective of this study was to assess whether GI samples obtained during life displayed α Syn pathology in subjects with post-mortem verified α Syn pathology in the brain.

Methods: During a 10-year period, 972 autopsies with a neuropathological assessment were carried out at Uppsala University Hospital. In 216 of the assessed brains α -synuclein pathology was observed. In 74 cases (34% of all cases with α Syn pathology), in addition to the brain, GI samples were available for this study. IHC method, applying four different antibodies was implemented on GI samples. A case was assigned as positive if labelled inclusions/neurites were observed in any of the tissue samples using any of the four antibodies.

Results: In 13.5% of the cases (10/74) clinical signs of PD were observed prior to death. In 92% (68/74) of all cases α Syn pathology was observed both in the brain and in the GI samples.

Conclusion: Our results indicate that assessment of α Syn in the GI biopsies can eventually be used as a diagnostic marker of α -synucleinopathy.

Disclosure: Nothing to disclose

EPR1009

Inhibitory synapse degeneration in Alzheimer’s disease: an array tomography study

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Background and aims: Synaptic degeneration is the strongest correlate of cognitive impairment in Alzheimer’s disease (AD), although it is yet unclear to what extent inhibitory synapses are affected from the pathological process. Clinical findings on the other hand, suggest an excitatory/inhibitory imbalance from the very early stages. Array tomography is a high-resolution imaging method,

providing precise quantification of synapses in nanoscale. This study is the 1st to investigate inhibitory synapse degeneration in human AD brain.

Methods: Human brain tissues from BA20/21 and BA17 regions of 10 AD ((4F, 6M); (6 ApoE4+, 4 ApoE3+)) and 5 control (2F, 3M) cases (mean age \pm SD: 80.9 \pm 7.4 and 78.8 \pm 1.4, respectively) were stained with GAD65/67 antibody immunohistochemistry for inhibitory cell count; array tomography ribbons from the same regions were stained for DAPI, GAD65/67, synaptophysin and 6e10 antibodies for nuclei, inhibitory and total presynaptic terminals and amyloid plaques, respectively; and imaged with immunofluorescence to quantify synaptic densities around and away from plaques (Figure 1).

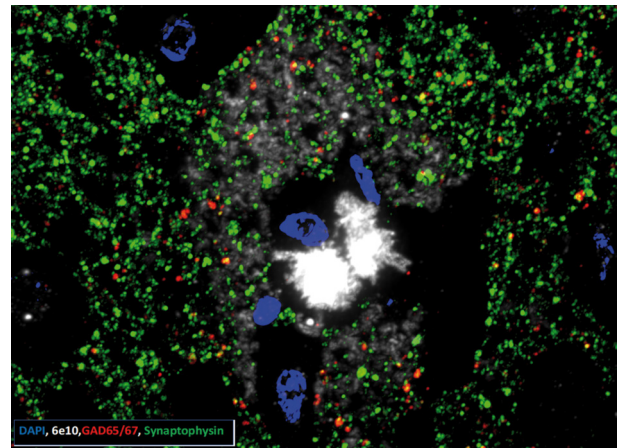


Figure 1: Image shows an amyloid plaque in the centre (6e10-white) surrounded by nuclei (DAPI-blue) and presynaptic terminals (Synaptophysin-green) and inhibitory presynaptic terminals colocalising with synaptophysin (GAD-red).

Results: Total GAD65/67+ cell count and GAD65/67 immunoreactivity was lower in AD in both brain regions. Cell numbers were the lowest in BA20/21 of ApoE4+ cases. Overall densities of GAD65/67+ presynaptic terminals were lower in both regions for AD, and plaque distance analysis showed a decrease in GAD65/67+ synapse densities in immediate surroundings of amyloid plaques.

Conclusion: Our results fall in line with previous studies showing lower GAD65/67 immunoreactivity in AD in temporal and occipital cortices. This effect was greater in ApoE4 allele+ cases. Inhibitory presynaptic terminals were decreased in general, and in a greater extent around amyloid plaques.

Disclosure: This study was funded by European Academy of Neurology under Research Training Fellowship funding scheme.

Autonomic nervous system disorders 1

EPR1010

Pain provocation during the tilt-table test in the diagnosis of reflex syncope

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Background and aims: To compare 2 tilt-table protocols in the evaluation of patients with transient loss of consciousness suggestive of reflex syncope.

Methods: Patients with a definite clinical diagnosis of reflex syncope were eligible for participation in the study and randomly assigned to 1 of the 2 tilt table protocols: A) The subjects were tilted to 70° for a maximum period of 10min. If there were no symptoms after initial 10min, a painful stimulus with the insertion of 0.7mm needle into the dorsum of hand subcutaneously for 30s was performed with patient tilted for further 30 minutes or until symptoms occurred; B) Standard 40min tilt without any provocation.

Results: Out of the 108 participants, 84 were assigned to protocol A (mean age 29.8±11.2, 66 females, median number of prior syncope 2) and 24 to protocol B (mean age 27.2±9.4, 18 females, median number of prior syncope 2). Syncope occurred more frequently in protocol A (66 (78.6%) participants) compared to protocol B (12 (50%) participants), p=0.009. There was no difference in timing of the syncope during the tilt test between the protocols (12 (range 3-37) in protocol A and 17.5 (range 1-37) in protocol B, p=0.181), however average duration of the tilt was significantly shorter for protocol A (13.5 (range 3-40) in protocol A and 38.5 (range 1-40) in protocol B, p=0.004).

Conclusion: The addition of painful provocation in the 10thmin of the tilt-table test increases the sensitivity of the test by 28%.

Disclosure: Nothing to disclose

EPR1011

Epidemiology of postural orthostatic tachycardia syndrome (POTS) in the population of Zagreb (Croatia)

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Background and aims: We aimed to estimate the incidence of POTS in the population of Zagreb, Croatia and to determine demographic and clinical characteristics of the studied population.

Methods: Cases of POTS from 2012-2017 were identified by retrospective analysis of medical records in the University Hospital Center Zagreb. Crude incidence rates were standardized by age using the method of direct standardization according to the European and world standard population.

Results: From 385 patients referred as suspected POTS, 23 were identified as having a definitive diagnosis of POTS. The annual incidence ranged from 3.3 to 14.8 per 1,000,000 for both sexes combined. The highest incidence rates were registered in the age groups 18-29 and 30-39 with female predominance. The mean age at time of diagnosis was 30.7 (SD±9.2, range 18 to 52 years). The median duration of symptoms at time of diagnosis was 7.5 months (range 3 to 180 months). Regarding associated comorbidities, there were 2 patients with chronic gastritis and the following comorbidities were identified in 1 patient each: epilepsy, prior subarachnoid hemorrhage, anxiety, mitral insufficiency, obstructive sleep apnea, hypothyreosis and irritable bowel syndrome. In the group of patients not fulfilling criteria for POTS, the most common alternative diagnoses were autonomic dysfunction due to multiple sclerosis in 22, anxiety disorder in 17, epilepsy in 16 and orthostatic tachycardia due to deconditioning in 13 patients.

Conclusion: Data obtained in this study are useful in providing better surveillance of disease in population, comprehensive assessment of disease burden, and organization of health care services.

Disclosure: Nothing to disclose

EPR1012

Impact and Distribution of Autonomic Dysregulation in Fatal Familial Insomnia: Data from the Published Cases

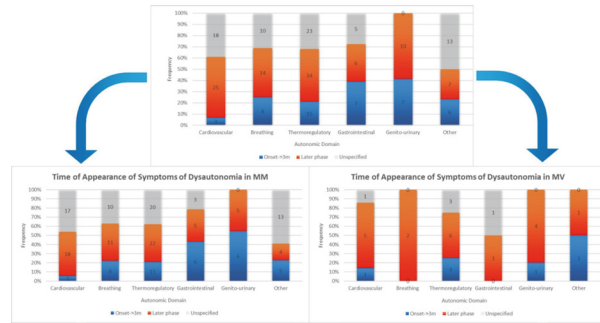
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Background and aims: Fatal Familial Insomnia (FFI) is a hereditary prion disease linked to a missense mutation at codon 178 of the prion-protein gene (PRNP). FFI is characterized by physiological sleep loss and 24-hours autonomic and motor hyperactivation. Autonomic dysfunction consists in sympathetic overactivation with disruption of circadian rhythms and dysregulation of physiological responses. However, the impact throughout the disease course has been poorly investigated.

Methods: We reviewed all published cases of FFI genetically and/or pathologically confirmed until November 2019. We analysed the signs and symptoms of autonomic dysregulation including time of onset and domain involved, according to PRNP mutation genotype (MM, MV or unspecified).

Results: We comprehensively evaluated 136 cases from 61 different publications, 94MM, 19MV and 23 with an unspecified genotype. The mean disease duration was 11.68±5.14 months in MM patients and 22.33±12.91 months in MV (p<0.001). Thermoregulatory and cardiovascular domains were the most frequently involved (45.5% and 33.8% of patients respectively) without any significant difference between genotypes (Fig.1). Gastrointestinal symptoms, when present, appeared in more than 50% of cases within 3 months from disease onset (Fig.2). In relation to life expectancy, patients with breathing disturbances presented a reduction of 3.88 months (CI95%=-7.69--0.06; p=0.047); alteration of pupillary accommodation resulted in a loss of survival time of 8.97 months (CI95%=-14.24--6.69; p=0.004). Finally, a nightly non-dipper blood pressure profile reduced the survival by 10.0 months in MM patients (CI95%=-14.97--5.03; p=0.004).



Correlation between symptoms of dysautonomia and time of appearance during the disease course in published cases of confirmed Fatal Familial Insomnia, homozygous (MM) and heterozygous (MV) at codon 129 as in Baldelli and Provini, 2019. The number of described cases has been indicated inside each column's section.

Conclusion: Dysregulation of specific autonomic domains leads to a marked reduction of life expectancy in FFI.

Disclosure: Nothing to disclose



Frequency of symptoms of dysautonomia throughout the disease course in published cases of confirmed (genetically and/or pathologically) Fatal Familial Insomnia, homozygous (MM) and heterozygous (MV) at codon 129 as in Baldelli and Provini, 2019. The number of described cases has been indicated inside each column's section.

EPR1013

Intensive rehabilitation of anomic aphasia is associated with beneficial autonomic effects by increasing parasympathetic autonomic modulation

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Background and aims: Anomic aphasia induces linguistic anxiety. Although the application of Constraint-Induced Aphasia Therapy (CIAT) (Pulvermüller et al., Stroke 2001;32:1621-6) has been proven to be effective in the treatment of anomic aphasia, its possible effect on cardiovascular autonomic modulation has not yet been studied. The objective of this study is to analyse whether the intensive rehabilitation of anomic aphasia has effects on cardiovascular autonomic modulation.

Methods: In 5 patients with chronic post-stroke aphasia (all men), we recorded RR-intervals (RRI) and continuous beat-to-beat blood pressure (BP) during a designation test of drawings (n=80) before and after 2 weeks (30 hours) of CIAT. We calculated parameters of total autonomic modulation [RRI standard deviation (RRI-SD)], mainly sympathetic cardiac modulation [RRI low frequency powers (RRI-LF-powers)], parasympathetic modulation [square root of the mean squared difference of successive RRIs (RMSSD) and RRI high frequency powers (RRI-HF-powers)] and sympatho-vagal cardiac balance (RRI-LF/HF-ratios). Values were compared before and after CIAT (paired t-test for normally distributed values; Wilcoxon-test for non-normally distributed values; significance: p<0.05).

Results: After CIAT, there was a significant increase in RRI-HF-powers (31.10±6.30 vs 39.04±10.64) and a significant decrease in RRI-LF-powers (68.74±6.34 vs 60.66±10.77) and RRI-LF/HF-ratios (2.32±0.71 vs 1.73±0.82). No significant differences were found in RRI, BP, RRI-SD and RMSSD.

Conclusion: CIAT has beneficial effects not only on anomic aphasia but also on cardiovascular autonomic modulation by increasing parasympathetic and decreasing sympathetic modulation, suggesting that intensive rehabilitation of anomic aphasia diminishes linguistic anxiety in aphasic patients.

Disclosure: Nothing to disclose

EPR1014

Exploring autonomous system during sleep: a key to understand sudden death in Prader Willi syndrome

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Background and aims: Patients with PWS have a higher cardiovascular risk but the underlying mechanism is unclear, possibly related to autonomic nervous system (ANS) dysfunction.

Methods: 57 children performed a polysomnography: 37 PWS (7.2 years, sex ratio 1.05) and 20 controls (8.5 years, sex ratio 0.81). At the genetic level, there were 54% deletion, 43% maternal disomy and 3% imprinting defect. All patients were treated with GH for an average of 5.4 years. Sleep structure and Respiratory events were analyzed according to the criteria of the AASM 2012. The Heart Rate Variability has (HRV) been analyzed (Kubios software) in the time domain (SDNN, NN50 and RMSSD) and in the frequency domain (LF and HF).

Results: HR is significantly higher in patients PWS compared to controls in N2 and REM (trend only in N3). In the time domain, the RMSSD is significantly reduced at all stages of sleep and PNN50 is significantly reduced in N2 and REM (tendency only in N3). In the frequency domain, the LF power is decreased in N3 in the PWS group. HF power (reflection of parasympathetic tone) more low in the PWS group without being significant. The parasympathetic activity in PWS is altered as we notice a significant reduction in pNN50 and RMSSD and downward trend in HF (p=0.06). The decrease in potency of LF could reflect an associated decrease in sympathetic tone.

Conclusion: These changes in CV ANS regulation may contribute to the increase of cardiovascular risk in PWS, and thereby a lack of reactivity during nocturnal respiratory event. Additional studies are needed to deepen the mechanisms probably central mediation.

Disclosure: Nothing to disclose

EPR1015

Barriers and facilitators to implement the European Society of Cardiology syncope guidelines in five Dutch hospitals

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Background and aims: Syncope is very common and has a broad differential diagnosis. Structuring syncope care abroad has been shown to improve diagnostic yield, reduce costs and improve quality of life. We implemented the European Society of Cardiology (ESC) 2018 syncope guidelines in 5 Dutch hospitals by changing procedures in Accident and Emergency (A&E) departments and establishing syncope units where none was present. We evaluated the implementation process to identify potential barriers and facilitators.

Methods: We conducted semi-structured interviews with 19 specialists and residents involved in syncope care from neurology, cardiology, internal medicine and emergency medicine. Interviews were audiotaped and transcribed in full. Reported barriers and facilitators were classified independently by 2 researchers according to the framework of Flottorp and analyzed with specific qualitative software (Atlas.ti).

Results: We identified 25 barriers and 18 facilitators. Most barriers concerned the individual health care professional, such as no experience of residents to work with the guideline at the A&E due to a high turnover, and the organizational context, e.g. no adherence to the guideline due to conflicting standardized procedures at the A&E. Most facilitators were reported at the level of innovation. The multidisciplinary syncope unit in particular was perceived as useful solution to a perceived need in clinical practice.

Conclusion: Implementing the ESC guideline on the A&E and starting syncope units facilitated a structured multidisciplinary work-up for syncope patients. Several barriers were identified in this study. Future implementation along similar lines can be improved by targeting these barriers.

Disclosure: This study was funded by the Netherlands Organization for Health Research and Development (843002707).

EPR1016

Disturbed microcirculation of the skin in patients with complex regional pain syndrome (CRPS)

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Background and aims: Complex regional Pain Syndromes (CRPS) are characterized by autonomic, sensory and motor disturbances. The pathophysiology of CRPS involves beyond others disturbances of the sympathetic nervous system and chronic ischemia also seems to play a role. Non-painful warmth-induced vasodilation of the skin is regulated by an early CGRP (=nerval)-induced vasodilation followed by a delayed NO (=endothelium)-induced vasodilation. Both mechanisms can be investigated and differentiated by functional Laser-doppler Flowmetry (fLDF).

Methods: Skin perfusion of the affected and unaffected extremity of patients with CRPS and patients with unilateral pain syndromes of other origins were investigated fLDF (PeriScan PIM 3 System). The 1st measurement was made at rest after adaptation of skin temperature to 32°C. Afterwards, the skin was slowly warmed up to 42°C with a water-loaded ring for 25 minutes and skin perfusion monitored continuously.

Results: On the affected extremity all patients showed the typical bimodal vasodilation of the skin, whereat CRPS-patients showed a similar rapid increase of skin perfusion until the first peak (20.2 vs 21.1min, p n.s.), but a reduced amplitude of the 1. peak (80.1 vs 187.6PU, p<0.05), reduced dip between 1. und 2. peaks (53.4 vs 98.1PU, p<0.05) with similar duration (25.6 vs 24.6min; p n.s.) and a reduced skin perfusion with a slower rise (p<0.05) when approaching the plateau with an end of the measurement after 40 minutes (150 vs 232.1PU, p<0.05).

Conclusion: Results point towards a disturbed nerval- and endothelium-induced vasodilation in CRPS.

Disclosure: Nothing to disclose

EPR1017

Sudomotor dysfunction in people with neuromyelitis optica spectrum disorders

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Background and aims: To analyze sudomotor function in people with neuromyelitis optica spectrum disorders (pwNMOSD).

Methods: We enrolled 41 NMO-IgG positive pwNMOSD (32 females, mean age 47.9±13.3, median EDSS 2.5, median disease duration 7 years) from Zagreb, Ljubljana and Belgrade. 27 patients had history of transverse myelitis, 30 optic neuritis and 7 area postrema/brainstem syndrome. Sudomotor function was evaluated with a validated questionnaire (COMPASS-31) and quantitative sudomotor axon reflex test (QSART). Sweat volumes were determined on 4 sites (hand, proximal and distal leg and foot) on the right side of the body and interpreted in the form of sudomotor index (SI) of Composite Autonomic Scoring Scale (CASS).

Results: Hypohidrosis and anhidrosis on the hand was present in 2 (4.9%) and 2 (4.9%), on the proximal leg in 4 (9.8%) and 4 (9.8%), on the distal leg in 2 (4.9%) and 5 (12.2%), and on the foot in 2 (4.9%) and 3 (7.35) pwNMOSD, respectively. Involvement of more than one site (hypohidrosis or anhidrosis) was present in 7 (17.1%) pwNMOSD. 2 participants reported reduced sweating in the COMPASS-31 questionnaire: 1 of them had hypo/anhidrosis on all sites, the other participant had normal QSART responses. The SI was pathological in 18 (43.9%) patients: sudomotor dysfunction was mild in 8 (19.5%), moderate in 6 (14.6%) and severe in 4 (9.8%) patients. Disease duration, EDSS, transverse myelitis or area postrema/brainstem syndrome were not associated with sudomotor dysfunction.

Conclusion: Sweating is frequently impaired in pwNMOSD, with up to 25% of patients showing moderate to severe sudomotor dysfunction.

Disclosure: Nothing to disclose

EPR1018

Cardiovascular autonomic testing in the work-up of cerebellar ataxia: insight from an observational single center study

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Background and aims: Cerebellar ataxias are a heterogeneous group of disorders of both genetic and non-genetic origin. In sporadic cases, 2 entities are recognized: multiple system atrophy of cerebellar type (MSA-C) and SAOA (Sporadic Adult-Onset Ataxia). The presence of severe cardiovascular autonomic failure reliably distinguishes MSA-C from other ataxias, but it may appear only late in the disease course. Herein, we aimed at evaluating the diagnostic yield of cardiovascular autonomic function tests in the work-up of cerebellar ataxia.

Methods: We applied a cardiovascular autonomic tests battery in consecutive patients with neurodegenerative cerebellar ataxia and matched healthy control. We recorded the presence of both orthostatic hypotension (OH) and blood pressure falls non-fulfilling the criteria of OH (non-OH BP). Sporadic cases were followed-up for an eventual conversion to MSA-C.

Results: 42 patients were recruited, 19 of whom with sporadic disease (2 probable MSA-C, 6 possible MSA-C, 11 SAOA). Sporadic and hereditary cases showed no difference concerning ataxia severity at baseline. At head-up tilt, non-OH BP falls were detected in 9 patients, but not in controls. This finding was significantly more frequent in sporadic cases (p=0.006) and was detected in 5 out of 7 patients that during follow-up converted to possible/probable MSA-C. Findings at standing test were normal in 4 out of 9 cases with non-OH BP falls at head-up tilt.

Conclusion: A complete cardiovascular autonomic battery with head-up tilt can detect early signs of BP dysregulation which may be missed at bed-side tests, thus warranting its application in the first line work-up of cerebellar ataxias.

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EPR1019

Validation of the neurogenic orthostatic hypotension ratio upon active standing

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Background and aims: Distinguishing neurogenic orthostatic hypotension (nOH) from other causes of blood pressure (BP) instability is of pivotal importance in clinical practice. Norcliffe-Kaufmann et al. recently showed that when the ratio between the heart rate increase and the systolic BP fall after 3 minutes of passive head-up tilt (HUT) is <0.492 , this indicates nOH. Here we aimed at validating this nOH ratio with standard arm-cuff BP measurements upon active standing (AS).

Methods: We screened all patients who had undergone cardiovascular autonomic function testing at the Innsbruck Medical University between January 2008 and September 2019.

Results: We included 51 patients (27 with Parkinson's disease, 22 with multiple system atrophy) diagnosed with orthostatic hypotension either upon AS or HUT. 49 patients showed no BP overshoot after the Valsalva maneuver and were thus classified as having nOH. Out of these, 27 patients showed a systolic BP fall ≥ 20 mmHg in both the HUT and the AS and were considered for further analysis. The nOH ratio was <0.492 for 20 patients during HUT and for 19 patients during the AS. The sensitivity of the nOH ratio for neurogenic OH was therefore 74% upon HUT and 70% upon AS. The correlation between the nOH-ratio upon HUT and AS was strong ($\rho=0.86$, $p<0.001$).

Conclusion: A nOH ratio <0.492 evaluated with standard arm-cuff heart rate and BP measurements has a good sensitivity for nOH both upon HUT and AS. This ratio can be therefore used as bedside nOH screening measure, if no tilt-test facilities are available.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EPR1020

Efficiency of rehabilitation after stroke:

A multifactor analysis

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Background and aims: The high prevalence of strokes makes the rehabilitation after stroke an important task. To better allocate the resources we need to understand the factors influencing the efficiency of rehabilitation in different time periods. In the previous study (Akhmadeeva L. R. et al, Effectiveness of rehabilitation after stroke in the hospital: quantitative analysis of motor function recovery, Problems of balneology, physiotherapy, and exercise therapy, 2019, 40, p. 4-9) we compared patients in acute stroke unit and rehabilitation ward. This study discusses patients in the early rehabilitation state (first six months after the stroke)

Methods: N=548 in-patients, (320 males and 228 females) were studied in the rehabilitation wards of two hospitals in Ufa, Russia. The average age was 65.5 years, standard deviation 10.8. Hospital A staff participated in a long-term training program. Rivermead Index change and other parameters were measured. Power was >0.999 for medium effects ($r=0.3$) and 0.65 for small effects ($r=0.1$) (5% level).

Results: We found a significant improvement in the Rivermead index after rehabilitation. Gender, the duration of hospital stay or the time after stroke did not have noticeable effect on the outcome. The improvement at the hospital with the specially trained staff is 1.08 points higher than at the other hospital. Younger age, better initial state or ischemic (as opposite to hemorrhagic) stroke had small positive effects.

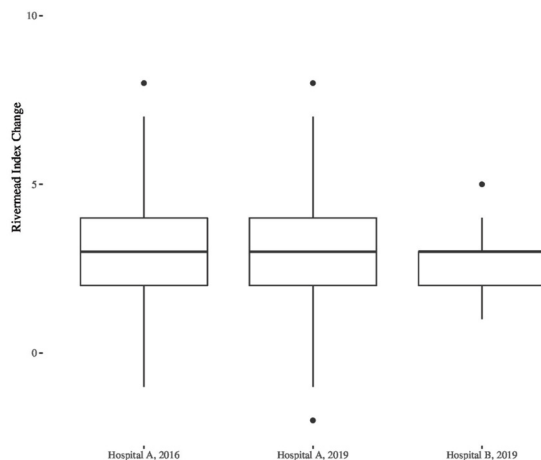


Figure 1: Average change in Rivermead Index

Average change in Rivermead Index

Table 1: Change in Rivermead Index for Different Hospitals

Hospital	Number of patients	Mean change	Standard deviation
Hospital A, 2016	104	3.11	2.29
Hospital A, 2019	410	3.11	1.93
Hospital B, 2019	34	2.76	1.13

Change in Rivermead Index for Different Hospitals

Table 2: Factors of patients' improvement

Factor	Change in Rivermead Index Improvement			p
	Mean	95% Interval		
		Min	Max	
Hospital B as compared to Hospital A	-1.0802	-1.8005	-0.3598	3.38×10^{-3}
Age (per year)	-0.0225	-0.0401	-0.0049	1.25×10^{-2}
Male sex	0.1345	-0.2295	0.4985	4.68×10^{-1}
Initial Rivermead Index	0.2208	0.1353	0.3062	5.67×10^{-7}
Days in rehab	0.0246	-0.0393	0.0885	4.50×10^{-1}
Ischemic stroke as compared to Hemorrhagic stroke	0.4745	0.0028	0.9462	4.87×10^{-2}
Days before rehab	-0.0004	-0.0036	0.0027	7.81×10^{-1}

Factors of patients' improvement

Conclusion: Rehabilitation is beneficial for all stroke patients. The effect of patients' age and initial state is quite small. Training of hospital staff is important for the rehabilitation.

Disclosure: Nothing to disclose

EPR1021

The association of paraoxonase-1 L55M single nucleotide polymorphism with recurrent ischemic stroke

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Background and aims: Ischemic stroke patients are often at significantly increased risk of stroke recurrence, even despite appropriate treatment. In the studies it has been stated that HT, atrial fibrillation, transient ischemic attack, and male gender are primary risk factors in recurrent strokes. In atherosclerotic processes such as coronary artery disease and stroke, Paraoxonase-1 (PON1) L55M polymorphisms have been often investigated. The aim of this study is to examine PON1 L55M polymorphism in patients with recurrent atherothromboembolic stroke and determined its effects on risk of recurrent stroke.

Methods: 110 patients with atherothromboembolic recurrent ischemic stroke (48 females, 62 males), for whom we excluded the possibility of cardioembolism with proper examinations were included in this study. 84 patients without stroke from the same age group (35 females, 49 males) were included as the control group. Hypertension, diabetes mellitus, smoking, and LDL levels of the patients were recorded. The frequency of the PON1 L55M was examined in patients and controls using a Polymerase Chain Reaction and Restriction Fragment Length Polymorphisms method.

Results: After adjusting for age, gender, and the prevalence of smoking, hypertension, diabetes mellitus, and hypercholesterolemia, the MM genotype (MM vs. LL+LM) was found to be associated with a decreased risk of recurrence ($p=0.002$). These data results showed a significant correlation between the PON1 L55M polymorphism and recurrent ischemic stroke in terms of genotypic frequency distribution (Table).

	Patients n: 110	Controls n: 84	p	O.R. (CI 95%)
PON1 L55M			0.0022	
LL	86 [78.2%]	46 [55%]		
LM	19 [17.3%]	28 [33%]		
MM	5 [4.5%]	10 [12%]		
Allele frequency			0.000	2.63(1.57-4.44)
L	191 [86.8%]	120 [71%]		
M	29 [13.2%]	48 [29%]		

Genotypic and allelic distribution of the PON1 L55M polymorphism among controls and recurrent ischemic stroke patients

Conclusion: The results of the present study suggest that PON1 L55M polymorphism may be one of many genetic factors for recurrent ischemic stroke susceptibility in Turkish population.

Disclosure: Nothing to disclose

EPR1022

Cognitive Impairment predicts stroke incidence and mortality: results from a population based study in an elderly Sicilian population

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Background and aims: Scanty population-based studies investigated predictors of cerebrovascular disease risk and mortality. Aims of this population-based study were to determine the characteristics of patients with CVD and to identify predictors of stroke mortality.

Methods: A prospective population-based study has been performed in the elderly population of Bagheria, Sicily. Differences in patient characteristics, cognitive impairment, premorbid risk factors, and hospital investigations were analyzed by t test or Chi square where appropriate. Relative risk, and Kaplan-Meier analyses were performed to investigate the effect of determinants on stroke occurrence and mortality. Statistical analyses were performed using SPSS software version 18.

Results: During the 9-year follow-up period 176 individuals out of a total population of 19800 person/years developed a CVD. Risk for stroke was significantly higher among individuals affected by cognitive impairment (RR 1.7; 95%CI 1.3-2.1). BMI distribution showed a significantly different pattern between individuals who developed aCVD compared to the others (p for trend= 0.01). We also observed a significant association between male sex and a higher stroke related mortality compared to women (RR 1.22; 95% CI 1.1-1.4). K-M estimates showed a cumulative probability for stroke occurrence during follow-up higher among patients affected by cognitive impairment (log rank test $p<0.0001$). Survival estimates showed also a significant association for a lower survival among individuals with a stroke having a cognitive impairment compared to the others ($p<0.0001$).

Conclusion: Findings of this study suggest that CI and BMI are associated with CVD occurrence and mortality displaying gender differences.

Disclosure: Nothing to disclose

EPR1023

The predictive value of collateral score in posterior circulation stroke

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Background and aims: Posterior circulation collateral score (PC-CS) is a quantitative grading tool to assess the status of collateralisation on computed tomography angiography (CTA). The study sought to examine the prognostic value of PC-CS to predict clinical outcome in patients with posterior circulation stroke.

Methods: Consecutive fifty-one patients with posterior circulation stroke with mean age 67.68 ± 13.84 years were retrospectively reviewed. The status of collaterals was graded using PC-CS assessed on a 10-points scale that quantifies the potential of collateral flow in posterior communicating and cerebellar arteries on pre-treatment CTA. PC-CS was dichotomised into poor (PC-CS: 0-6) and good (PC-CS: 7-10) collaterals. Association of collateral status with clinical outcome at 90 days (assessed using modified Rankin score (mRS)) was studied (poor outcome $mRS > 2$; good outcome $mRS 0-2$).

Results: Twenty-four patients (47%) had poor (PC-CS: 0-6) and 27 patients (53%) had good (PC-CS: 7-10) collaterals. In a multivariate regression model, poor (PC-CS: 0-6) collateral status (OR 28.3, CI 3.5-229.1) was significantly associated with poor outcome ($mRS > 2$) when adjusted for time to emergency presentation since stroke onset, treatment (thrombolysis and/or thrombectomy) and stroke severity at admission.

Conclusion: The pre-treatment collateral status assessed using PC-CS is an independent predictor of clinical outcomes at 90 days in posterior circulation stroke.

Disclosure: Nothing to disclose

EPR1024

Early neurological deterioration following thrombolysis for mild stroke with isolated internal carotid artery occlusion: incidence, predictors and mechanismsN. Boulenoir¹, P. Seners¹, J.-C. Baron¹, G. Turc²,
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Background and aims: The incidence, predictors and mechanisms of early neurological deterioration (END) following intravenous thrombolysis (IVT) for acute stroke with mild symptoms and isolated internal carotid artery occlusion (ICAO) are little known.

Methods: From a multicenter retrospective database we extracted all patients with both $NIHSS < 6$ and isolated ICAO (i.e. not involving the circle of Willis) on admission, intended for IVT alone (i.e. including those receiving rescue thrombectomy). END was defined as ≥ 4 NIHSS point increase within the first 24hrs. END and no-END patients were compared for i) pre-treatment clinical and imaging variables including occlusion site, completeness of Willis circle and perfusion, and ii) presence of intracranial arterial occlusion or haemorrhage on follow-up imaging.

Results: Of the 74 included patients (mean age 64yrs, median NIHSS 3, supra-bulbar ICAO in 35%), 30% experienced END, of whom 63% received rescue thrombectomy. There was no occurrence of parenchymal haemorrhage on follow-up imaging, but new intracranial occlusion was present in 75% of END patients vs. 0% of no-END patients ($P < 0.0001$). Supra-bulbar ICAO was the only admission predictor of END after stepwise variable selection (OR=4.0; 95%CI 1.2-12.5; $P=0.017$). As compared to no-END, END was strongly associated with poor 3-month outcome ($mRS \leq 1$: 71% vs. 20%, $P < 0.0001$).

Conclusion: END is a frequent and highly deleterious event after IVT for minor stroke with isolated ICAO. This study identified distal embolism as underlying mechanism in 3 out of 4 patients. The strong association with ICAO site may reflect a different response of the thrombus to IVT, which may depend on underlying stroke etiology.

Disclosure: Nothing to disclose

EPR1025

Predictors of outcome in 1-year survivors of large middle cerebral artery infarcts treated by decompressive hemi-craniectomy.

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Background and aims: Decompressive hemi-craniectomy (DH) increases survival without severe dependency in patients with large middle cerebral artery (LMCA) infarcts. The objective was to identify predictors of 1-year outcome after DH for LMCA infarct in clinical practice.

Methods: We conducted this study in consecutive patients who underwent DH for LMCA infarcts, in a tertiary stroke centre. Using multivariable logistic regression analyses, we evaluated predictors of (i) 30-day mortality, and (ii) poor outcome after 1 year (defined as a modified Rankin scale 4 to 6) in 30-day survivors.

Results: Of 212 patients (133 men, 63%; median age 51 years), 35 (16.5%) died within 30 days. Independent predictors of 30-day mortality were infarct volume before DH (odds ratio [OR], 1.09 per 10 ml increase; 95% confidence interval [95%CI] 1.03 to 1.15), and midline shift 24 hours after DH (OR 2.31; 95%CI 1.01 to 5.30). The optimal cut-off to predict death at 30-days before DH was an infarct volume of 210ml or more. Amongst the 177 survivors at day-30, 77 (43.5%) had a poor outcome at 1-year. Independent predictors of poor outcome at 1-year were age (OR 1.08 per 1-year increase; 95%CI 1.03 to 1.12) and weekly alcohol consumption of 300g or more (OR 5.30; 95%CI 2.20 to 12.76), but not infarct volume.

Conclusion: In patients with LMCA infarcts treated by DH, stroke characteristics (infarct volume before DH and midline shift after DH) predict 30-day mortality, while patients' characteristics (age and excessive alcohol intake) predict 1-year outcome in 30-day survivors.

Disclosure: Nothing to disclose

EPR1026

Extending intravenous thrombolysis time window guided by CT Perfusion

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Background and aims: Intravenous thrombolysis (IVT) beyond 4.5 hours from symptom onset is contraindicated. Recent clinical trials have suggested that IVT window may be extended in patients with favorable radiological findings on CT perfusion or MRI. We present our experience with IVT beyond 4.5 hours.

Methods: Retrospective analysis of prospective registry of patients treated with IVT within 9 hours from symptom onset selected by CT perfusion (RAPID software) at our comprehensive stroke center from January 2019 to December 2019. Clinical and radiological variables were collected.

Results: 14 patients were included, (65% were females; mean age 73±14.19). Median NIHSS was 9.5 (range 2-25). Infarct core volume was 13.2ml (range 0-109.86), volume of salvageable tissue was 32.16ml (range 0-103.83) and mismatch ratio determined by RAPID was 3.3 (range 1.9-9.3). CT angiography showed vessel occlusion in 11 patients. Time onset of symptoms to the beginning of alteplase was 319min (range 280-510). Alteplase dose used was 0.9mg/kg in 13 patients and 0.6mg/kg in 1. None of them presented intracranial or systemic hemorrhagic complication. At 3 months, 63.3% patients were independent (mRS≤2) and the median mRS was 1.5 (range 0-4).

Conclusion: In our experience, selecting patients for IVT beyond 4.5 hours guided by CT perfusion is safe and effective, and is associated with a good neurological prognosis at 3 months.

Disclosure: Nothing to disclose

EPR1027

Stress Hyperglycaemia Associated with Poor Functional Outcomes in Acute Ischaemic Stroke Patients treated with Intravenous Thrombolysis

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Background and aims: Transient hyperglycaemia in the context of illness with or without known diabetes has been termed as 'stress hyperglycaemia'. This has been demonstrated to be associated with an increased risk of recurrent stroke in patients with a minor ischemic stroke or transient ischemic attack. We investigated the association between stress hyperglycaemia ratio (SHR) and clinical outcomes in acute ischaemic stroke patients undergoing recanalisation therapy with intravenous thrombolysis (IVT).

Table 1: Comparing High (SHR \geq 0.97) with Low Stress Hyperglycaemia Ratio (SHR<0.97) in Patients with Acute Ischaemic Stroke Undergoing Intravenous Thrombolysis

	High SHR (\geq 0.97, n=219)	Low SHR (<0.97, n=447)	Mean Difference/Odds Ratio (95% CI)	p-value
Age	67.9 (\pm 15.2)	63.5 (\pm 13.6)	4.5 (2.1 – 6.8)	<0.001
Gender (Male)	49.8%	68.0%	0.64 (0.53 – 0.77)	<0.001
Smoking	6.4%	18.3%	0.88 (0.83 – 0.92)	<0.001
Diabetes	23.7%	16.6%	1.09 (1.01 – 1.19)	0.026
Hypertension	66.7%	57.3%	1.28 (1.03 – 1.59)	0.020
Hyperlipidaemia	49.3%	45.9%	1.07 (0.91 – 1.25)	0.401
Atrial Fibrillation	20.8%	13.4%	1.12 (1.04 – 1.22)	0.002
Fasting Glucose (mmol/L)	8.6 (\pm 3.0)	6.0 (\pm 1.7)	2.6 (2.2 – 2.9)	<0.001
HbA1c (%)	6.2 (\pm 1.4)	6.3 (\pm 1.5)	-0.1 (-0.4 – 0.1)	0.233
Haematocrit	39.5 (\pm 6.0)	41.2 (\pm 5.4)	-1.8 (-2.7 – -0.8)	<0.001
NIHSS at onset	16.7 (\pm 7.4)	13.3 (\pm 7.0)	3.4 (2.3 – 4.6)	<0.001
Systolic blood pressure at onset (mmHg)	159.5 (\pm 24.3)	150.5 (\pm 23.7)	8.9 (5.1 – 12.9)	<0.001
Diastolic blood pressure at onset (mmHg)	85.4 (\pm 15.6)	82.1 (\pm 15.5)	3.3 (0.8 – 5.9)	0.010
Mortality	5.0%	1.8%	1.03 (1.01- 1.07)	0.019
Good Functional Outcome (mRS 0-2 at 90 days)	37.0%	62.6%	0.59 (0.51 – 0.69)	<0.001

Table 1

Methods: We examined 666 consecutive acute ischaemic stroke patients who underwent IVT in our centre between 2006-2017 and had glucose and HbA1c tested at admission. SHR was calculated by fasting plasma glucose (FPG) divided by HbA1c. Univariate and multivariate analyses were employed [modified Rankin Scale (mRS) 0-2 at 90 days].

Results: 361 patients (54.2%) had good functional outcomes. These patients were younger (60.7 ± 12.7 vs 70.0 ± 14.4 years, $p<0.001$), of male gender (70.7% vs 51.5%, $p<0.001$), had lower prevalence of atrial fibrillation (13.0% vs 20.7%, $p=0.008$) and lower SHR (0.88 ± 0.20 vs 0.99 ± 0.26 , $p<0.001$). Patients with higher SHR were older, more significantly associated with diabetes mellitus, higher mortality rates and worse functional outcomes at 90-days

(Table 1). On multivariate analyses, SHR remained independently associated with good functional outcomes (adjusted OR 0.26, 95%CI 0.11-0.63, $p=0.003$).

Conclusion: SHR is an important predictor of functional outcomes in patients with AIS undergoing IVT. Further studies are necessary to validate this finding and determine if it can be targeted as a potential treatment variable.

Disclosure: Nothing to disclose

EPR1028

The association between carotid atherosclerosis and the coronary artery calcification

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Background and aims: Carotid atherosclerosis and coronary artery calcification has been suggested as a predictor of future coronary artery disease. The association between carotid Doppler ultrasound (US) and coronary artery calcium score (CACS) has not been investigated. The purpose of this study was to investigate the association between the carotid artery atherosclerosis and CACS.

Methods: We retrospectively enrolled subjects who had both carotid US and cardiac computed tomography as part of health examinations from March 2007 to April 2019. Subjects were categorized into four groups according to CAC score as assessed by cardiac computed tomography: zero (0), low (1-99), intermediate (100-399), or high (≥ 400). Then, the presence of the carotid plaque and the mean of carotid intima-media thickness (IMT, mm) in each CAC score group was assessed.

Results: A total of 2,941 subjects (mean age: 55.0 \pm 9.9 years; percentage male: 65.4%) were included for analysis. Carotid plaques were detected in 1006 subjects (34.2%). The presence of carotid plaque and the mean IMT significantly increased as the CACS increased (21.4%, 46.3%, 68.1%, 79.9%, respectively, p for trend <0.001; 0.64 \pm 0.23, 0.74 \pm 0.33, 0.77 \pm 0.37, 0.83 \pm 0.42, respectively, p for trend <0.001). Multivariate logistic regression analysis showed CACS was an independent risk factor for the presence of carotid plaque (adjusted odds ratio = 3.18; 95% confidence interval = 2.63-3.83). Multivariable linear regression analysis showed the IMT increased as the CACS increased (β =0.076, p<0.001).

Conclusion: A high CAC score was associated with the presence of carotid plaque and the increased IMT.

Disclosure: Nothing to disclose

EPR1029

Long-term EEG monitoring for the detection of epileptic activity in the acute phase of stroke

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Background and aims: Stroke is a common cause of seizures, especially in the elderly population. However, the incidence, associated factors and influence on outcome of interictal epileptic discharges and subclinical electrographic seizures in the acute phase of stroke are unknown.

Methods: In this prospective study, 55 patients underwent long-term video-EEG monitoring within 3 days after intracerebral haemorrhage or ischemic stroke. Epileptic activity on the EEG, including spikes, spike-waves and electrographic seizures, was analysed and correlated with clinical and neuroradiological patient characteristics, the occurrence of clinical seizures and functional outcome.

Results: Data analysis is ongoing. In a preliminary analysis, data of the first 35 patients was investigated. Epileptic activity was seen on the EEGs of 8/35 (23%) patients. 3/35 (9%) of patients had electrographic seizures, and spikes or spike waves were seen in 6/35 (17%) of subjects. Ictal electrographic activity and early clinical seizures (<7 days post-stroke) were significantly correlated (p=0.018) in patients with ischemic stroke. No other significant associations were found between the occurrence of epileptic discharges and clinical or radiological features, nor with outcome.

Conclusion: Data analysis of all patients is ongoing and will be presented for the 1st time at the conference. In a preliminary analysis of the first 35 patients, epileptic discharges were frequently found in the acute phase post-stroke. Ictal electrographic activity was associated with the occurrence of early clinical seizures.

Disclosure: Nothing to disclose

EPR1030

Neural progenitor cell-derived extracellular vesicles induce neuroprotection via regulation of the multidrug resistance transporter ABCB1 after ischemic stroke

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Background and aims: Extracellular vesicles (EVs) derived from neural progenitor cells (NPCs) enhance post-stroke neurological recovery, albeit the underlying mechanisms remain elusive. In light of previous research describing an enhanced post-stroke integrity of the blood-brain barrier (BBB) upon systemic transplantation of NPCs, we wondered whether or not NPC-derived EVs affect BBB stability and which cellular mechanisms might be involved in the process.

Methods: Using an in vitro model of brain endothelial cells (ECs) and astrocytes, cells were treated with EVs or PBS and exposed to oxygen-glucose-deprivation (OGD) injury. The readout parameters focused on the expression of ABCB1, an ATP-binding cassette (ABC) transporter expressed on ECs contributing to BBB integrity. Further in vitro analysis examined the pro-inflammatory NF- κ B pathway, the paracellular permeability and the transcellular electrical resistance (TER) of cultured ECs. In vitro data was finally confirmed using a rodent stroke model.

Results: Cultured ECs displayed increased ABCB1 levels when exposed to OGD, which was reversed by treatment with EVs. The latter was due to an EV-induced inhibition of the NF- κ B pathway. Using a BBB co-culture model of ECs and astrocytes exposed to OGD, EVs stabilized paracellular permeability and ABCB1 levels without affecting TER. Likewise, EVs yielded reduced Evans blue extravasation, decreased ABCB1 expression as well as an inhibition of the NF- κ B pathway and downstream matrix metalloproteinase 9 activity in stroke mice. EV-induced inhibition of the NF- κ B pathway finally resulted in a post-stroke modulation of immune responses.

Conclusion: EVs enhance post-stroke BBB integrity via ABCB1 transporter regulation attenuating inflammatory cell recruitment via inhibition of the NF- κ B pathway.

Disclosure: Nothing to disclose

EPR1031

Cancelled

Cerebrovascular diseases 2

EPR1032

Endocan: a novel predictor of endothelial dysfunction in silent brain infarction

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Background and aims: Silent brain infarction (SBI) has been proposed as a subclinical risk factor for symptomatic stroke in the future. In this study, we aimed to investigate the relationship between serum inflammatory markers and SBI.

Methods: We included 54 patients diagnosed with SBI as the study group and 52 individuals as the control group. SBI was defined as hypointense area on T1 and hyperintense on T2-weighted images sized >3mm diameter. The levels of endocan, PTX-3 and CRP in plasma were evaluated.

Results: The mean age (53.8±7.1 vs 52.5±8.5 years, p=0.527) and gender distribution (female/male, 39/15 vs 38/14, p=0.921) were similar between patient and control groups, respectively. Serum levels of endocan (p=0.036) and hsCRP (p=0.022) were significantly higher in patients with SBI than the controls. PTX-3 sedimentation, WBC, lymphocyte, monocyte, neutrophil, platelet, LDL, HDL, TG values were not significantly different between the groups with and without SBI (p>0.05). There was a significant correlation (p=0.16/r=-0.196) between hsCRP and endocan levels in the SBI group.

Conclusion: Endocan, a new biomarker of endothelial pathology, is significantly increased in patients with SBI and may predict future events of stroke.

Disclosure: Nothing to disclose

EPR1033

Platelet-to-lymphocyte ratio correlates with hemorrhagic transformation and a worse outcome at 90 days following stroke

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Background and aims: Inflammation has been associated with worse outcome in acute stroke. Platelet-to-lymphocyte ratio (PLR) is an inflammatory parameter that was associated with worse outcome in previous studies. In this study we evaluate the association between PLR, hemorrhagic transformation and functional independence at 90 days following stroke, in patients with ischemic stroke who received intravenous thrombolysis and/or mechanical thrombectomy.

Methods: We included patients with anterior circulation ischemic stroke who received revascularization therapy, between January 2017 and December 2018. We collected demographic, clinical, analytical and imagiological data. Hemorrhagic transformation was classified according to the Fiorelli criteria in H1, H2, PH1 and PH2+remote clot. The functional status was classified according to the modified Rankin scale (mRS). We further applied regression models to assess association between variables.

Results: 375 patients were included, 67% received intravenous thrombolysis and 61% were treated with mechanical thrombectomy. Hemorrhagic transformation occurred in 94 patients (25%). In the multivariate model, we found that higher levels of PLR were associated with greater hemorrhage severity, after adjusting for other variables (OR 1.34, 95% CI 1.05; 1.72). Lower PLR levels, on the other hand, were associated with functional independence at 90 days following stroke (p<0.01).

Conclusion: In this study, platelet-to-lymphocyte ratio was associated with hemorrhagic transformation and severity and worse functional outcome at 90 days. This is in line with previous studies which suggest that inflammation might be harmful in acute stroke. In the future, PLR might be useful in stratifying stroke patients in order to understand who may benefit from immunomodulatory therapies.

Disclosure: Nothing to disclose

EPR1034

Haematoma volume, secondary expansion and 3-month-mortality in patients on antiplatelet therapy. A systematic review and meta-analysis

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Background and aims: We aimed to assess the influence of prior antiplatelet therapy (APT) at onset of intracerebral haemorrhage (ICH) on hematoma characteristics and outcome.

Methods: We performed a systematic review and meta-analysis of studies comparing ICH outcomes of patients on APT (APT-ICH) with patients not taking APT (non-APT-ICH). Primary outcomes were haematoma volume (mean difference and 95%-confidence interval (95%-CI)), haematoma expansion, in-hospital- and 3-month mortality. Odds ratios (OR) were calculated with Maentel-Haenszel random-effects method and 95%-CI.

Results: Out of 1205 identified publications, 28 studies on 31,063 patients with APT-ICH and 62,789 patients with non-APT-ICH matched our in- and exclusion criteria. Patients on APT were older (6.8 years, 95%-CI 5.71 - 7.90, $p < 0.00001$, I^2 for heterogeneity = 69%, $p < 0.00001$), had larger haematoma volume (mean difference 3.6 ml, 95% - CI 1.43 - 5.28, $p = 0.0006$; $I^2 = 60%$, $p = 0.0009$), higher short-term-mortality (OR 2.02, 95%-CI 1.41 - 2.90, $p = 0.0001$; $I^2 = 76%$, $p < 0.00001$), higher 3-month-mortality (OR 1.5, 95%-CI 1.24 - 1.81, $p < 0.0001$; $I^2 = 70%$, $p = 0.0001$). Risk for haematoma expansion was insignificantly higher in APT-ICH (OR 1.26, 95%-CI 0.83 - 1.91, $p = .027$). We found insufficient data for comparison of single vs dual APT-ICH.

Conclusion: APT is a relevant risk factor for larger haematoma volume and higher mortality in patients with ICH. However, estimating the real-life impact remains difficult concerning the large heterogeneity amongst studies. Data on differences in single and dual APT-ICH are scarce and warrant further investigation.

Disclosure: MG has received a Young Talents in Clinical Research Grant by the Swiss Academy of Medical Sciences and the Bangert-Rhyner-Foundation

EPR1035

Ischemic stroke in young adults: retrospective cohort study in Republic of Moldova's tertiary neurology center

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Background and aims: Ischemic stroke in young adults is a rising health problem with multiple risk factors and socio-economic impacts. The aim of the study was to characterize the cohort of Moldovan patients.

Methods: Retrospective medical records evaluation of 1687 patients with ischemic stroke treated in tertiary neurology center from January 2018 till December 2019 was performed and 59 patients aged 50 and less were included. Was analyzed the risk factors profile, clinical presentation, neuroimaging, and comorbidities.

Results: The study cohort consists of 67.9% men and 32.1% women, mean age – 42.95±6.7. In 82.1% was the 1st-ever stroke and 17.9% - recurrent. The middle cerebral artery territory was affected by 76.8%, mostly in the left hemisphere – 46.4% and posterior territory – 19.6% with brainstem location in 12.5%. The first clinical presentation was motor deficit – 60.7%, speech impairment – 23.2%. NIHSS 10.03±5.14. Neuroimaging shows: ischemic lesion – 94.6%, concomitant lacunar infarcts/leukoaraiosis – 28.6%, old strokes – 19.6%. Large vessel occlusion was documented in 12.5% (left side – 75%), stenosis – 30.4% (mean 43.5±15.7%) and vertebral artery hypoplasia – 25%. In 55.4% of patients, the sedimentation rate was elevated and in 26.8% - leukocytosis. Only 41.1% of patients were on anterior treatment and 7.1% had anticoagulants. In 26.8% patient different types of infection were documented prior to stroke onset. The risk factor profile is presented in table 1.

Nr.	Risk factors/comorbidities	% (abs)
1.	Hypertension	78.6% (44)
2.	Diabetes Mellitus	26.8% (15)
3.	Obesity	21.4% (12)
4.	Dislipidemia	33.9% (19)
5.	Atrial fibrillation	16.1% (9)
6.	Ischemic heart disease	8.9% (5)
7.	Large vessel atherosclerosis	32.1% (18)
8.	Smoking	17.9% (10)
9.	Alcohol	10.7% (6)
10.	Anterior C-V event	12.5% (7)
11.	Familial history of CV disease	17.9% (10)
12.	Infections	26.8% (15)
13.	Cancer	7.1% (4)
14.	Rheumatic heart disease	5.4% (3)

Conclusion: Moldovan cohort of young adults with ischemic stroke presents the same risk factor profile as older adults with the trigger role of infections in the stroke onset.

Disclosure: Nothing to disclose

EPR1036

T.E.D.R.A.S.- Trial: Transesophageal Echocardiography as Dysphagia Risk in Acute Stroke

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Background and aims: Dysphagia is common in patients with acute stroke and deteriorates the overall outcome. Transesophageal echocardiography (TEE) is routine examination in the diagnostics of stroke etiology. In cardiac surgery it is known as cause of postoperative dysphagia. The prevalence of dysphagia in acute stroke patients undergoing TEE is unknown. The aim of T.E.D.R.A.S. was to assess the influence of TEE on swallowing in acute stroke patients.

Methods: T.E.D.R.A.S., included 34 patients in 2 groups: 19 in the intervention group (IG), 15 in the control group (CG). Flexible endoscopic evaluation of swallowing (FEES) analyzed swallowing in the IG (1) one day before TEE, (2) max. 2-4 hours after TEE, (3) 24 hours after TEE. In the CG FEES was performed on 3 consecutive days with TEE after the last FEES. Validated scores assessed dysphagia severity. Difference scores were built from pre to post TEE for all dysphagia measures.

Results: In between group comparison dysphagia measures increased in the IG immediately after TEE and 24 hours after TEE in penetration-aspiration-score for saliva ($p < 0.001/p = 0.007$), for small liquid bolus ($p = 0.009/p = 0.059$) and for large liquid bolus ($p = 0.009/p = 0.025$). Secretion severity score is increased immediately after TEE and 24 hours after TEE in the IG ($p \leq 0.001/p \leq 0.001$) as well as the residue severity score for saliva, liquid boli and for puree.

Conclusion: The results of T.E.D.R.A.S. indicate that TEE has a negative influence on swallowing in acute stroke patients.

Disclosure: Nothing to disclose

EPR1037

Faster logistics of thrombolytic treatment in stroke centers with prenotification. Findings from a nation-wide survey in the Czech Republic.

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Background and aims: Acute ischemic stroke (AIS) patients with pre-hospital prenotification are treated faster with intravenous thrombolysis (IVT) than patients arriving to hospital without prenotification. However, it is not clear how much pre-hospital and in-hospital logistical steps contribute to the delay of thrombolytic treatment. We sought to investigate whether there are differences in in-hospital logistics of stroke centers with prenotification.

Methods: Logistical processes in Czech stroke centers from January 1st, 2017 to March 31st, 2018 were assessed by a questionnaire. Door-to-needle times (DNT) were obtained from SITS registry. The results of the study were analyzed by descriptive statistics.

Results: All 45 stroke centers in the Czech Republic responded. Due to one reorganization in 6 centers and 2 reorganizations in 2 centers, 55 center-datasets were analyzed. Prenotification was reported in 50 (91%) centers. Following differences between stroke centers with prenotification versus those without prenotification were found: median (IQR) DNT 26 vs. 40 (21-30 vs. 34-42) minutes, patients' admission to CT in 18 vs. 0 (36 vs. 0%) centers, admission to ER in 22 vs. 4 (44 vs. 80%) centers, admission to out-patient office in 10 vs. 1 (20% vs. 20%) center, no patients' transfers before IVT in 16 vs. 0 (32 vs. 0%) centers, and IVT initiation on CT table in 34 vs. 0 (68 vs. 20%) centers.

Conclusion: Stroke centers with prenotification had faster logistics of thrombolytic pathway. Prenotified AIS patients arriving to the hospital were more likely to be admitted to pre-prepared CT and have IVT initiated on CT table.

Disclosure: Supported by the project no. LQ1605 from the National Program of Sustainability II (MEYS CR).

EPR1038

Safety and efficacy of percutaneous transluminal angioplasty for atherosclerotic stenosis of vertebral artery origin

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Background and aims: The aim was to find out how the presence of severe impairment of other cerebral feeding arteries and concomitant carotid artery stenting (CAS) affected the periprocedural risk and long-term effect of balloon angioplasties for atherosclerotic stenosis of vertebral artery origin (VAO).

Methods: We used a retrospective analysis of consecutive balloon angioplasties for $\geq 70\%$ VAO stenosis. The patients were divided into groups with an isolated VAO stenosis and multiple stenoses. We investigated the frequency of periprocedural complications in the 1st 72h and the risk of developing restenosis and ischemic stroke/transient ischemic attack (TIA) during the follow-up period.

Results: In the set of 66 patients aged 66.1 ± 9.1 years, concurrent severe polystenotic impairment was present in 56 (84.8%) patients. 21 (31.8%) patients received endovascular treatment for a stenosis on one or more other arteries in addition to VAO stenosis (15 of them had CAS). In the periprocedural period, none of the patients suffered from ischemic stroke or died. 1 case of TIA in the carotid artery territory (1.6%) occurred in the polystenotic group with concurrent CAS. During the mean follow-up period of 36 months, we identified 8 cases (16.3%) of $\geq 50\%$ asymptomatic VA restenosis. In addition, 4 (8.9%) cases of ischemic stroke occurred in the polystenotic group.

Conclusion: The presence of a severe polystenotic impairment or concomitant CAS had no adverse effects on the overall low periprocedural risk of balloon angioplasty of VAO stenosis or the risk of developing restenosis during the follow-up period.

Disclosure: Study was supported in part by the Ministry of Health of the Czech Republic (DRO – UHHK 00179906) and Charles University, Czech Republic (PROGRES Q40).

EPR1039

Risk of post-operative ischemic lesions after carotid endarterectomy and stenting

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Background and aims: Silent infarctions is frequently detected after carotid endarterectomy (CEA) or carotid stenting (CAS). Aim was to compare risk of new brain infarctions between CEA and CAS in 2 time periods.

Methods: All patients with ICA stenosis $>70\%$ indicated for CEA or CAS in 3 grant projects in 2 time periods (2004-2008 and 2014-2018) were included to the post-hoc analysis. Changes in the surgery (different plaque extraction technique and perioperative heparin dose) and stenting (different stent type, distal protection) were implemented in the 2nd time period. Brain diffusion-weighted magnetic resonance imaging (DW-MRI) was performed prior to intervention and 24h after intervention for new infarctions detection.

Results: 73 patients (47 males; age 64.9 ± 7.0 years) underwent CEA and 77 patients (58 males; age 65.6 ± 7.3 years) underwent CAS in the 1st time period (2004-2008); 247 patients (177 males; age 67.4 ± 7.5 years) underwent CEA and 121 patients (93 males; age 70.5 ± 7.6 years) underwent CAS in the 2nd time period (2014-2018). New infarctions were found after CEA in 18 (24.7%) patients in the 1st time period and in 37 (15.0%) in the 2nd time period ($p=0.05$). New infarctions were found after CAS in 38 (49.4%) patients in the 1st time period and in 34 (28.1%) patients in the second time period ($p<0.01$). New infarctions on control MRI were found more frequently in patients after CAS compared to CEA in both time periods ($p<0.01$).

Conclusion: Changes in the intervention techniques improve the risk of new brain infarctions after CEA/CAS. CEA had lower silent brain infarction risk compared to CAS.

Disclosure: Supported by the Ministry of Health of the Czech Republic grant No. NV19-04-00270.

EPR1040

In-thrombus Thrombin Activity in Acute Ischemic Stroke – New Diagnostic Marker of Cardio Embolic Origin

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Background and aims: Identifying stroke subtype is essential for the 2ndary prevention of ischemic stroke, specifically differentiating cardio embolic from other causes. Histological profiling of clots retrieved by endovascular intervention has limited yield. This study measured for the 1st time thrombin secreted from retrieved clots.

Methods: Clots were retrieved from 68 patients with acute ischemic stroke that were classified by standard criteria into 18 patients with proven atrial fibrillation (AF), 15 patients with atherosclerotic origin and 35 with other, including cryptogenic causes). Standard samples from the clots were assayed for thrombin secretion and for general histology. A fluorescent substrate thrombin assay measured levels secreted from the clots every hour.

Results: Clots of AF origin secreted decreasing levels of thrombin with time in contrast to increasing levels of thrombin secreted by atherosclerosis origin thrombi ($p < 0.0001$ by repeated measures ANOVA). Using a summary measure of the ratio of thrombin secreted after 7/1 hours a diagnostic sensitivity of 100% and specificity of 73% were found for the present data. The group of cryptogenic stroke were indistinguishable from the AF group.

Conclusion: These results suggest thrombin secretion pattern from a clot may serve as a novel marker which will enable a fast, sensitive and specific diagnosis of stroke etiology thus providing an early and appropriate secondary prevention therapy.

Disclosure: Nothing to disclose

EPR1041

Early FLAIR Enhancement in Reversible Cerebral Vasoconstriction Syndrome

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Background and aims: Reversible cerebral vasoconstriction syndrome (RCVS) is a relatively new clinical and neuro-radiological entity, with potentially devastating ischemic outcomes. No predictive marker for syndrome severity or ischemic outcome exists up to date.

Methods: In this retrospective cohort of 18 female patients admitted to an acute stroke unit in 2018-2019, we report an early MRI marker of posterior leptomeningeal enhancement in the absence of CSF pleocytosis.

Methods: In this retrospective cohort of 18 female patients admitted to an acute stroke unit in 2018-2019, we report an early MRI marker of posterior leptomeningeal enhancement in the absence of CSF pleocytosis.

Results: 12 out of 15 (80%) RCVS patients that underwent brain MRI exhibited this sign during the disease course. The degree of enhancement was scored and had shown a trend of positive correlation ($p=0.04$, Pearson's correlation analysis, $R^2=0.3$) to RCVS severity depicted by radiological and clinical syndrome extent (number of affected vessels, ischemic stroke, seizure or subarachnoid hemorrhage). In the 2 most devastating cases, early leptomeningeal enhancement preceded by days the development of diffuse vasoconstriction.

Conclusion: This phenomenon may be of substantial clinical utility in early diagnosis and treatment in RCVS, as well as in elucidation of this syndrome's pathophysiology.

Disclosure: Nothing to disclose

EPR1042

Outcome of patients treated by mechanical thrombectomy for anterior circulation strokes during off-hours

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Background and aims: At off-hours, stroke patients have higher mortality and disability rates. The question of whether this off-hour effect exists in patients treated with mechanical thrombectomy (MT) remains unknown.

The aim of our study is to compare outcomes of patients treated by MT for cerebral ischaemia at off-hours vs. at working time.

Methods: We prospectively included consecutive adults who underwent MT alone or in combination with recombinant tissue – plasminogen activator (rt-PA) for a large-vessel occlusion in the anterior circulation between 2015 and 2019 in 12 stroke units. They underwent magnetic resonance imaging-scans at admission and 22-36 hours later. We evaluated outcomes at 3 months with the modified Rankin scale (mRS). To classify patients we used the time of groin puncture.

Results: We included 1,179 patients (631 women, 53.5%; mean age 72 years; median baseline NIHSS 17; 680 treated at off-hours, 57.7%; 734 treated with rt-PA, 62.3%; median delay between stroke recognition and end of MT 281 minutes). No patient was lost to follow-up. At 3 months, patients treated at off-hours did not differ for the proportion of patients with a mRS 0-1 (adjusted odds ratio [adjOR] 0.91; 95% confidence interval [CI] 0.68-1.22), or 0-2 (adjOR 0.92; 95%CI 0.68-1.23), and death (adjOR 1.24; 95%CI 0.89-1.73).

Conclusion: The slight tendency towards worse outcomes at off-hours was not significant. Therefore, off-hours effects can be minimized by a coordinated organisation of stroke care.

Disclosure: Unité Inserm U1171

EPR1043

Laboratory examinations – lessons learned from 120 cases treated with idarucizumab in Germany

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Background and aims: Recently we have shown that idarucizumab application in acute stroke patients treated with dabigatran improves clinical outcome parameters. In this retrospective series of 120 cases positive effects of dabigatran reversal could be documented regarding mortality and modified Rankin scale in patients with acute hemorrhagic stroke (aHS). At the same time, individuals with acute ischemic stroke (aIS), regained eligibility for intravenous thrombolysis, thereby improving substantially in NIH Stroke Scale (NIHSS).

Methods: We asked all German neurological/neurosurgical departments to contribute their retrospective data collected from administration of idarucizumab following product launch in January 2016 to June 2018.

Results: In aHS, 15 of 40 patients were on dabigatran 150mg bid, while 25 took 110mg bid. CrCl was above 50ml/min in all cases while thrombin time (TT) upon admission was elevated substantially in almost all cases examined. aPTT was normal in 79.5%. In aIS, 32 patients received 150mg, 48 received 110mg dabigatran bid. The vast majority of patients with ischemic stroke had a CrCl above 50ml/min. TT was prolonged above 35 seconds in 91.4% of cases while aPTT values were normal in 48.1% of patients.

Conclusion: These data underline the necessity to prescribe the appropriate dosage recommended in the prescription protocol to all patients. Furthermore, global hemostasis parameters like aPTT again prove to be not useful for therapeutic decisions. Finally, inclusion of TT values into emergency laboratory examination in patients with acute stroke under dabigatran is helpful to identify patients with impaired hemostasis potentially benefitting from idarucizumab application.

Disclosure: Nothing to disclose

Child neurology/developmental neurology; Clinical neurophysiology

EPR1044

Blink reflex habituation in patients with frontotemporal dementia: a preliminary study

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Background and aims: Blink reflex has a plethora of research applications including neurodegenerative disorders, migraine, psychiatric disorders and more. The aim of the present study is to test the value of the R2 habituation in patients diagnosed with frontotemporal dementia (FTD) in comparison to healthy individuals.

Methods: 10 healthy controls and 7 FTD patients participated in the study. Electrical stimulation was applied to the supraorbital (SO) nerve with stimulus intensities ranging from 15 to 25mA. Surface EMG responses were recorded from the orbicularis (Medtronic Keypoint 31A02). Paired stimuli at interstimulus intervals (ISIs) of 100, 200, 400 and 769ms were separated by 15 to 30s to minimize habituation. For each ISI we calculated the R2 amplitude ratio (expressed as R2 peak-to-peak amplitude of the conditioned response, divided by the R2 peak-to-peak amplitude of the unconditioned response). We evaluated the R2 habituation index by plotting the R2 amplitude ratio for all the tested ISIs.

Results: At ISI of 100ms the mean value of the R2 amplitude ratio was 0.740 for FTD patients and 0.276 for healthy controls, which was statistically different ($p=0.007$), and at ISI of 200ms the mean value of the R2 amplitude ratio was 0.737 for FTD patients and 0.327 for controls, which was also significantly different ($p=0.017$). No significant difference was found at ISIs of 400ms and 769ms.

Conclusion: FTD patients show a marked lack of habituation of the R2 response at high frequency paired stimulation. This might indicate a deficient cortico-bulbar control in this patient group.

Disclosure: Nothing to disclose

EPR1045

Influence of chronic radiofrequency electromagnetic fields exposure on sleep structure in preterm neonates: preliminary results

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Background and aims: While hospitalized, preterm neonates are exposed to radiofrequencies (RF). Disruption of sleep mechanisms by RF exposure may disrupt their neurophysiological development. We investigated the influence of chronic RF exposure on sleep structure in preterm neonates.

Methods: Individual, continuous measurements of RF levels were performed on 25 preterm neonates (gestational age: 29 ± 2 wk, birth weight: $1,247\pm 367$ g) during the 1st 3 weeks after birth. An overnight polysomnography was performed on the last day of measurements. Individual RF exposure level over the whole recording period was expressed as the median (0.03 ± 0.01 V/m), the 99.9th percentile (P99.9, 0.1% of the highest values, 0.67 ± 0.29 V/m) and the highest value (maximum, 1.75 ± 0.66 V/m). Linear relationships were computed between RF exposure levels and sleep structure parameters: frequency, duration and percentage of sleep stages and wakefulness episodes.

Results: No significant relationship was found between the median level and sleep structure parameters. P99.9 was associated positively with rapid eye movement (REM) sleep frequency ($r^2=0.207$, $p=0.0223$) and negatively with both non-REM (NREM) proportion ($r^2=0.215$, $p=0.0195$) and the NREM longest episode ($r^2=0.168$, $p=0.0422$). The highest exposure value was also associated positively with REM sleep frequency ($r^2=0.165$, $p=0.0441$) but negatively with the average duration of REM episodes ($r^2=0.209$, $p=0.0217$) and the REM longest episode ($r^2=0.540$, $p=0.0054$).

Conclusion: These preliminary results suggest that sleep structure of preterm neonates is altered when exposed to chronic, low levels of RF during early life. Such alterations may depend on exposure levels. This finding raises the question of the repercussions of these sleep disturbances on the child's neurobehavioral and physiological outcomes.

Disclosure: Nothing to disclose

EPR1046

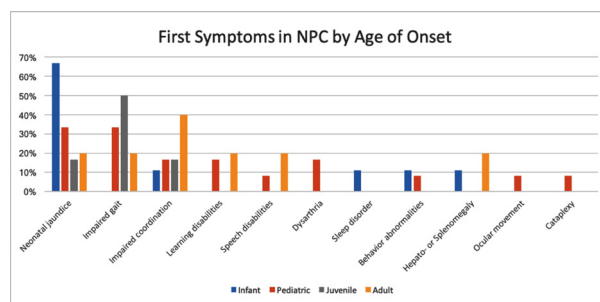
First symptoms in Niemann-Pick disease type C observed by family members: Clues for diagnosis?

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Background and aims: To comprehensively characterize the 1st symptoms noticed by family members in patients with Niemann-Pick type C (NPC).

Methods: 36 family members from 5 countries (Germany, UK, Greece, Slovakia, Czech Republic) responded to a paper or online questionnaire so far.

Results: Median age was 17 years (n=36, 49% F; interquartile range (IQR) 10-19), the age at the diagnosis was 6 years (IQR 1-16). Time from 1st symptom till diagnosis (MTTD) was 1 year (IQR 0-2.5), but varied largely. The infantile-onset MTTD was 1 year (IQR 0-1) and neonatal jaundice was the most frequent 1st symptom occurring in 67% of patients. This was also true for pediatric-onset MTTD (IQR 0-2.5) and impairment of gait was the most common 1st symptom (33%). In the juvenile-onset patients, MTTD was 0 years (IQR 0-16) and the most frequent symptom was impairment of gait (50%). In the adult group, MTTD was 2 years (IQR 0-21) and impairment of coordination was the most common symptom. Cataplexy was the most common 1st symptom observed by family versus physician (86% vs. 7%). Vertical supranuclear gaze palsy (VSGP) was present in 81% of patients, noticed in 54% by physician and in 42% by family. Hepato- or splenomegaly was most frequently 1st noticed by a physician than family (83% vs. 8%).



First Symptoms in NPC by Age of Onset

Conclusion: We present preliminary data of a multinational cohort on first symptoms observed by the family before the diagnosis of NPC was made. Hereafter, this essential knowledge may help to establish the diagnosis earlier and, thus, to faster allocate treatment.

Disclosure: Nothing to disclose

EPR1047

Single-fiber electromyography as an integral part of the diagnostic work-up of myasthenia gravis

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Background and aims: Stimulation single-fiber electromyography (sSF-EMG) is currently recognized as a more sensitive method than repetitive stimulation (RS) for the diagnosis of myasthenia gravis (MG), but presents a higher demand for technical expertise. We aimed to evaluate the diagnostic yield of the introduction of sSF-EMG in the everyday work-up of patients with suspected MG in a tertiary centre.

Methods: Patients submitted to sSF-EMG from 2016 to 2018 in our centre's Neurophysiology Department were retrospectively reviewed, and their clinical and electrophysiological data was collected.

Results: 93 patients met the inclusion criteria. 30 of those patients had the final diagnosis of MG by their attending neurologist, of whom: 11 presented with an altered RS and sSF-EMG (10 with clear criteria, 1 with borderline criteria), of which 9 were seropositive, with 3 ocular forms and 8 generalized forms; 5 presented with an altered sSF-EMG and normal RS (4 clear criteria and 1 borderline criteria), all of them seronegative, with 4 ocular forms and 1 generalized form; 14 patients presented with normal sSF-EMG and RS, of which 7 were seropositive, with 8 ocular forms and 6 generalized forms. 6 of these 7 seropositive patients were under immunosuppression at time of the exam. The 7 seronegative patients without neurophysiological alterations were diagnosed based on clinical presentation and response to treatment with pyridostigmine/immunosuppressant agents, and presented with less typical cases of MG. 2 patients with altered sSF-EMG presented diagnoses other than MG.

Conclusion: sSF-EMG demonstrated an increased diagnostic benefit compared with RS in patients with seronegative MG.

Disclosure: Nothing to disclose

EPR1048

Single EEG with standardised interpretation a specific predictor of poor outcome after cardiac arrest in everyday clinical setting

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Background and aims: A single routine EEG with standardised interpretation has been shown, in a clinical trial, to predict poor outcome after cardiac arrest with 100% specificity. We aimed to replicate this finding in a routine clinical setting and compare the predictive value of EEG to somatosensory evoked potentials (SSEP).

Methods: Consecutive patients after primary cardiac arrest who had not regained consciousness after therapeutic hypothermia were included in the study. A standard 20-minute EEG was performed during working hours, described according to ACNS guidelines and categorised as highly malignant, malignant or benign as proposed by Westhall et al. Retrospectively EEG categorisation was revised by dedicated EEG specialists. Other investigations were performed at the attending physician's request. Poor outcome was defined as best Cerebral Performance Category 3-5.

Results: Included in the analysis were 76 patients, 63 had a poor outcome. EEG was recorded on average 3.8 (2-7) days after cardiac arrest. SSEP were performed in 65 patients. All patients with either absent SSEP or very malignant EEG had a poor outcome (100% specificity and 100% positive predictive value) with either original or specialist-revised EEG interpretation. Sensitivity for predicting poor outcome of very malignant EEG was 38%, of absent SSEP 31% and for the combination of both 47%.

Conclusion: Using standardised interpretation, EEG has 100% specificity in predicting poor outcome after cardiac arrest, same as SSEP. Combining both methods improves the proportion of patients correctly recognised as having poor prognosis. The described use of EEG is feasible in everyday clinical care.

Disclosure: Nothing to disclose

EPR1049

Use of sw LORETA qEEG to study the role of default mode network (DMN) in empathy processing

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Introduction: The number of studies using swLORETA qEEG technologies in neurobehavioral science has increased in recent years. The interest for these methodologies relies in their high-temporal resolution and greatly improved spatial resolution.

The brain's default mode network (DMN) include the posterior cingulate cortex (PCC) and medial prefrontal cortex (MPFC). DMN is the most extensive of the 3 major neural networks in the human brain.

Empathy is the ability to identify with another person's feelings or thoughts based on memory and self-referential mental simulation. The DMN in particular is related to self-referential empathy.

Objective: Using swLORETA qEEG to study whether individual differences in the core components of empathy are related to DMN effective connectivity (EC).

Methods: In order to study the possible neural mechanisms underlying empathy, we investigated the EC of the DMN in subjects from a general population. swLORETA qEEG imaging data were acquired from 19 subjects during a resting state and while watching an image with empathetic content. An independent component analysis was used to identify the DMN. Differences in EC strength were compared between the participants.

Results: The results obtained allow us to distinguish 2 groups. The low-empathy group showed lower EC of the MPFC (Brodmann areas 10, 11) and PCC (Brodmann areas 29, 31) within the DMN, compared to the high-empathy group. The results of the study suggest that empathy is related to EC of the MPFC/PCC within the DMN.

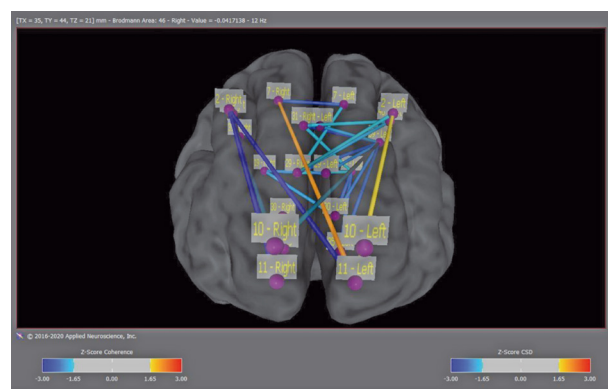


Fig.1 Effective connectivity in the DMN in a participant from the low-empathy group

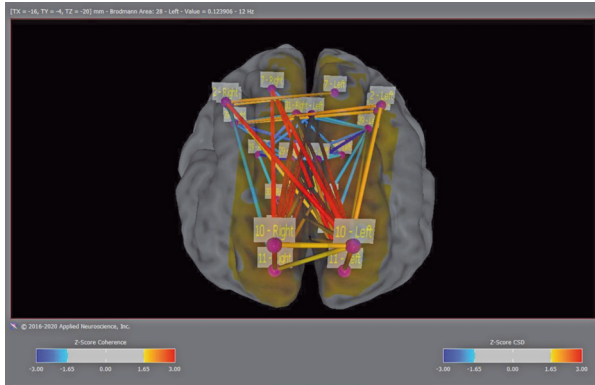


Fig.2 Effective connectivity in the DMN in a participant from the high-empathy group

Conclusion: Functional decreases in EC among low-empathy subjects may reflect an impairment of self-referential mental simulation.

Disclosure: Nothing to disclose

EPR1050

The improvement in diagnosis and epilepsy managing in children with progressive myoclonus epilepsy during the last decade – a single tertiary center experience

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Background and aims: The aim is to explore if diagnosis and epilepsy managing in children with progressive myoclonus epilepsy (PME) have been improved during last ten years.

Methods: The retrospective study included children with PME treated during 25-year period, divided in 2 groups: treated before December 2010 (I), and after, up to December 2019 (II). Only patients aged 0.2-18 years, with proven PME diagnosis by enzyme, genetic and/or histopathology investigations were included. Evaluated parameters were: etiology, seizure onset, the period from disease onset to diagnosis, and, as a measure of epilepsy control -SE frequency and recurrence rate. Statistical analysis included tests: Chi-Square, Mann-Whitney and ANOVA, using SPSS version 25.

Results: The study included 51 patients with PME, 27 in I and 24 in II group. The underlying diseases were: NCL (30), Gaucher (5), Niemann-Pick (4), mitochondrial (4), Lafora (3), Krabbe (2), KCNC1 gene mutation (2). Average duration from initial symptoms to diagnosis was 3.2 ± 3 years (I) vs. 1.4 ± 0.9 years (II). In 35 patients (68.6%) seizure was among initial symptoms. Both SE frequency 55.5% (15/27) vs. 37.5% (9/24), and recurrence rate (66.7% vs. 22.2%) were higher in the 1st group showing tendency towards, but not statistically significant difference.

Conclusion: The diagnosis and epilepsy managing in children with PME improved during the last decade. Earlier genetic diagnosis, its impact on appropriate antiseizure medications, together with better education of parents/caregivers as well as availability of effective prehospital rescue medications contributed to significantly decreased frequency and recurrence rate of SE.

Disclosure: Nothing to disclose

EPR1051

Hyperconnectivity and network rearrangement as a predictive biomarker of neurodegenerative dementia: results from a multicenter EEG study on Frontotemporal Dementia and Alzheimer's disease.

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Background and aims: EEG studies of functional connectivity have provided new measures of brain organization in neurodegenerative diseases, especially Alzheimer's disease (AD). We aim to study the macroscale modifications occurring in another neurodegenerative condition, Frontotemporal dementia (FTD), in comparison with AD.

Methods: Mutual information (MI) (measure of functional connectivity) and MI-based graph theory analysis (topological network descriptors) were measured on resting state EEG signals recorded in the prodromal stage of dementia, at onset of dementia and at 3 years follow-up in 18 FTD and 18 AD in comparison with 20 healthy controls.

Results: MI showed hyperconnectivity in FTD and AD vs. controls at the prodromal stage of dementia. Main hubs, present in controls, were lost in both disease groups, and substituted by provincial hubs in frontal leads in FTD and in parieto-occipital leads in AD. FTD and AD networks appeared to be rearranged in new small worlds.

Conclusion: Hyperconnectivity, increased small world propensity and local efficiency in salient areas of the neurodegenerative process of FTD and AD could be used as an early diagnostic biomarker of neurodegenerative dementia.

Disclosure: Nothing to disclose

EPR1052

Cognitive task-related functional connectivity alterations in temporal lobe epilepsy

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Background and aims: We investigated cognitive task-related functional connectivity (FC) in patients with temporal lobe epilepsy (TLE). Using visual 3 stimulus paradigm we studied cognitive large-scale networks and impact of TLE on connectivity outside the temporal lobe.

Methods: High density EEG of 19 TLE patients with hippocampal sclerosis and 10 healthy controls (HC) were recorded during performing paradigm. Scalp data were reconstructed into the source space and FC was measured using phase lag index. Correlating with the neuropsychological data, possible compensatory mechanisms were investigated.

Results: Significant changes were found in FC of regions outside the epileptogenic network, most significantly between structures involved in the visual stimulus processing. These changes were more widespread in left temporal lobe epilepsy (LTLE). There were no significant differences in task performance in comparison with HC; implying that there must be compensatory mechanism. When correlated with neuropsychological data we found that mainly the right hemisphere was responsible for compensating for network alterations.

Conclusion: Our findings confirm the hypothesis that LTLE is the more pervasive form of disease. Even though the network alterations in LTLE are more severe, compensatory mechanisms reduce the impact of epilepsy on cognitive functions. Our suggestion of the compensatory role of the non-dominant hemisphere in TLE is novel.

Disclosure: Nothing to disclose

EPR1053

The changes of theta event-related synchronization/desynchronization in patients with post-operative cognitive dysfunction after on-pump coronary artery bypass grafting

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Background and aims: The risk of neurological complications after cardiac surgery remains currently significant. The aim of the study was to investigate the theta event-related synchronization/desynchronization (ERS/ERD) changes during visual selection task in patients after on-pump coronary artery bypass grafting (CABG) with and without postoperative cognitive dysfunction (POCD).

Methods: The study included 32 patients who underwent on-pump CABG, mean age 57.2 ± 6.08 years. All patients underwent extended neuropsychological testing and computer electroencephalography 3-5 days before and at 7-10 days after CABG. The POCD was determined according to the criterion: 20% decrease of cognitive indicator compared to one at baseline on 20% of the neuropsychological battery tests. Statistical processing was performed using the STATISTICA 10.0.

Results: The frequency of POCD was 69 % (22 patients). At the 7-10 days after CABG, the POCD patients had less pronounced theta ERD in the left fronto-central regions during the stage of 200-400ms in comparison to patients without cognitive decline. Only the patients without POCD had a decrease of event-related theta activity in the left parietal leads compared with baseline. During the stage of 600-800ms, the POCD patients also had less theta ERD in both fronto-central and parietal regions of right hemisphere compared to patients without POCD.

Conclusion: The patients with POCD after CABG had the pathological changes in the event-related theta activity. An analysis of event-related synchronization/desynchronization can be used as objective marker of POCD.

Disclosure: The reported study was funded by RFBR and Kemerovo region, project number 20-415-420005.

EPR1054

Internet addiction in Central Siberia urban adolescents: the prevalence and comorbidity with recurrent headache

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Background and aims: Numerous studies have convincingly demonstrated Internet addiction (IA) comorbidity with a broad range of psychopathologic conditions such as depression and anxiety. Psychosomatic symptoms prevalence and types in Internet-addicted adolescents is not studied well. We aimed to investigate IA prevalence and its comorbidity with recurrent headache in Central Siberia urban adolescents.

Methods: 2950 urban Siberian (Krasnoyarsk) school-based adolescents (aged 12-18; boys/girl ratio 1348/1602) were tested with Chen Internet Addiction Scale (CIAS). Based on the CIAS, score Internet users were categorized into three groups: adaptive Internet users (AIU-1) (scoring 27-42); maladaptive Internet users (MIU) (scoring 43-64); and pathological Internet users (PIU) (scoring ≥ 65). Adolescents were also asked about headache presence/frequency and according to answer were divided into 3 groups: (1) No headache group, (2) frequent episodic headache with episodes frequency 1-15 per month, and (3) chronic headache with episodes frequency >15 per month. Chi-square test was used.

Results: The prevalence of AIU, MIU, and PIU were 50.4%, 42.8%, and 6.8%, respectively. Significant positive associations were detected between CIAS scores and headache, especially for chronic headache group ($p_{1-2}=0.0047$, $p_{1-3}<0.0001$, $p_{2-3}=0.0008$, where 1-AIU, 2-MIU, 3-PIU; Fig. 1).

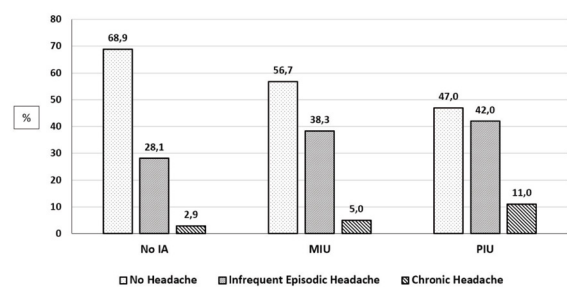


Fig. 1. Recurrent headache presence/frequency in Internet addicted adolescents.

Conclusion: The prevalence of Internet addiction (PIU) in Central Siberia urban adolescents is 6.8%. Internet addiction group have significantly higher headache frequency that may be explained by the presence of common risk factors such as emotional stress, depression, and anxiety.

The reported study was funded by RFBR according to the research project № 18-29-22032\18.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 1

EPR1055

Imaging correlates of action slowing in cortical neurodegenerative diseases

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Background and aims: Although action slowing has been recently identified as a leading deficit in early stages of degenerative cortical neurocognitive disorders (NCD), its mechanism and imaging correlates remains unknown. The objective was to determine imaging correlates using multivariate voxel based morphometry (VBM) of action slowing (focusing on simple reaction time (SRT)) in patients with cortical NCD.

Methods: We included 30 patients (16 mild NCD and 14 major NCD (Alzheimer's disease (n=9), Lewy body disease (n=3) and behavioral frontotemporal degeneration (n=2)) with a MMSE \geq 20, in Amiens academic memory center. Attentional and sensory-motor components of SRT (5th (C5) and 50th (C50) SRT percentiles z scores) were extracted using individual distribution analysis and age- and education adjusted using normative data. Following conventional VBM analysis ($p < 0.001$), significant clusters of voxels were submitted to multivariate linear general model according to a validated method.

Results: SRT were significantly slower in patients. SRT C5 was negatively associated with gray matter density of the right dorsolateroprefrontal cortex and the total intracranial volume (TIV) (model $R^2=0.287$, $p=0.004$). SRT C50 was negatively associated with the gray matter density of the left supramarginal region and the TIV (model $R^2=0.468$, $p < 0.001$).

Conclusion: Our results support action slowing at an early stage of cortical degenerative diseases and indicate that sensory-motor and attentional component depend on different structures: right DLPFC and left supramarginal. Right DLPFC role supports our earlier findings in fMRI activation study; the contribution of the left supramarginal, will be further explored using additional structural and functional connectivity analyses.

Disclosure: Nothing to disclose

EPR1056

Increased sensitivity to uncertainty guides decision-making in hippocampal dysfunction

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Background: The hippocampus plays an important role in many functions including memory and spatial cognition. However, its contribution to decision-making and valuation is under-investigated and yet to be established.

Objective: To determine the hippocampal contribution to information gathering behaviour and decision-making under uncertainty.

Methods: 17 patients with focal bilateral hippocampal atrophy (mostly as a result of autoantibody-associated limbic encephalitis) and 30 healthy matched controls underwent a novel behavioural task to investigate information gathering and decision-making under uncertainty, together with standard screening cognitive measures of memory and executive function.

Results: When actively gathering information to maximise rewards and reduce uncertainty, patients with hippocampal atrophy gathered significantly more information than controls prior to making a decision. This effect persisted when the need for memory was eliminated: when making decisions to accept or reject potential rewards in exchange for tolerating uncertainty, patients with hippocampal damage weighted uncertainty more, resulting in lower acceptance of the high-reward low-uncertainty offers. The results did not change after controlling for the differences in cognitive screening scores between patients and controls.

Conclusion: The results point to a potential role of the hippocampus in weighing up uncertainty against rewards. They indicate that the hippocampus and its functional networks might be involved in the psychopathology of behavioural syndromes that could result from deficits in processing of uncertainty and rewards, such as anxiety, an important feature of many brain disorders.

Disclosure: Nothing to disclose

EPR1057

Do deficits in Mitochondrial Spare Respiratory Capacity contribute to Neuropsychological changes seen in Alzheimer's disease (AD)?

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Background and aims: In clinical settings, AD is defined by characteristic deficits in neuropsychological testing supported by amyloid/tau biomarkers and neuroimaging abnormalities. The cause of neuropsychological changes is unknown. Tau deposition correlates with, but does not fully account for all neuropsychological impairments. Mitochondrial spare respiratory capacity (MRSC) is lowered in AD patient fibroblasts. This study investigates if fibroblast mitochondrial functional correlates with neuropsychological/neuroimaging changes in AD.

Methods: 10 AD patient and 10 control fibroblast were assessed. ATP and extracellular lactate were measured using luminescent and fluorescent protocols. Mitochondrial membrane potential (MMP) was measured using tetramethylrhodamine. Mitochondrial respiration and glycolytic function were measured using a Seahorse XF Analyzer. Neuropsychological testing and brain structural MRIs were undertaken on all participants. Correlations were performed between MMP, MRSC and neuropsychological/MRI AD markers.

Results: Reductions in delayed ($p<0.0001$), immediate recall ($p<0.0001$), semantic fluency ($p<0.0001$), phonemic fluency ($p=0.0033$) and MMSE ($p=0.0009$) scores were seen in AD patients. Controlling for age, education and brain reserve; left hippocampal ($p=0.001$), left parietal ($p=0.002$), right parietal ($p=0.001$) and anterior medial prefrontal cortical ($p=0.017$) gray matter volumes were reduced. AD fibroblasts had reduced MMP ($p=0.001$), MRSC ($p<0.0001$), glycolytic reserve ($p=0.05$), and extracellular lactate ($p<0.05$) levels. MRSC and MMP correlated significantly with immediate recall ([MRSC, $p=0.0041$], [MMP, $p=0.0115$]), delayed recall ([MRSC, $p=0.0013$], [MMP, $p=0.0138$]) and semantic memory ([MRSC, $p=0.0039$], [MMP, $p=0.009$]) tests. The correlations between MRSC and neuropsychological measures remained after controlling for age, education and brain reserve. No correlations were seen with grey matter volumes.

Conclusion: In-depth metabolic analysis of sporadic AD fibroblasts identifies functional abnormalities that correlate with neuropsychological features of AD.

Disclosure: This work has not received commercial support

EPR1058

TRIANA TEST: A preliminary evaluation of a new logical memory test

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Background and aims: "Triana Test" (TT) is a new logical memory test based on the exciting love story between a flamenco dancer and a Japanese student. The aim was to study the diagnostic accuracy of TT to discriminate patients with Amnesic Mild Cognitive Impairment (aMCI) from normal controls (NC).

Methods: A phase I validation study. TT was administered to aMCI patients ($n=38$; memory complaints corroborated by a reliable informant, a total score on the Memory Associative Test of the district of Seine-Saint-Denis (TMA-93) $\leq 10^{\text{th}}$ percentile, and no functional impairment) and NC ($n=55$; no memory complaints, a total score on TMA-93 $\geq 25^{\text{th}}$ percentile, and no functional impairment). 4 variables were scored (maximum score for each=12 points): immediate free recall (IFR), immediate cued recall (ICR), deferred free recall (DFR), and deferred cued recall (DCR). The diagnostic accuracy of TT was estimated by the area under curve (AUC) using ROC curve analysis.

Results: For TT, scores on IFR (6.2 ± 2.2 vs 3.4 ± 2.4 , $p<0.001$), ICR ($9.8\pm 1.8\pm 7.7\pm 2.6$, $p<0.001$), DFR (6.8 ± 2.6 vs 2.7 ± 2.7 , $p<0.001$), and DCR (9.8 ± 1.9 vs $7.6\pm 7.6\pm 2.6$, $p<0.001$) were significantly lower in aMCI group vs NC group. The ROC curve analysis determined an AUC of 0.80 (95% CI, 0.70-0.89) for IFR, 0.74 (95% CI, 0.64-0.84) for ICR, 0.84 (95% CI, 0.76-0.92) for DFR, and 0.74 (95% CI, 0.64-0.84) for DCR, to discriminate aMCI patients from NC.

Conclusion: TT showed a good diagnostic accuracy to distinguish aMCI patients from NC.

Disclosure: Nothing to disclose

EPR1059

The Association of Personality Dimensions with Quality of Life in Parkinson's disease patients with motor fluctuations

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Background and aims: As in most chronic disease, Quality of Life (QoL) is affected in Parkinson's disease (PD) patients. Moreover, it was shown that both physical and psychological health are impacting QoL, therefore personality dimensions are probably also associated with QoL in chronic neurological diseases such as PD. We have thus studied the association between different QoL scores and personality dimensions in fluctuating PD patients waiting for Deep Brain Stimulation of the Sub-Thalamic Nucleus (DBS-STN).

Methods: Data from all PD patients awaiting DBS-STN included in the French multicentric cohort study PREDI-STIM were used. The "Temperament and Character Inventory" (TCI) and the "Parkinson Disease Questionnaire 39" (PDQ-39) were filled before surgery. Adjusted univariate generalized linear regression models were used to study the association between PDQ-39 scores and TCI dimensions.

Results: In all fluctuating PD patient (n=363), there were a significative negative association between the Harm Avoidance temperament and QoL ($p=3e-11$, $R^2=0,18$), and a significative positive association between Self-Directedness and Cooperativeness characters and QoL (respectively, $p=2e-11$, $R^2=0,19$; $p=1e-3$, $R^2=0,1$). This association between personality and QoL was even more important with the mental component of QoL.

Conclusion: Low Harm Avoidance and high Self-Directedness and Cooperativeness scores are associated with a better QoL in fluctuating PD patients, mainly at an emotional and social level of QoL. Thus, focusing on the personal resources of these patients as therapeutic education seems to be important to improve their QoL.

Disclosure: The study was funded by the France Parkinson charity and French Ministry of Health (PHRC national 2012). This is an ancillary study to Protocol ID: 2013-A00193-42; ClinicalTrials.gov: NCT02360683.

EPR1060

Neuropsychological features at baseline and dementia conversion in a memory clinic sample

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Background and aims: Cognitive assessment scales [Mini-Mental State Examination (MMSE), Addenbrooke Cognitive Examination (ACE)] are used to determine cognitive dysfunction and may be useful in predicting conversion to dementia in patients with memory complaints. We studied which items of the MMSE and ACE at baseline differed in patients presenting with memory complaints who later converted to dementia compared to non-converters.

Methods: Retrospective study of patients presenting to a memory clinic with primary memory complaints, without impaired activities of daily living (ADL), measured by the IADL questionnaire, with a follow-up >6 months. Objective cognitive impairment was defined as a score <1.5SD for age and ACE or MMSE (patients ≤1 year of education). Dementia was defined according to DSM-5 Criteria.

Results: Of 174 patients, 83 were included in the study. 42 (50.6%) patients converted to dementia (median time 20 months), with similar age, gender, education and global ACE and MMSE compared to non-converters at baseline. Converters showed significant worse scores at baseline on the recall item of the MMSE (median 2 vs 1; $p=0.006$) and free delayed recall (median 0 vs 1; $p=0.006$) of the ACE, which remained significant after logistic regression analysis controlling for age, sex and education.

Conclusion: In our sample, converters showed significant worse free delayed recall at baseline compared to non-converters, in line with previous studies of episodic verbal memory tests. Our results also highlight the need to consider performance in individual items of global assessment scales, apart from the global score, in predicting cognitive outcomes.

Disclosure: Nothing to disclose

EPR1061

ANTI-STIGMA training reduces stereotypes and increases GPs confidence in managing Neurocognitive disorders

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Background and aims: Neurocognitive Disorders (NCD) affect approximately 9 million people in Europe. Negative stereotypes and lack of knowledge about benefits of timely diagnosis can result in delayed diagnosis and poor management. This pilot studied the impact of an “Antistigma” training to empower GPs to diagnose and act on NCDs.

Methods: In the context of the “Act On Dementia” European Joint Action, 4 medical universities (Limoges and Lyon in France, Sofia in Bulgaria, and Lublin in Poland) invited GPs and residents to an “Antistigma” training based on an ethical approaches and case studies. Pre- and post-questionnaires were performed to explore GPs’ and residents’ stereotypes about NCD and their self-confidence in NCD management, before and after the training.

Results: In 2018, 8 sessions of the “Antistigma” training were held in Limoges, France (3), in Lyon, France (1), in Bulgaria (2) and in Poland (2). Participants were 192 GPs and residents. There were no significant differences between the training centers, or between residents and GPs.

Before training, participants expressed high stereotypes about disclosure of NCD. After training, stereotypes were reduced significantly ($p<0.001$), and especially stereotypes about NCD disclosure ($p<0.001$). Participants’ confidence increased significantly in general and for each step of the pathway: initiating diagnosis, disclosure of NCD, managing care and anticipating needs ($p<0.001$).

Conclusion: During European Joint Action “Act On Dementia”, “Antistigma” training proved positive impact on GPs’ and residents’ attitudes and practices towards NCDs. Practices for NCD can be reinforced and harmonized in primary care across Europe.

Disclosure: Nothing to disclose

EPR1062

Combined social cognition measures improve the diagnostic accuracy of the behavioral variant of frontotemporal dementia

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Background and aims: Severe socio-emotional impairments characterize the phenotype of the behavioral variant of frontotemporal dementia (bvFTD). Literature however reports social cognition disorders in other neurodegenerative syndromes. In this study, based on a clinical setting, we investigated accuracy of single social cognition task performance and combined social measures in the differential diagnosis of bvFTD.

Methods: We included 32 bvFTD, 26 Alzheimer's disease (AD), 16 primary progressive aphasia (PPA), 17 corticobasal syndrome (CBS) patients and 40 healthy control (HC) subjects. Ekman-60 faces Test (Ek-60F) and Story-based empathy task (SET) were administered to each subject. The emotion recognition and processing ERA index and the balance angle between SET sub-conditions were calculated. 1-way ANOVA was used to compare performances among groups, while receiver operating characteristic (ROC) curve tested ability to distinguish subjects with and without bvFTD.

Results: Compared to HC, all patient groups showed impaired performance at social tasks. ROC analysis showed good discriminative value for the ERA index + angle combination (bvFTD vs AD = AUC 0.73, cut-off 102.6, sens 0.62, spec 0.85; bvFTD vs PPA = AUC 0.75, cut-off 91.5, sens 0.56, spec 0.88; bvFTD vs CBS = AUC 0.80, cut-off 103.3, sens 0.63, spec 0.75; bvFTD vs HC = AUC 0.89, cut-off 143, sens 0.94, spec 0.70).

Conclusion: Accuracy analysis supported the advantages of a combined social measure over single task performance for the differential diagnosis of bvFTD. The use of a short battery in clinical settings may thus reduce uncertainties and improve the identification of the bvFTD phenotype.

Disclosure: Nothing to disclose

EPR1063

Evaluation of discriminative and early detection abilities of social cognition measures for the diagnosis of the behavioral variant of frontotemporal dementia: a systematic review

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Background and aims: Although loss of empathy is currently considered a core feature of the behavioral variant of frontotemporal dementia (bvFTD), the use of social tasks in the neuropsychological assessment of bvFTD is at present not required by any diagnostic guideline. In this systematic review, we explored the clinical maturity of social cognition measures in the early and differential diagnosis of bvFTD.

Methods: Papers were selected searching the PubMed and Medline databases. The search was limited to the available evidence regarding emotion recognition, empathy, theory of mind, and other social cognition skills. Only papers reporting indices of accuracy and/or sensitivity/specificity in classifying bvFTD from controls or other diseases were considered.

Results: Among the 160 papers initially included in the paper selection, only 14 papers were eligible for the scope of the present review. The accuracy of social cognition tasks for the early bvFTD detection in comparison with normal controls, as well as for the discrimination with Alzheimer's disease and psychiatric patients have been addressed in a very restricted number of studies, mainly focused on emotion recognition and theory of mind. The use of different cognitive measures hampers study comparability.

Conclusion: Study results suggest that no recommendation concerning the use of a specific social task in bvFTD is currently available. Although the literature seems to suggest that emotion recognition and ToM tasks could be the best choice to ensure a high diagnostic accuracy in clinical settings, there is the need of further specific investigations, including comparison studies.

Disclosure: Nothing to disclose

EPR1064

A retrospective assessment of the prognostic value of initial neuropsychological assessment in the syndrome of transient epileptic amnesia

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Background and aims: The syndrome of transient epileptic amnesia (STEA) is related to mesial temporal lobe alterations and occurs commonly in the elderly. Consequently, there are STEA cases that inaugurate a neurodegenerative disease. These patients may possibly be identified early by the use of neuropsychological tests. Our work explored such hypothesis.

Methods: 97 STEA patients with sufficient follow-up (≥ 6 years) were included in this retrospective monocentric study. 33 were thereafter excluded because of missing data. In the 64 remaining patients, 2 groups were identified according to their cognitive status over time: 6 were “decliners” (progressive decrease of the MMSE score during follow-up) and 58 were “non-decliners” (stable or slightly fluctuating MMSE score). The 2 groups were compared for initial neuropsychological performances.

Results: The “decliners” were diagnosed with Alzheimer’s disease (AD) during follow-up. Our main result shows that “decliners” and “non-decliners” significantly differed on initial 16-items Free and Cued Selective Reminding Test (FCSRT) performances. All FCSRT trials (immediate recall, free and cued recalls, delayed free and cued recalls) were significantly decreased ($p < 0.01$) in “decliners” compared to “non-decliners”. Not all decliners had initial performances $< 2SD$, but using a composite score, they were identified with Sensitivity=87.9% and Specificity=100%.

Conclusion: An underlying AD is the possible etiology for few STEA patients (9.4% of our cohort). These patients can be detected early based on initial cognitive examination when using the FCSRT.

Disclosure: Nothing to disclose

Critical care; Education in neurology; Ethics in neurology

EPR1065

Digital Brain - digital collection of the Institute Psychiatry and Neurology

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Background and aims: Human brain tissue derived from patients with neurological diseases remains the most appropriate material for research of the human brain under pathological conditions. Institute of Psychiatry and Neurology in Warsaw has an extensive and only in Poland collection of human brains obtained postmortem from patients with neurological diseases. Creating a digital, open-wide and easy-access database of collected brain tissue would allow quick and precise search of cases for the scientific or educational purposes.

Methods: We digitalize 5273 fixed whole and fragmented brains, 24372 paraffin blocks, 34558 histological sections, neuropathological protocols and medical data collected since 1952 in Institute of Psychiatry and Neurology. For project purposes, an internet platform was created to search, view and share digitized cases.

Results: Currently, most of the material has been verified, described and placed in correct locations in Institute of Psychiatry and Neurology. About 1000 cases were completely introduced into the created database. Website is under construction and will operate at www.digitalbrain.ipin.edu.pl. Project completion is estimated for 2022.

Conclusion: The digital, wide-open, easy-access database of the Institute of Psychiatry and Neurology human brains collection provides several, unique opportunities. It will allow quick search and evaluate of cases for the scientific, clinical, diagnostic and educational purposes both by obtaining desired material and by working directly on internet platform. We hope that it will establish extensive scientific cooperation, promote science and public awareness of nervous system diseases.

Disclosure: Project is supported by the „Digital Brain - digital collection of the Institute Psychiatry and Neurology” (Project No.POPC.02.03.01-00.0042/18).

EPR1066

Predicting the Quality of Clinical Performance in Neurology Residents

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Background and aims: It is very difficult to predict how well a student, still in university, will develop as a competent or even superior clinical neurologist during Neurology residency.

Methods: We collected data available at the time of application for Neurology residency positions and sought a correlation with clinical excellence as assessed by the Neurology residency program director. Data included: age at entry; US Medical Licensing Examination (“step”) scores; evaluations or grades in university Internal Medicine and Neurology rotations; overall clinical performance in university; perceived reputation of the university at which Medicine was studied; whether or not the applicant had additional years of clinical training (e.g. in Internal Medicine); time spent on research, and publications; and at what position the candidate was listed on the electronic ‘match’ list for resident selection.

Results: Data were collected covering 194 Neurology residents who began residency from 2008 until 2016 and completed residency training by June 2019 in 2 relatively large Neurology programs affiliated with the same university. Outcome was assessed at the conclusion of training 4 years later by the Neurology residency program directors who had worked with them throughout the residency -- by rank ordering residents within each class (year of training) in terms of relative clinical excellence.

Conclusion: Correlations between data available before the start of residency and the quality of clinical performance of Neurology residents by the end of training will be displayed, and a predictive model will be developed. Terminology and discussion will be adapted for suitability to European and other medical education systems.

Disclosure: Nothing to disclose

EPR1067

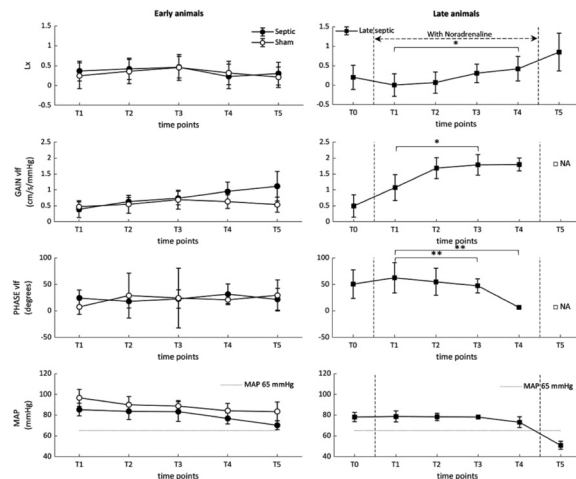
Dynamic cerebral autoregulation and neurovascular coupling impairments occur late in sepsis

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Background and aims: Prior studies suggest that sepsis alters the regulation of cerebral-blood-flow (CBF) (i.e. dynamic cerebral autoregulation (dCA) and neurovascular coupling (NVC)), which could lead to septic encephalopathy in up to 75% of cases. The temporal evolution of dCA and NVC impairment during sepsis progress is still unknown because relevant animal models are lacking. We studied dCA and NVC in a clinically relevant ovine model of septic shock.

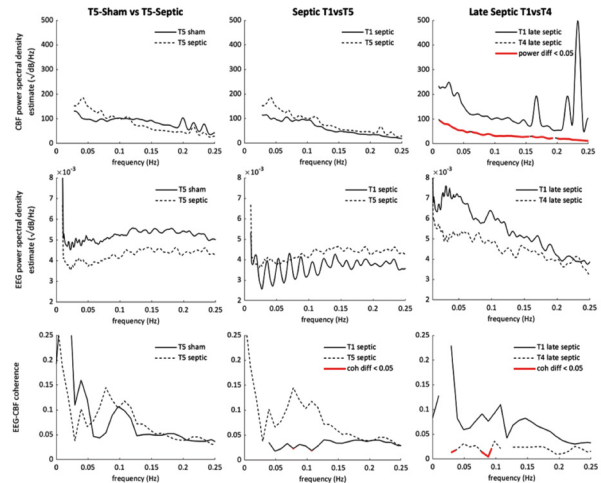
Methods: Mechanically ventilated sheep were randomized to brief (<24h) faecal peritonitis (sepsis, N=13), prolonged (>24h) faecal peritonitis (late-sepsis, N=7) or sham procedure (N=15). dCA was evaluated by the Lx index and transfer-function-analysis; results were compared between the sham and the septic groups. The late-sepsis group served as its own control. The magnitude-squared-coherence (MSC) between electrical cortical activity and CBF was employed to estimate NVC. Repeated-measure ANOVA and Friedman test were used for statistical analysis.

Results: There were no differences neither in the Lx nor in the TFA parameters between the sepsis and the sham group, but dCA was statistically impaired in the late-sepsis-group (FIG.1). The MSC differed only in the late-group where a statistically significant reduction in the CBF power spectral density was noted (FIG.2); this confirms a disruption in the NVC due to a reduced efficiency of cerebral vessels to adjust CBF to cortical activity. dCA/NVC impairment was associated with cortical dysfunction (i.e. decrease in alpha-delta ratio (FIG.3)). No differences in MAP-PaCO₂-temperature were noted between groups.

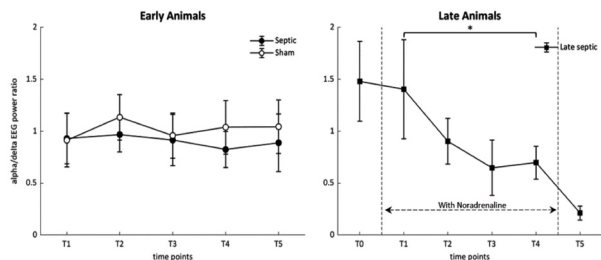


Early animals: sepsis and sham group. Late animals: late sepsis group (T0 corresponds to the last time point before noradrenaline infusion)

which was started around 15h after sepsis induction when response to fluid challenge became suboptimal, in order to maintain MAP around 80mmHg). NA: data not significant because of a too low TFA coherence



EEG-CBF coherence corresponds to the MSC. In red, the frequencies where a difference between time points were statistically significant (i.e. in the bottom right panel, a loss of MSC is evident for frequencies below 0.1Hz between the last time point before noradrenaline withdrawal (T4) and the T1)



The alpha/delta power ratio of the EEG signal, a surrogate to quantify cortical function, was significantly decreased at T4 in the late-sepsis group, suggesting the presence of a brain dysfunction induced by NVC/dCA impairment.

Conclusion: dCA/NVC alteration develop late after sepsis induction and they are associated with brain dysfunction.

Disclosure: Nothing to disclose

EPR1068

Ethical decision-making in the management of pediatric patients with severe disorders of consciousness: A qualitative study

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Background and aims: The emergence of technologies that potentially extend the survival of patients with severe brain damages and uncertain prognoses poses clinical, legal and ethical challenges. This study aims to understand the criteria that guide physicians' decision-making in the management of pediatric patients with severe consciousness disorders such as unresponsive wakefulness syndrome and minimally conscious state.

Methods: Between January 2019 and January 2020, we conducted a qualitative study using a grounded theory approach and interviewed 18 Italian-speaking neurologists, intensivists and pediatricians based in Swiss hospitals.

Results: Not only participants use a variety of criteria to guide their decision-making (including etiology, quality of life, prognosis and invasiveness of the treatment) but they also interpret them differently and attribute different levels of importance to them. As a result, the interviewees differ in their strategies adopted during the decision-making process. A small number of the participants consult the scientific literature or discuss the approach with other peers outside their team, while the majority involve the team, follow the patient's family's wishes, or discuss the decision with colleagues from other specialties who are directly involved in the care of the patient. Moreover, for the majority of the interviewees, a pivotal role in managing a fruitful relationship with the patient's family is played by physicians' empathy, experience, communication skills, authoritativeness and emotional maturity.

Conclusion: The divergences in decision-making among physicians that we captured in this study suggest the need for novel, specific guidelines with regard to the management of pediatric patients with severe consciousness disorders.

Disclosure: Nothing to disclose

EPR1069

Breaking Bad News Training is Insufficient in Neurology Residencies in Brazil

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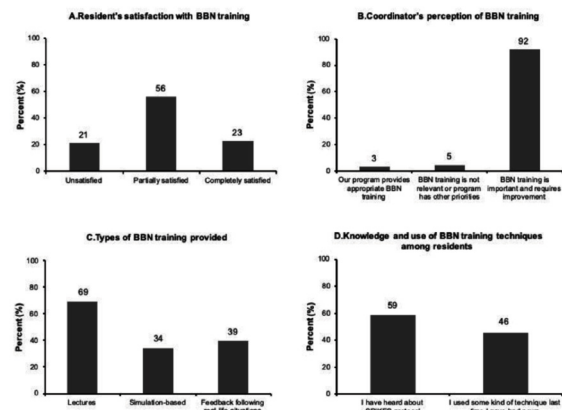
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Background and aims: Developing good communication skills is essential in order to establish successful doctor-patient relationships. Communication skills becomes even more important when it comes to breaking bad news (BBN). In neurology, the ability to deliver bad news is especially important as many diseases have poor prognosis, resulting in chronic disability or death.

The aim of this project was to evaluate how BBN training is carried out in neurology residency programs in Brazil.

Methods: Preceptors and residents of neurology were asked to fill out surveys about how BBN skills were taught and practiced in residency programs.

Results: We collected 174 responses from 45 institutions in 17 states of Brazil. More than 90% of preceptors believe their programs require substantial improvement and more than 70% of residents are dissatisfied with current training. Only 16% of preceptors reported formal or simulation-based training, while 31% of the residents denied ever receiving specific training. In addition, 60% of the residents reported never having received feedback on how well they communicated bad news and 58.7% of preceptors admitted this was not standard practice in their programs.



Overview of BBN training in Neurology residencies in Brazil. A) Resident's and newly certified neurologists (NCN)' satisfaction with BBN training provided during residency; B) Coordinators' perception of BBN training provided by their programs; C) Types of BBN training provided; D) Knowledge and use of BBN techniques among residents and NCN.

Conclusion: This study suggests that the current BBN training is deficient in neurology residency programs across Brazil. Given the relevance of such a skill to patients' care, every effort should be made to provide structured training opportunities during residency.

Disclosure: Thaiza Lima, MD. received a grant from the Ethics Committee of CREMESP (Conselho Regional de Medicina do Estado de São Paulo*) for performing this research. *São Paulo State Regional Medical Council

EPR1070

Time matters in brain health: how should society prepare for a growing population at risk of neurodegenerative diseases?

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Background and aims: As people live for longer, the number of individuals who will develop neurodegenerative diseases is predicted to rise. Identifying those at greatest risk is the 1st step in prevention. Cultivating an attitude within society that accepts preventive approaches in neurology and encourages individuals to proactively prioritise their own brain health is vital.

Methods: A multidisciplinary, geographically representative group with expertise in dementia, Parkinson's disease, genetics, epidemiology, public health, patient advocacy and ethics developed an evidence-based set of recommendations to prepare a framework for a preventive approach to neurodegenerative diseases.¹

Results: The group produced 18 recommendations, targeting stakeholders involved in health promotion (5 recommendations), clinical practice (2) and research/decision-making (11). Recommendations covered the need for effective treatments, accurate diagnostic and progression markers, affordable tests to detect and diagnose disease and appropriate support for individuals seeking further information about 'brain health' and associated checks.

Conclusion: In the absence of suitable biomarkers and disease-modifying treatments, neurodegenerative diseases do not currently meet established screening criteria. Further work is needed to develop treatments for neurodegenerative diseases and validate diagnostic tools to identify people at risk. Meanwhile, healthcare decision-makers should start to pave the way for the advent of national programmes that facilitate risk assessment and earlier disease detection and

intervention, with appropriate consideration of the ethical implications. Stakeholders need to work together for these common goals.

1. Giovannoni G, Noyce AJ, Scheltens P et al. Time matters. A call to prioritize brain health. 2019. Available from: <http://www.oxfordhealthpolicyforum.org/reports/brain-diseases/brain-diseases-report>

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EPR1071

Resting-state NIRS-EEG in unresponsive patients with acute brain injury

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Background and aims: Levels of consciousness in patients with acute brain injury are often difficult to assess. Near-infrared spectroscopy (NIRS) and electroencephalography (EEG) can be performed serially at the bedside at low costs, an important advantage in the ICU. However, combined NIRS-EEG has never been evaluated for acute brain injury and disorders of consciousness in the ICU.

Methods: We explored resting state oscillations in 8-channel NIRS oxyhemoglobin and 8-channel EEG band-power signals to classify levels of consciousness in patients with traumatic or nontraumatic brain injury in the ICU (n=9). Conscious neurological patients from step-down units and wards served as controls (n=14). We also explored NIRS-EEG to characterize changes in the levels of consciousness over multiple days in unresponsive ICU patients with repeated measurements (n=5).

Results: Neurovascular coupling between NIRS oxyhemoglobin (0.07-0.13Hz) and EEG band-power (1-12Hz) at frontal areas was sensitive and prognostic to changing consciousness levels. Unsupervised adaptive mixture independent component analysis (AMICA) revealed a mixture of 5 models, with the relative probabilities of these models reflecting levels of consciousness over multiple days. Weighted k-nearest neighbor classification of AMICA probabilities distinguished unresponsive patients from conscious controls with >90% accuracy (positive predictive value 93%, false discovery rate 7%) and, additionally, identified patients who subsequently failed to recover consciousness with >99% accuracy.

Conclusion: We suggest that NIRS-EEG for monitoring consciousness levels after acute brain injury is worthy of further exploration. Neurovascular coupling may be a marker of consciousness levels, and normalization of neurovascular coupling may herald recovery of consciousness after acute brain injury.

Disclosure: Nothing to disclose

EPR1072

Public perception and legislation of brain death, cardiac death and organ donation

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Background and aims: How the public perceives the difference between brain death and cardiac death and how this may influence attitudes towards organ donation, remains poorly understood. We investigated the public perception of brain death versus cardiac death and documented inconsistencies in the legislations of countries with different geographical, cultural and socioeconomic backgrounds.

Methods: Using a crowdsourcing approach, we randomized 1072 participants from 30 countries to either a case report of organ donation after brain death or to 1 following cardiac death. Further, we reviewed the scientific literature and sampled guidelines from 24 countries and 5 continents.

Results: Of all participants, 73.1% would be willing to donate all organs, while 16.0% would want to donate some of their organs. Exposure to “brain death” was not associated with a lesser likelihood of participants agreeing with organ donation (82.1%) compared to “cardiac death” (81.9%; RR 1.02, 95% CI 0.99 to 1.03; p=0.11). However, participants exposed to “cardiac death” were more certain that the patient was truly dead (87.9%±19.7%) than participants exposed to “brain death” (84.1%±22.7%; Cohen’s d 0.18; p=0.004). Sampling of guidelines and literature review revealed large differences between countries regarding procedures required to confirm brain death and cardiac death, respectively.

Conclusion: Implementation of organ donation after cardiac death is unlikely to negatively influence the willingness to donate organs, but legislation is still brain death-based in most countries. The time may be ripe to adjust legislations and increase the rate of cardiac death-based organ donation.

Disclosure: Nothing to disclose

EPR1073

Risk factors for hyperactive delirium after subarachnoid hemorrhage

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Background and aims: Hyperactive delirium is common in patients with subarachnoid hemorrhage (SAH). In this study we aimed to identify risk factors for delirium and to evaluate its role on patients' outcomes.

Methods: In 276 SAH-patients admitted to a neurological ICU, daily RASS (Richmond Agitation Sedation Scale) and ICDSC (Intensive Care Delirium Screening Checklist) scores of the 1st 30 days were retrospectively collected by chart review. Hyperactive delirium was defined as ICDSC \geq 4 when RASS $>$ 0. Risk factors for delirium and its association with outcome (3-month mRS) were analysed using multivariable GLM. Patients without delirium reaching at least once a RASS \geq 0 served as reference group.

Results: Patients were 56 (IQR 47-67) years old and had an admission H&H grade of 3 (IQR 1-5). 65 (24%) patients developed hyperactive delirium at median 6 (IQR 3-16) days after SAH. 49 (18%) patients never reached a RASS \geq 0. In multivariable analysis, intubation $>$ 48hrs, aneurysm detection, lower H&H grade and pre-existing psychiatric disorder were associated with the development of delirium (Table 1). In matched analysis, the cumulative dose of midazolam before delirium onset was higher in patients with delirium compared to the control group (p=0.031). Overall, delirium was not associated with worse outcome (p=0.136). Interestingly, patients with delirium more often had a mRS of 1-3 (77%) compared to an mRS of 0 (14%) or 4-6 (9%).

Table 1: Risk factors for the development of hyperactive delirium			
Variable	Adjusted Odds Ratio	95% Confidence Interval	p-Value
Detection of an aneurysm (compared to non-aneurysmal SAH)	4.38	1.48-12.97	0.008
Intubation $>$ 48 hours	4.46	1.89-10.56	0.001
Pre-existing psychiatric disorder	3.17	1.14-8.83	0.027
Hunt and Hess grade (I-V)	0.63	0.48-0.83	0.001
Age, years	0.99	0.97-1.01	0.425

Table 1

Conclusion: Our data suggest that delirium has the highest incidence in patients with intermediate outcomes, suggesting that both, a certain severity degree and a minimum of neuronal connectivity is needed for the development of delirium.

Disclosure: Nothing to disclose

EPR1074

Low-resolution pressure reactivity index and its derived optimal cerebral perfusion pressure in adult traumatic brain injury: a CENTER-TBI study

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Background and aims: After traumatic brain injury (TBI), brain tissue can be further damaged when cerebral autoregulation is impaired. Regulating CPP according to computed optimal CPP (CPPopt) values based on cerebrovascular reactivity indices might contribute to prevent this. In this study, we examined the predictive value of a low-resolution long pressure reactivity index (L-PRx) and a multi-window, weighted CPPoptLPRx algorithm.

Methods: Using the multi-center CENTER-TBI study dataset, the association of L-PRx (correlation between 1min averages of intracranial pressure (ICP) and arterial blood pressure (ABP) over a moving time frame of 20min) and PRx (correlation between 10sec averages of ICP and ABP over a moving time frame of 5min) to outcome was assessed using univariate and multivariate regression analysis. CPPopt values were calculated using a multi-window algorithm that was either based on L-PRx or PRx and discriminative power was compared.

Results: L-PRx and PRx were both significant predictors of mortality in univariate and multivariate regression analysis. PRx displayed a higher discriminative ability, although the difference in area under the curves between L-PRx and PRx was not significant (DeLong's test). Similarly, deviations of actual CPP from calculated CPPoptLPRx and CPPoptPRx values were significantly associated with outcome in univariate and multivariate analysis with the CPPoptPRx trending towards more precise predictions.

Conclusion: Although LPRx and CPPoptLPRx did not reach the predictive power of the PRx and CPPoptPRx, they were still significantly associated with outcome. A prospective trial is needed to assess if CPP management according to CPPoptLPRx can improve clinical outcome.

Disclosure: LR received a scholarship from the CENTER-TBI study to visit the Brain Physics Lab in Cambridge.

EPR1075

Transcranial doppler ultrasound for brain death confirmation.

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Background and aims: Transcranial doppler (TCD) is a useful method of ancillary testing for determination of brain death (BD). The aim of this study is to describe TCD patterns found in patients with BD, assess the sensitivity and specificity results and contrast with literature.

Methods: We conducted an observational, prospective TCD examination of consecutive patients with clinical diagnosis of BD. We used the database register of the neurology ultrasonology laboratory. There were 49 BD studies of 13589 database registers between April 2009 and December 2018, 37 of them with clinical diagnosis of BD.

Results: We found male prevalence (71.4%), an age average of 51 years and the main cause of BD was brain hemorrhage. The temporal brain window was the most used and the middle cerebral artery was the most explored. 2 (5.4%) patients had inadequate transtemporal window. We registered increased pulsatility in 3 (8.1%), reverberating flow in 11 (29.7%), small systolic peaks in early systole in 14 (37.9%) and complete absence of flow with previously known adequate transtemporal window in 7 (18.9%). This study showed a sensitivity of 86% and a specificity of 100% of TCD for confirming BD.

Conclusion: Our results show high sensitivity and specificity of TCD for confirming BD, similar than previously reported and higher than other non-invasive methods. TCD is an useful, noninvasive and high-available method of ancillary testing for the determination of BD by an expert neurosonologist.

Disclosure: Nothing to disclose

Epilepsy 1

EPR1076

Cenobamate is a Novel Anti-Epileptic Drug with a Unique, Dual, Complementary Mechanisms of Action

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Background and aims: Cenobamate is a novel anti-epileptic drug (AED) recently approved by the FDA. However, its mechanism of action has been only partially described. Here we present data supporting cenobamate's dual mechanism of action (MoA) increasing GABAA-receptor-mediated inhibitory currents and preferentially blocking persistent sodium excitatory currents.

Methods: Cenobamate was tested in models of radioligand binding displacement to assess its binding on GABAA receptors. Relative activities on human GABAA receptor subtypes were studied on 6 human GABAA ion channel subtypes expressed in heterologous cells. Potentiation of GABA-induced currents and effects on both phasic/tonic GABAA currents were assessed in rat hippocampal CA3 neurons, dentate gyrus granule cells (DGGC), and mouse/rat hippocampal CA1 neurons. Conventional whole-cell patch clamp assays obtained electrophysiological recordings.

Results: Cenobamate enhanced the current induced by 1 μ M GABA in a concentration-dependent manner, demonstrating positive modulation of GABAA receptors. Enhancement of GABAA receptor-mediated inhibitory currents occurred in both the phasic and tonic modalities in rodent hippocampal neurons. In addition to its modulation of several properties of voltage-gated Na⁺ channels, cenobamate acts as a preferential INaP inhibitor in neuronal voltage-gated Na⁺ channels to exert its anti-epileptic efficacy.

Conclusion: Most current AEDs either decrease neuronal excitation or increase neuronal inhibition. Cenobamate impacts both: it acts as a positive allosteric modulator of the GABAA receptor, binding to a site distinct from benzodiazepines and preferentially blocks persistent sodium currents enhancing the inactivated state of voltage-gated sodium channels. This complementary mechanism of action might be a key contributor to the high rates of responders shown during the placebo-controlled clinical trials.

Disclosure: Nothing to disclose

EPR1077

A comprehensive machine learning-based software pipeline to classify EEG signals: a case study on PNES vs control subjects.

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Background and aims: Diagnosis of psychogenic non-epileptic seizures (PNES) by electroencephalography (EEG) is a not trivial task during clinical practice for the neurologist. No clear PNES electrophysiological biomarker has been found yet, and only video-EEG monitoring with recording of typical episodes is the gold standard for diagnosis

Methods: In this study, we analysed 10 EEG time series recordings from 10 patients (2 males, age 28 \pm 12.4) with PNES and 10 healthy subjects (3 males; age 33 \pm 13.93). PNES diagnosis was made based on a typical episode recorded during video-EEG, with EEG showing neither concomitant ictal activity nor post-ictal changes.

A novel software pipeline that consists of a semi-automatic signal processing technique and a supervised Machine Learning (ML) classifier to aid discriminative diagnosis of PNES via EEG time series, is proposed. The software framework consists of (i) artifact rejection EEG module; (ii) feature extractor in frequency domain; (iii) classifiers based on different ML algorithms, such as Support Vector Machine (SVM), Linear Discriminant Analysis (LDA) and Bayesian Network. The classification scores were evaluated using Random Split and Leave One Out-Validation.

Results: The first experiments on a dataset including PNES and control subjects showed good accuracy (between 75% and 87%, depending on classifiers and validation methods). LDA with LOO-Validation had the best accuracy (87%).

Conclusion: The promising results of the proposed software pipeline suggest that it may be a valuable tool to support existing clinical diagnosis.

Disclosure: Nothing to disclose

EPR1078

Relation between caffeine consumption and risk of seizure-related respiratory dysfunction in patients with drug-resistant focal epilepsy

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Background and aims: About 33% of focal seizures are associated with central apnea resulting in transient hypoxemia. Caffeine promotes spontaneous breathing by antagonizing adenosine. However, the relation between caffeine consumption and risk of seizure-related respiratory dysfunction in patients with drug-resistant focal epilepsy remains unknown

Methods: We reviewed the video-EEG recordings of 108 patients with drug-resistant focal epilepsy included in the SAVE study to identify those with ≥ 1 focal seizure, valid SpO₂ measurement and information about coffee consumption. This latter was collected at inclusion using a standardized self-questionnaire and further classified into four groups: none, rare (less than 3 cups/week), moderate (from 4 cups/week to 3 cups/day) and high (more than 4 cups/day). Ictal/post-ictal hypoxemia (IH) was defined as SpO₂<90% during at least 5 seconds. Association between hypoxemia and person- or seizure- specific variables was analyzed after correction for individual effects and the varying number of seizures.

Results: All data were available for 83 patients and 315 seizures. IH was observed in 64 seizures. Occurrence of IH was independently associated with temporal lobe epileptogenic zone ($p < 0.001$) and coffee consumption ($p = 0.003$). In comparison with high coffee consumption, odds ratio for no, rare and moderate coffee consumption was 9.34 (95% CI 2.6-34.0), 3.57 (95% CI 0.99-12.8) and 2.03 (95% CI 0.54-7.69). Duration of IH and SpO₂ nadir were not associated with coffee consumption.

Conclusion: The risk of IH dramatically varied as a function of coffee consumption, with preventive effect of high consumption. This result needs to be further investigated in interventional studies.

Disclosure: Nothing to disclose

EPR1079

Efficacy and Safety of Cenobamate in European Epilepsy Patients with Uncontrolled Focal-Onset Seizures

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Background and aims: There is a need for more effective anti-epileptic drugs (AEDs) since approximately 40% of patients do not achieve seizure freedom despite treatment with 2 AEDs. Here, we present the results of cenobamate, a novel AED, in European epilepsy patients with uncontrolled focal onset seizures (FOS).

Methods: This was a post-hoc analysis of a double-blind, placebo-controlled trial. Adults with uncontrolled FOS treated with concomitant 1-3 AEDs were assigned to once-daily adjunctive cenobamate 100mg, 200mg, 400mg, or placebo. There was a 6-week titration and a 12-week maintenance phase. Primary European endpoint was responder rate ($\geq 50\%$ reduction in seizure frequency from baseline) in the maintenance phase; prespecified secondary included seizure freedom (maintenance phase). Safety and tolerability were assessed.

Results: In Europe, 250 patients were enrolled. Median disease duration ranged from 21-28 years. Responder rates during the maintenance phase were 42%/52%/63% for 100mg/200mg/400mg cenobamate vs 31% for placebo. Seizure freedom occurred in 4%/15%/25% in patients receiving 100mg/200mg/400mg vs 2% for placebo. Overall, the most common AEs ($\geq 10\%$) were somnolence, dizziness, headache, fatigue, and diplopia. Efficacy and safety were consistent with the overall study population.

Conclusion: Complete control of seizures is the ultimate goal of therapy, but the probability of achieving seizure-freedom diminishes with each failed treatment to less than 5% after the second AED. Adjunctive treatment with cenobamate showed significantly higher percentage of responders compared with placebo, including 100% responders. Cenobamate is a novel AED with the potential of improving outcomes for FOS patients with uncontrolled epilepsy. Results here were consistent with the overall patient population.

Table 1. Responder Rates, %	Cenobamate 100mg (N=57)	Cenobamate 200mg (N=60)	Cenobamate 400mg (N=60)	Placebo (N=58)
$\geq 50\%$ Reduction	42.1% <i>P</i> =0.2486	51.7% <i>P</i> =0.0262	63.3% <i>P</i> =0.0005	31.0%
$\geq 75\%$ Reduction	19.3% <i>P</i> =0.1133	35.0% <i>P</i> =0.0007	45.0% <i>P</i> <0.0001	8.6%
$\geq 90\%$ Reduction	7.0% <i>P</i> =0.4385	23.3% <i>P</i> =0.0022	31.7% <i>P</i> <0.0001	3.4%
100% Reduction	3.5% <i>P</i> =0.6184	15.0% <i>P</i> =0.0167	25.0% <i>P</i> =0.0002	1.7%

P-values vs placebo

Responder rates

Disclosure: Study 017 (NCT01866111) was sponsored by SK Life Science, Inc. and the analyses supported by Arvelle Therapeutics International GmbH

EPR1080

Distinctive electrographic patterns of clinical and subclinical focal seizures

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Background and aims: Ambulatory EEG devices are becoming a common tool in the neurological praxis for the follow up of patients with epilepsy. However, since many seizures are imperceptible or remain disregarded by the patient and considering the presence of EEG artifacts, the scrutiny of epileptic seizures could become a tough task in the interpretation of long-term EEG data. This study was designed to identify distinctive electrographic patterns of clinical and subclinical seizures for evaluation of long-term scalp EEG data.

Methods: Scalp EEGs of 50 patients (n=468, age 7-68y, 30 male) with focal epilepsy, structural and non-structural (40 epilepsy temporal lobe, 10 extratemporal patients) were retrospectively evaluated regarding the total duration of electrographic seizure patterns, the number of electrodes involved, extension to ipsilateral or contralateral electrodes, and the presence of ictal patterns. Results were analysed with Wilcoxon Rank-Sum and Fisher exact tests.

Results: Statistically significant differences between subclinical and clinical seizures were found for all studied aspects. Subclinical seizures showed a shorter duration, a low number of involved electrodes and less frequent propagation beyond the temporal lobe and to the contralateral cerebral hemisphere ($p=2.41 \cdot 10^{-8}$; $p=2.494 \cdot 10^{-7}$; $p=0.001113$ and $p=7.182 \cdot 10^{-13}$ respectively). Furthermore highly variable electrographic patterns of frequency and configuration were observed in either form of electrographic patterns within the same patient.

Conclusion: This study demonstrates the existence of several electroencephalographic features distinguishing clinical and subclinical seizures which may allow the scrutiny of interpretations of long-term EEG data. Moreover, it takes a step forward the understanding of epileptic dynamics across different brain regions.

Disclosure: Nothing to disclose

EPR1081

Incidence of epilepsy in Denmark 1977-2016

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Background and aims: Long-time trends of epilepsy incidence from large cohorts have not been previously studied.

Methods: Study population: We estimate the incidence of epilepsy among individuals born in Denmark, who were alive and living in Denmark at the start of follow-up (birth or 1. January 1977, whichever comes later) N=7,360,166. Identification of individuals with epilepsy: Using data from the Danish National Patient Registry, we identified all epilepsy diagnoses (ICD-8: 345, excl. 345.29 and ICD-10: G40).

Identification of individuals with psychiatric disorders: Using data from the Danish Central Psychiatric Register, we identified all psychiatric disorders diagnoses (ICD-8: 290-315 and ICD-10: F00-F99).

For each calendar year, age and sex, we calculated the incidence of epilepsy as the number of persons diagnosed for the 1st time with epilepsy divided by the total number of people alive and living in Denmark at that age and year.

Results: The incidence of epilepsy was higher in males than in females and particular high in persons with co-morbid psychiatric disorders (Table 1).

Table 1. Overall sex specific incidence of epilepsy in Denmark from 1995 to 2016.

	Person-years	Incident epilepsy patients (n)	Incidence rate, per 100,000 person-years
Overall	108,622,700	85,728	78.9 (95% CI: 78.4-79.5)
Males	53,891,950	45,719	84.8 (95% CI: 84.1-85.6)
Females	54,730,750	40,009	73.1 (95% CI: 72.4-73.8)
With psychiatric disorder			
Overall	7,014,431	15,080	215.0 (95% CI: 211.6-218.4)
Males	3,124,086	7,864	251.7 (95% CI: 246.2-257.3)
Females	3,890,345	7,216	185.5 (95% CI: 181.3-189.8)
Without psychiatric disorder			
Overall	101,608,270	70,648	69.5 (95% CI: 69.0-70.0)
Males	50,767,864	37,855	74.6 (95% CI: 73.8-75.3)
Females	50,840,406	32,793	64.5 (95% CI: 63.8-65.2)

Table 1.

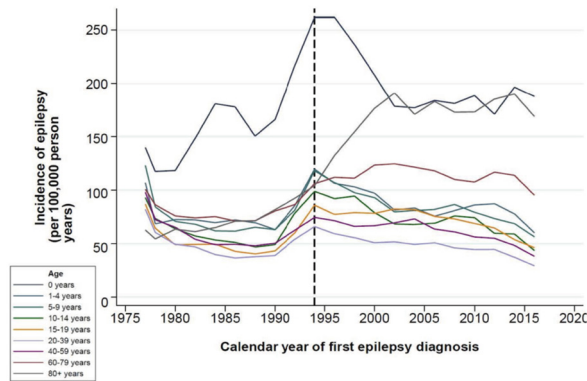


Figure 1

Conclusion: The incidence of epilepsy is highly age and sex specific and associated with psychiatric disorders. The incidence was remarkable stable in recent decades.

Disclosure: The study was supported by the European Union (www.esbace.eu)

EPR1082

Analysis of thalamic oscillatory activities may predict responsiveness to DBS of the anterior nuclei of the thalamus

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Background and aims: Deep brain stimulation (DBS) of the anterior nuclei of the thalamus (ANT) is a promising therapeutic approach in patients with intractable epilepsy.

Methods: We analyzed intracerebral recordings from externalized DBS electrodes targeted bilaterally in the ANT in 14 patients with more than 1 year of follow up. Electrode contacts were located in the ANT and adjacent structures. 8 patients were responders with at least 50% seizure reduction; 6 were non-responders.

3 types of bipolar EEG were defined: recorded from 2 contacts in the ANT (IN), from 1 contact in the ANT and a 2nd 1 out of the ANT (BRIDGE), and from both contacts out of the ANT (OUT).

In the local field EEG, spectral power (PW) and power spectral entropy (PSE, describing system complexity) were analyzed. We calculated normalized spectral power and normalized power spectral entropy in the following passbands: 1-4Hz, 4-8Hz, 8-12Hz, 12-20Hz, 20-45Hz, 65-80Hz and HFO: 80-200Hz (ripple), 200-500Hz (fast ripple).

Results: PW analysis displayed significant differences between positive and negative outcomes in the delta, theta, high-gamma, ripple, and fast ripple frequency bands. PSE analysis displayed significant differences between positive and negative outcomes in all frequency bands. Differences were significant in the BRIDGE; there were no significant differences in the OUT and IN.

Conclusion: Significant differences in thalamic EEG oscillatory activities between responders and nonresponders with bilateral ANT DBS were detected. We suggest that analysis of EEG recorded from the ANT could predict response to ANT DBS.

Disclosure: Nothing to disclose

EPR1083

Slow titration of Cannabidiol add-on treatment in patients with drug resistant epilepsy provides a better safety profile

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Background and aims: To assess adverse events (AE) and efficacy of add-on Cannabidiol (CBD) with a slower titration compared to randomized controlled trials (RCTs).

Methods: We conducted a prospective, open-label, multi-center study involving 6 centers (French reference centre for rare epilepsies). All patients had a slow titration reaching target doses within at least 1 month. Follow-up included efficacy and AE evaluation at 1, 2 and 6 months.

Results: 125 patients were enrolled (62 Lennox-Gastaut, 48 Dravet, 5 Tuberous sclerosis, 10 other etiologies). Median concomitant anti-epileptic drugs (AEDs) was 3 (range 2-3), treatment duration 9 months (range 6-11) with a mean dose of 10mg/kg/day at M1 (M1), 15mg/kg/day at M2 and 17mg/kg/day at M6. 25 patients (20%) discontinued CBD, 21 due to lack of efficacy, 3 due to AE and 1 due to SUDEP.

AE were observed in 61 patients (48.8%). The most common were somnolence (19.2%), aggressivity (13.6%) and fatigue (12%). Somnolence and fatigue were significantly associated with the number of AEDs (P=0.012) but not with any specific AED.

Abnormal liver function tests >3X the upper limit were reported in 11.2% and significantly associated with valproate (P=0.04) or clobazam (P = 0.04).

Seizures frequency decreased without significance between baseline and M1, 2 and 6. Parents and practioners' satisfaction about CBD were significantly higher at M6 compared to M1 and M2 (P = 0.001).

Conclusion: Results showed that a slower titration of CBD dose is better tolerated comparing our results to RCTs.

Disclosure: Nothing to disclose

EPR1084

In vivo interictal signatures of human periventricular nodular heterotopia

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Background and aims: Periventricular nodular heterotopia (PNH) is a common cause of drug-resistant epilepsy, characterized by nodules of ectopic neurons adjacent to the lateral ventricles. In contrast to other types of cortical malformations, no unique interictal patterns have been described in PNH. The goal of our study was to identify interictal LFP signatures and the underlying neuronal substrates that originate within the epileptogenic nodules in PNH.

Methods: Interictal patterns were described on an unprecedented level of microscopic detail by means of microelectrode recordings from three PNH nodules in 2 patients. LFP patterns were identified on the basis of their morphological and pathological features and then described in the time and frequency domains. Single units were extracted using spike-sorting algorithms, after which extracellular spike-width and peak-trough time were used to describe units on the basis of detected morphological and electrophysiological features

Results: Highly consistent interictal activities were identified in all 3 nodules 1) trains of periodic slow waves (n=2855), 2) isolated slow deflections (n=1631), both with superimposed fast activity, and 3) epileptic spikes (n=6986). Patterns were highly local and largely invisible on the adjacent macro-electrode contacts. Spike analyses showed that the vast majority of units (n=25) were strongly modulated during all interictal patterns. The same units were involved in all 3 patterns, while showing different patterns of firing rate modulation during the interictal events.

Conclusion: These results are consistent with an altered regulation of cellular excitability and suggest that periodic patterns may result from fluctuation in inhibition and rebound excitation in the same neuronal network.

Disclosure: This study was supported by the program "Investissements d'avenir" ANR-10-IAIHU-06, and grants from the OCIRP-ICM and the Fondation de l'APHP pour la Recherche - Marie-Laure PLV Merchandising.

EPR1085

20-year experience with Vagus Nerve Stimulation Therapy for drug-resistant epilepsy in a single centre.

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Background and aims: To analyse the efficacy and tolerability of Vagus Nerve Stimulation (VNS) Therapy as treatment for drug-resistant epilepsy (DRE).

Methods: A retrospective study including patients which started VNS Therapy for DRE at Cruces University Hospital from 1998 to 2018 was performed. The following data were collected: age, seizure and epilepsy types, number of previous and concomitant anti-epileptic drugs (AEDs), monthly seizure frequency and adverse events at 6 and 12 months and last follow-up visit. Good response was defined as a $\geq 50\%$ reduction in monthly seizure frequency compared with the baseline.

Results: 104 patients were included. All but 2 had the electrode implanted in the left vagus nerve. 14 patients were younger than 12 years. 92% suffered from partial onset epilepsy, and were experiencing a median number of 14.5 seizures per month. Median number of AEDs used in the past was 8. Median number of concomitant AEDs was 3. Median treatment duration was 57.8 months. The responder rate was 30 % at 6 months, 34.6% at 12 months and 44% at last follow-up visit. Adverse events were experienced by 39.4%, the most common being hoarseness. Right sided VNS did not lead to cardiovascular adverse effects. VNS Therapy was discontinued in 34%, mostly due to lack of efficacy. Fibrosis and infection led to the device removal in 7 patients.

Conclusion: In this long term study, VNS Therapy showed efficacy in 44% of patients with DRE. Tolerability was good, and right sided VNS did not lead to hemodynamic adverse effects.

Disclosure: Nothing to disclose

EPR1086

Predictive factors of recurrent Status Epilepticus. A 35-year cohort study

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Background and aims: It is well-known that status epilepticus (ES) is associated with high short and long-term morbidity and mortality. The risk of developing recurrent SEs is also known, but the predictors are poorly defined. This study aims at identifying the factors associated with the occurrence of ES in patients with a diagnosis of epilepsy and the predictors of its recurrence.

Methods: We enrolled 252 patients with at least one ES that were consecutively observed at our center in the period going from 1983 to 2018 (median follow-up 3,16 years); in addition, a randomized selection of 714 patients with epilepsy diagnosed without ES history was enrolled, with a 3:1 ratio. Different clinical-demographic variables were evaluated and were then included in a univariate/multivariate logistic regression model and a Cox regression model.

Results: The occurrence of ES was independently correlated with age of onset of ES ($p < 0.001$; OR 1.018; 95% CI 1.010-1.026), absence of known etiology ($p < 0.001$; OR 0.231; 95% CI 0.153-0.348) and number of anti-epileptic drugs taken at the last observation ($p < 0.01$; OR 1.4; 95% CI 1.19-1.69). Interestingly, the recurrence of ES was negatively correlated to its onset in an acute symptomatic context ($p = 0.034$; OR 0.26; 95% CI 0.075-0.906).

Conclusion: Late onset and the presence of a known etiology predict the occurrence of ES in a large cohort of patients. The occurrence of the 1st ES in an acute symptomatic context reduces the risk of recurrence.

Disclosure: Nothing to disclose

EPR1087

Impact of epilepsy training on school teachers and counselors: an intervention study in Lebanon

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Background and aims: The study evaluated the immediate impact of an epilepsy training through the administration of a questionnaire on the attitudes and knowledge of teachers and counselors before and immediately after the intervention in public and private schools in Lebanon.

Methods: This project is part of an epilepsy awareness campaign in Lebanon applied to teachers and counselors in a 1.5-3-hour session. It consisted of a pretest, a unified and interactive Powerpoint conference and a posttest. The statistical analysis used the McNemar and Stuart Maxwell tests with a statistical significance level of 0.05.

Results: 73 participants completed the pre and posttest questionnaires. The majority were female (68.5%) aged <39 years (57%). A positive impact of the training was found, regardless of its duration, by comparing the pre- and postintervention results of questions relating to the effect of epilepsy on schooling, the manifestations of seizures, their psychological or behavioral effects, seizure 1st aid and the possibility of curing epilepsy with surgery. Most of our teachers recognized that children with epilepsy have a comparable IQ to others. They had a poor discriminatory attitude against people with epilepsy in terms of the direct attitude towards them or hiring them. However, 24% preferred avoiding marrying a person with epilepsy, and this was not modified by the training.

Conclusion: This is 1 of few studies worldwide and the 1st in Lebanon to demonstrate an immediate positive effect of training on epilepsy among school teachers using an arabic questionnaire. Future research should be undertaken to develop robust training models to destigmatize epilepsy.

Disclosure: Nothing to disclose

Headache and pain 1

EPR1088

Characterisation of prescription patterns in episodic and chronic migraine patients starting treatment in a real life setting with erenumab in Germany (SPECTRE) – A real world evidence study

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Background and aims: Antibodies as prophylaxis are novel in the migraine field, thus it is important to collect information about their application in the local clinical routine outside of randomized controlled trials. Erenumab, a Calcitonin Gene-Related Peptide (CGRP)-receptor antagonist, was approved with two monthly dosages: 70mg and 140mg. The aim of the SPECTRE study is to understand the choice of the starting dose as well as dose switching based on migraine characteristics and comorbidities.

Methods: This is an observational, non-interventional, multicenter, open label, single arm study comprising migraine patients receiving erenumab treatment. The study is conducted at 150 centers in Germany and aims to enroll 1960 adult migraine patients. Patients either can be new on the treatment or have started treatment recently, but not more than 3 months before entering the study. Apart from a headache diary, the patient-reported-outcome questionnaires HIT-6 and TSQM are used to assess the efficacy of erenumab and the satisfaction of the patients with the drug.

Results: The results of the 1st interim analysis of 100 patients will be presented. This will include patients' baseline migraine characteristics as well as the percentage of patients on each starting dose of erenumab stratified by the major reasons for prescription and comorbidities.

Conclusion: The SPECTRE study will give us valuable insights into the clinical routine of erenumab prescriptions in Germany. Characterization of the prescription pattern and analysis of the respective therapy response will possibly allow to develop individual treatment strategies for each patient.

Disclosure: Charly Gaul received honoraria for consulting and lectures within the past 3 years from Allergan Pharma, Ratiopharm, Boehringer Ingelheim Pharma, Eli Lilly, Novartis Pharma, Desitin Arzneimittel, Cerbotec, Bayer Vital, Hormosan Pharma, electroCore, Grünenthal, Reckitt Benckiser, and Teva. He does not hold any stocks of pharmaceutical companies or medical device companies. Mirja Koch and Caroline Baufeld are employees of Novartis Pharma GmbH. This study was funded by Novartis Pharma GmbH, Nürnberg, Germany.

EPR1089

Onabotulinumtoxin A Treatment Improved Health-Related Quality of Life in Adults with Chronic Migraine in the PREDICT Study: Results from Study Completers

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Background and aims: The PREDICT study aimed to assess long-term health-related quality of life (HRQOL) in Canadian adults with chronic migraine (CM) treated with onabotulinumtoxin A.

Methods: Canadian, multicentre, prospective, observational study (NCT02502123) in adults naïve to onabotulinumtoxin A for CM. Onabotulinumtoxin A (155-195U recommended) was administered every ~12 weeks over 2 years (7 cycles), per the Canadian product monograph. Primary endpoint: mean change in Migraine-Specific Quality of Life (MSQ) Tx4 vs. baseline. Secondary endpoint: headache days (daily headache diary). Unless noted, data presented as mean(SD); number of patients (n).

Results: 197 participants were enrolled; 123 (62.4%) completed all 7 treatment cycles and 74 (37.6%) discontinued the study (lost to follow-up [n=23], withdrew consent [n=8], adverse event [n=3], non-compliance [n=2], protocol violation [n=1], other [n=37]). 184 participants (average 45 years, predominantly female [84.8%] and Caucasian [94.6%]) received ≥1 treatment with onabotulinumtoxin A. At baseline, participants reported 20.9 (6.7) headache days/month, which decreased over time (range: -3.5 [6.3] at Tx1 [n=184] to -6.5 [6.6] at Tx4 [n=150]; all timepoints versus baseline, p<0.0001). Significant increases in MSQ post-Tx4 (n=150; restrictive: 21.5 [24.3], preventive: 19.5 [24.7], emotional: 22.9 [32.9]) were observed versus baseline, exceeding minimal important differences (all, p<0.0001). Additionally, completers reported 20.1 (6.7) headache days/month at baseline, which decreased over time (range: -3.9 [6.3] Tx1 [n=109] to -6.5 [6.5] Tx4 [n=107]; all timepoints versus baseline, p<0.0001). Significant increases in MSQ post-Tx4 (n=123; restrictive: 22.5 [23.5], preventive: 21.2 [24.7], emotional: 25.8 [32.7]) were also observed versus baseline in completers, exceeding minimal important differences (all, p<0.0001).

Conclusion: Real-world data from PREDICT demonstrate that onabotulinumtoxinA treatment for CM reduced headache days and improved HRQOL, with even greater improvements observed in study completers following long-term treatment.

Disclosure: This study was sponsored by Allergan Inc., Markham, Ontario, Canada.

EPR1090

Eptinezumab Reduced the Frequency of Migraine Days in Patients with Chronic Migraine and Medication-Overuse Headache: Subgroup Analysis of PROMISE-2

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Background and aims: Eptinezumab is a monoclonal antibody that inhibits CGRP for the prevention of migraine. This analysis evaluated the impact of eptinezumab on migraine frequency in patients with chronic migraine (CM) and medication-overuse headache (MOH) in the pivotal PROMISE-2 study.

Methods: PROMISE-2 randomized patients with CM to eptinezumab 100mg, 300mg, or placebo for 2 intravenous doses administered every 12 weeks. Trained investigators diagnosed MOH at screening based on 3 months of medication history and ICHD-3b criteria. Endpoints included change from baseline in monthly migraine days (MMDs) and $\geq 50\%$ and $\geq 75\%$ migraine responder rates over Weeks 1-12 and 13-24. In addition, during Days 1-7, the percentage of patients experiencing migraine was calculated.

Results: Of 1072 patients with CM treated, 431 (40.2%) were diagnosed with MOH (100mg, n=139; 300mg, n=147; placebo, n=145). During the 28-day baseline period, MOH patients experienced 16.7 migraine days (each arm). Over Weeks 1-12, eptinezumab-treated patients experienced greater reductions from baseline in MMDs than placebo patients (100mg, 8.2; 300mg, -8.5; placebo, -5.2). About twice as many eptinezumab-treated patients were $\geq 50\%$ (60.4%; 61.9%; 34.5%) or $\geq 75\%$ migraine responders (27.3%; 29.9%; 14.5%). Similar results were observed during Weeks 13-24. The percentage of patients experiencing migraine on Days 1 through 7 was lower with eptinezumab than placebo (baseline: ~59.7% across groups; Day 1: 27.8%; 30.1%; 45.5%).

Conclusion: Eptinezumab is efficacious in patients diagnosed with CM and MOH, with greater reductions in migraine days compared with placebo at week 12, and with effect as early as Day 1 and sustained through 24 weeks.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark

EPR1091

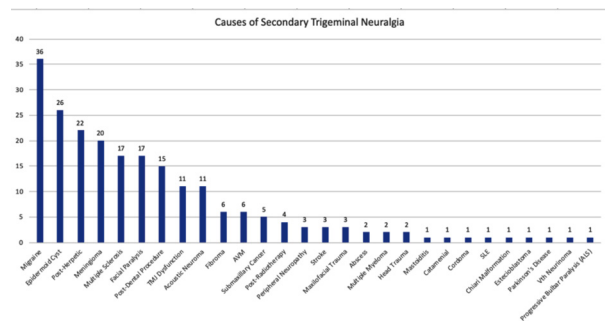
Etiological Diversity of 2ndary Trigeminal Neuralgia

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Background and aims: According to the American Academy of Neurology trigeminal neuralgia (TN) is classified regarding its etiology in classical, 2ndary to another disease and idiopathic when the cause is unknown. Although the 1st class represents about 70% of the total, there is a wide variety of diseases that can affect the trigeminal nerve and cause a 2ndary neuralgia. The aim of our study was to review and discuss all the causes of this type of TN seen in our clinic in the last 6 years.

Methods: A prospective recollection of all the cases of TN seen in our clinic from Jan 2014-Dec 2019 was performed. Patients diagnosed with classical or idiopathic TN were excluded from the final analysis and the frequency of each cause of secondary TN was registered.

Results: 1592 cases of TN were seen in our clinic between 2014-2019 of which 254 were 2ndary. We found 28 different causes of 2ndary TN, the most common pathologies were: migraine (16%), epidermoid cyst (12%), post-herpetic (10%), meningioma (9%) and multiple sclerosis (8%). Other causes found were: AVM, neurinoma, stroke, SLE, ALS and Catamenial TN.



Causes of 2ndary TN

Conclusion: TN can be 2ndary to a wide variety of diseases. It is important to always keep in mind that even though the majority of cases are due to a neurovascular contact, it is always wise to obtain a full clinical history and perform a proper physical examination complemented with a MRI in each patient, in order to rule out other causes in which the treatment and prognosis varies considerably.

Disclosure: Nothing to disclose

EPR1092

Pooled Analysis of Tolerability With Fremanezumab Treatment in Patients With Episodic or Chronic Migraine and Cardiovascular Medication Use at Baseline

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Background and aims: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. Adverse events (AEs) were evaluated in a subgroup of patients with episodic migraine (EM) or chronic migraine (CM) and cardiovascular (CV) medication use at baseline in this pooled analysis of phase 3 trials of fremanezumab.

Methods: This analysis included data from three phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. AEs reported for patients with baseline CV medication use were evaluated.

Results: Overall, 280 of 2,842 patients across these 3 studies were receiving CV medications at baseline, with similar proportions receiving CV medications across all treatment groups (9-11%). The most common type of CV medications used were agents acting on the renin-angiotensin system (3-4% across all treatment groups) and beta-blockers (3-4%). The most common AEs were injection-site-related (pain, erythema, and induration; Table). Cardiac disorder AEs were infrequent across all treatment groups (placebo, <1%; quarterly fremanezumab, 0%; monthly fremanezumab [675/225/225mg], 2%; monthly fremanezumab [225/225/225mg], 0%), as were vascular disorder AEs (0%, 1%, 6%, and 0%, respectively). No new safety signals were identified over 12 weeks of double-blind treatment.

Conclusion: This pooled analysis demonstrates that fremanezumab treatment over 12 weeks was well tolerated, with low and similar cardiac and vascular disorder AEs to placebo, in patients with migraine using CV medications at baseline.

Table. AEs With an Occurrence ≥5% of Patients in Any Treatment Group.

n (%)	Placebo (N=102)	Quarterly fremanezumab		Monthly fremanezumab	
		675mg/placebo (N=87)	675mg/225mg/225mg (N=54)	225mg/225mg/225mg (N=37)	225mg/225mg/225mg (N=37)
Patients with ≥1 AE	54 (53)	57 (66)	38 (70)	20 (54)	20 (54)
Injection-site pain	19 (19)	25 (29)	10 (19)	8 (22)	8 (22)
Injection-site erythema	10 (10)	17 (20)	7 (13)	5 (14)	5 (14)
Injection-site induration	8 (8)	16 (18)	12 (22)	10 (27)	10 (27)
Upper respiratory tract infection	5 (5)	3 (3)	3 (6)	3 (8)	3 (8)
Nasopharyngitis	3 (3)	5 (6)	4 (7)	3 (8)	3 (8)
Injection-site hemorrhage	2 (2)	2 (2)	3 (6)	1 (3)	1 (3)

AE, adverse event.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPR1093

Spinal nociceptive modulation and lipid mediators levels during the glyceryl trinitrate induction test in episodic migraine patients

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Background and aims: A derangement of the nociceptive system control as the disease progresses was found in migraine subjects. The endocannabinoids and their congeners may modulate the nociceptive pathways. Here, we evaluated the facilitation of nociceptive spinal modulation, anandamide (AEA) and palmitoylethanolamide (PEA) release, in patients affected by episodic migraine after glyceryl trinitrate (GTN) administration.

Methods: We enrolled 20 patients (33.8±8.4 years, 17 female) and 17 healthy controls (HC - 29.5±7.7, 12 female). In patients with a negative induction test (MIG-) and in HC, nociceptive withdrawal reflex, AEA and PEA plasma levels were recorded at baseline and 30, 60 (T-60) and 120 (T-120) minutes after sublingual GTN administration. Patients with a positive induction test (MIG+), were evaluated when a specific migraine-like headache reached an intensity of 5 on a 0-10 nociceptive rating scale (T-MIG) and after 1 hour (T-1h).

Results: 10 patients developed a migraine-like headache after GTN administration. The average latency of migraine onset was 63.0±55.0 minutes, therefore T-MIG and T-1h were compared with T-60 and T-120 respectively. After GTN, spinal sensitization was identified in MIG+ and MIG-, described as a decrease of single stimuli and temporal summation thresholds (p=0.016 and 0.001, respectively). After GTN, PEA levels significantly increased only in MIG+ patients at T-1h (p=0.031 vs baseline). AEA levels significantly increased in all subjects at T-120/T-1h (p=0.035 vs baseline), without significant differences between groups. Central sensitization parameters and lipid mediators' levels didn't correlate at each time point.

Conclusion: PEA release appears to be associated to the pain of migraine attack, as compensatory anti-inflammatory/analgesic mechanism.

Disclosure: Nothing to disclose

EPR1094

CGRP plasma levels and peripheral expression of specific microRNAs in chronic migraine with medication-overuse: changes induced by detoxification

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Background and aims: Chronic migraine (CM) is frequently associated to symptomatic medication overuse (MO) but the mechanisms underlying the development of MO remain unknown. Calcitonin gene related peptide (CGRP) is involved in sensitization phenomena and likely, in migraine chronification. MicroRNA expression patterns may be useful as disease biomarkers and for predicting individual risks of chronic pain.

Methods: We evaluated CGRP plasma levels and the expression of miR-34a-5p and miR-382-5p in peripheral blood mononuclear cells of subjects with episodic migraine (EM, N=30) and CM-MO (N=27), to investigate their role in reduction of headache frequency. CM-MO group was tested at baseline and 2 months after detoxification.

Results: Baseline levels of CGRP and microRNAs were significantly higher in CM-MO subjects compared with EM patients. All the CM-MO subjects completed successfully the detoxification and were overuse-free at 2 months. During the follow-up we recorded an overall 50% decrease in headache days/month reduction (26.23±5.24 vs 13.4±10). When stratifying the CM-MO group after detoxification in EM and CM, based on the mean headache number days during the 2-month follow-up (<15 or >15), in the EM (n=15) group, we found that both CGRP and microRNAs levels were significantly reduced as compared to baseline values. By contrast, in the CM group (n=12) we only observed a decrease in microRNAs, while CGRP plasma levels did not differ from baseline.

Conclusion: Increased CGRP plasma levels are associated to migraine severity, whereas miR-34a-5p and miR-382-5p changes are a consequence of MO.

Disclosure: This study was supported by Italian Ministry of Health to IRCCS Mondino Foundation, Pavia, Italy (RC19015D).

EPR1095

The Humanistic Disease Burden of Episodic and Chronic Migraine in France, Spain and the United Kingdom

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Background and aims: Migraine is a disabling disease affecting 14% of the population worldwide. Real-world data were collected on patients with episodic migraine (EM) and chronic migraine (CM) who had failed ≥2 preventive treatments in the UK, France, and Spain, with a focus here on health-related quality-of-life (HRQoL) outcomes.

Methods: A cross-sectional, web-based survey was conducted among eligible patients with EM and CM in the UK, France, and Spain. HRQoL was assessed using the Migraine Disability Assessment (MIDAS) and EuroQol 5-Dimension 5-Level (EQ-5D-5L) questionnaire (assessed for health “today” and during most recent migraine headache). Descriptive statistics were calculated at the country level and qualitatively compared across countries.

Results: Patients (n=316) were included from the UK (n=106; 80EM), France (n=105; 80EM), and Spain (n=106; 80EM). Of the CM patients, 63% were female, while of the EM patients, 48% were female. CM patients experienced greater migraine disability versus EM patients (median MIDAS score, 30 vs 12). For their most recent migraine, CM patients reported lower health status than EM patients, based on the EQ-5D-5L visual analog scale (median, 40 vs 60) and total index (median, 0.35 vs 0.52) scores. Among EM patients, MIDAS scores were highest in Spain (median, 19) followed by France (13) and the UK (8). EQ-5D-5L index scores for most recent migraine were comparable across countries (median, UK, 0.57; Spain, 0.55; France, 0.41).

Conclusion: Results reveal substantial migraine disability among patients who have failed previous preventive therapies and that unmet needs may be greater in certain countries.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPR1096

Procalcitonin levels in chronic migraine patients

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Background and aims: Procalcitonin (proCT) is a peptide released in situations of stress such as sepsis or major trauma. It is coded by the same gene as calcitonin-gene related peptide (CGRP), located in chromosome 11. According to current research, CGRP is the main molecular biomarker for migraine. Our aim is to evaluate the levels of proCT in chronic migraine (CM) patients and to correlate them with biomarkers of systemic inflammation such as interleukin-6 (IL-6) and C-reactive protein (CRP) and biomarkers of neurogenic inflammation such as soluble TNF-like weak inducer of apoptosis (sTWEAK) and calcitonin-gene related peptide (CGRP).

Methods: Cross-sectional study including 117 CM (ICHD2013) patients (48.6±11.2 years old; 97.4% women) and 70 healthy controls (47.4±10.7 years old; 97.1% women). Blood samples were obtained during interictal periods and levels of proCT were determined by electroquimioluminescence. Levels of IL-6, CRP, sTWEAK and CGRP were determined by ELISA. Results were compared using T-test and One-Way ANOVA and associations were evaluated by adjusted logistic regression.

Results: ProCT levels were significantly higher in CM patients (0.040±0.019 vs. 0.030±0.023ng/ml; p=0.003). Pro-CT levels were correlated with CGRP levels (r=0.498, p<0.001), but no correlation was found with IL-6, sTWEAK or CRP levels.

Conclusion: Our results point to a possible role of proCT as an inflammation-related biomarker in CM and a proxy biomarker of CGRP levels in this pathology.

Disclosure: Nothing to disclose

EPR1097

Retrospective cohort study of patients with predominantly nocturnal headache.

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Background and aims: Hypnic headache is a rare primary headache characterized by strictly sleep-related attacks yet, there is also an ill-defined group of patients with predominantly nocturnal headache (PNH), without criteria for hypnic headache or other entity.

Methods: Retrospective analysis of a cohort of adults with PNH identified through screening of medical records of a tertiary hospital headache clinic. Demographic variables, pain characteristics, previous and current acute and prophylactic medications, days of analgesic usage, and previous history of headache were collected.

Results: We identified 30 patients with PNH (25 females; mean age of onset 56.8 years (σ=9,4), 16 (64%) postmenopausal). Patients had a median of 17.3 days (IQR=9-30) of headache per month, occurring mostly between 2 and 4am. All patients had a moderate to severe pain that lasted more than 15 minutes and 12 patients had features of migraine. Half of them had tried 3 or more prophylactics, usually without clinically significant improvement, and 14 (46%) patients filled the criteria for medication-overuse headache (MOH). 21 (70%) patients had a previous diagnosis of migraine: in 12 the pain changed characteristics and became nocturnal; in 6 it disappeared before onset of a new strictly nocturnal pain and in 3 patients it became diurnal and nocturnal.

Conclusion: PNH is frequently associated with a history of migraine. It can lead to MOH because of its severity and the lack of response to prophylactics. Whether envisioned as part of migraine natural history or as a new entity, more studies on PNH are needed to optimize management of these patients.

Disclosure: Nothing to disclose

Headache and pain 2

EPR1098

Real-world Trends in Characteristics of Migraine Patients Newly Initiated on Erenumab in the United States

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Background and aims: Erenumab-aooe (erenumab; Aimovig[®]) is indicated for the preventive treatment of migraine in adults. While its efficacy and safety in migraine patients have been evaluated in multiple clinical trials, real-world use of erenumab has not been fully investigated. This retrospective analysis aimed to characterise migraine patients initiating erenumab in real-world setting using a US electronic health record (EHR) database.

Methods: Adult patients with ≥ 1 erenumab written prescription/administration between 5/1/2018-3/31/2019 were identified from Optum EHR database (index date=date of the 1st erenumab prescription/administration). Patient characteristics and initial prescriber specialty were assessed. The real-world trend of the patients' profile was assessed by the month of erenumab initiation.

Results: This study included 10,076 patients initiating erenumab; female (86.3%), average age 46.5 (standard deviation=13.0) years, patients were most commonly Caucasian (87.9%), Non-Hispanic (90.6%) and commercially insured (60.8%) at the index date. Commonly observed comorbid conditions during the 12-month pre-index period were anxiety (29.1%), depression (29.0%), and hypertension (21.7%). The mean Elixhauser comorbidity score in the 12-month pre-index period decreased over the month of erenumab initiation (Figure 1). More neurologists/headache specialists than general practitioners initiated erenumab in more severe migraine patients. Over time, there was an increase in general practitioners' prescribing erenumab, and prescription in less severe migraine patients (a proxy of declining trend in chronic migraine and triptan use) (Figure 2).

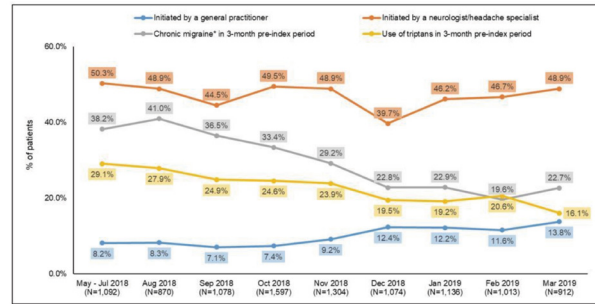


SD, standard deviation

Note:

The Elixhauser comorbidity index measures the baseline comorbidity based on inpatient and outpatient administrative claims data. The score is generated via the summation of points from each disease and the range of possible scores is from -19 (lesser disease burden) to +69 (greater disease burden).

Figure 1. Elixhauser comorbidity score assessed over 12-month pre-index period in patients initiating erenumab over time



* Diagnosis code of chronic migraine without aura was used.

Figure 2. Initial prescriber specialty, chronic migraine diagnosis & triptan use prior to erenumab initiation over time

Conclusion: Patients initiating erenumab had a higher comorbidity burden (anxiety, depression, and hypertension) in real-world compared with the general migraine population. Over time, a broader population of migraine patients received erenumab, and more general practitioners prescribed erenumab.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland.

EPR1099

Response to prophylactic treatment in Linear Headache: a series of 16 patients

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Background and aims: Linear Headache (LH) was described in 2014 and combines features of Nummular Headache (NH) and Epicrania Fugax (EF). It is not yet clarified whether it constitutes a subtype of the former, a focal manifestation of migraine or a singular disorder. We aim to analyze the response to acute and preventive medication in LH patients.

Methods: We prospectively included patients with 1) Continuous or intermittent head pain with the following characteristics: A) Sharply contoured, B) fixed in size and shape, C) linear shape; 2) absence of movement within the trajectory; 3) no circumscription of the pain to the territory of any nerve. We describe the number of patients that used each treatment and the response, defined by 50% reduction in monthly headache days.

Results: From April 2014 to April 2019, 14 patients fulfilled criteria, being 8 of them women. Mean age at onset was 40.6±21.6 years and mean time of evolution was 6.6±10.5 years. Prophylactic treatment had been used by 13/16 patients, with a mean of 4 treatments (range 1-6). Number of patients with response per drug was 1/5 for amitriptyline, 1/3 for lamotrigine, 1/2 with betablockers, 0/3 to topiramate and 0/2 pregabalin, gabapentine, duloxetine and zonisamide. Anesthetic blockade was used in 7 patients with 1 positive response and onabotulinumtoxinA was used in 7 cases, with 50% response in all cases, being excellent (>75%) in 4.

Conclusion: Response to prophylactic in LH patients resembles more NH than EF or migraine, being onabotulinumtoxinA the treatment with the better responder rate.

Disclosure: Nothing to disclose

EPR1100

Changes in Work Productivity and Interictal Burden: Results from a Randomized, Double-Blind, Placebo-Controlled Clinical Trial Evaluating Galcanezumab in Adults with Treatment-Resistant Migraine (CONQUER)

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Background and aims: We evaluated changes in work productivity/activity impairment and interictal burden attributed to migraine among patients treated with galcanezumab or placebo.

Methods: Patients with episodic or chronic migraine, who had multiple previous migraine preventive treatment failures, were randomized to galcanezumab 120mg/month (with a 240mg loading dose; n=232) or placebo (n=230) in this 3-month double-blind study (#NCT03559257). Absenteeism, presenteeism, work productivity loss, and activity impairment were assessed using the Work Productivity and Activity Impairment Questionnaire (WPAI) and calculated as impairment percentages; group comparison was conducted using ANCOVA. Burden between attacks was assessed using the Migraine Interictal Burden Scale (MIBS; score range 0-12; 0=none; ≥5=severe); group comparison was conducted using mixed model repeated measures.

Results: A total of 97.6% patients completed the 3-month, double-blind phase. The mean reductions of WPAI scores from baseline were significantly greater (all p≤0.0004) in the galcanezumab group compared with placebo in the percent of activity impairment (20.7% vs 8.6%), presenteeism (12.5% vs 2.6%), and overall work impairment (14.3% vs 3.5%); absenteeism was not significantly different. On the MIBS, mean change from baseline of 5.5 (indicative of severe interictal burden) was greater for the galcanezumab group (1.8) compared with placebo (0.8; p<0.0001).

Conclusion: Significantly greater reductions in migraine-related work productivity/activity impairment and interictal burden were seen in galcanezumab-treated patients relative to placebo.

Disclosure: This research was supported by Eli Lilly and Company. ClinicalTrials.gov: #NCT03559257 (15Q-MC-CGAW)

EPR1101

First data collection on the use of prophylactic migraine treatments including the monoclonal antibody Erenumab focused on the patient's personal experience

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Background and aims: The perspective of patients regarding a new therapeutic option is not systematically captured. Quality of life including daily activity, time with the family and the wellbeing of the patient are deciding factors in migraine management. Thus, it is imperative to understand the patients' perspective on treatment with erenumab, a fully human monoclonal antibody targeting the CGRP receptor, available since November 2018 in Germany.

Methods: From July 2019 to December 2019, an online survey of German patients diagnosed with migraine collected details regarding their disease and experience with migraine therapies. Patients who had been on erenumab for at least 3 months were further asked about their treatment outcome and impact on their lives.

Results: An interim analysis covered 19740 migraine patients of which 39% had prior prophylactic treatment and 37% are using non-pharmaceutical treatments. The analysis included 91 erenumab patients with a mean of 18 years disease duration. These erenumab patients have tried 6.1 different pharmacologic prophylactic therapies on average. 85% of erenumab-patients stated that they can cope better with daily activities, 83% have fewer days lost to migraine since therapy initiation and 47% could already feel an improvement of their migraine symptoms after the 1st injection. For EAN congress, the full data set of >20,000 migraine patients will be presented.

Conclusion: PERISCOPE provides us the 1st real world data of German patients treated with erenumab and shows that patients' benefit from erenumab treatment with regard to improvement of quality of life and reduction of migraine specific symptoms.

Disclosure: This study has been funded by Novartis Pharma GmbH.

EPR1102

Galcanezumab in migraine prevention: a systematic review and meta-analysis of randomized controlled trials

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Background and aims: Galcanezumab along with other three monoclonal antibodies targeting the calcitonin gene related peptide (CGRP) pathway represent the latest and the unique disease-specific and mechanism-based treatments for the prophylaxis of migraine. The aim of this study is to provide a pooled safety and efficacy analysis of all phase 3 randomized-controlled trials of galcanezumab, in the preventive therapy of migraine.

Methods: A computer-based literature search was conducted on MEDLINE and the US National Institutes of Health Clinical Trials Registry for phase 3 randomized-controlled trials of galcanezumab in migraine prevention. The primary outcome was the mean change in monthly migraine headache days (MHDs). The proportions of patients who reported at least one adverse event (AE), one serious AE or withdrew from the study were used as safety outcomes.

Results: 3 trials were included in the meta-analysis. Migraine preventive treatment with subcutaneous galcanezumab, at both 120mg and 240mg dosages, was associated with a significantly greater reduction in the mean number of monthly MHD vs. placebo (120mg MD=-1.98 95% CI=-2.33 to -1.63; p<0.0001) or (240mg MD=-1.86 95% CI=-2.2 to -1.53 p<0.0001). Galcanezumab was found to be more efficacious in all key 2ndary outcomes as well. Regarding safety, most of the adverse events were mild to moderate while drop-out rates and serious adverse events were low.

Conclusion: Galcanezumab is an efficacious and well-tolerated preventive treatment for migraine. Larger clinical trials with longer follow-up periods need to be conducted in order to provide more safety data of the above-mentioned drug.

Disclosure: Dr. P. Gklinos reports no disclosures. Dr. D.D. Mitsikostas has received honoraria, research and travel grants from Allergan, Amgen, Biogen, Cefaly, Eli Lilly, Electrocore, Mertz, Novartis, Roche, Sanofi, Specifar and Teva.

EPR1103

Natural course of Visual Snow Syndrome: a long-term follow-up studyM. Graber¹, P.J. Goadsby², A. Scutelnic¹, C. Schankin¹¹Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Berne, Switzerland, ²Headache Group, Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom, London, United Kingdom**Background and aims:** Visual Snow Syndrome (VSS) is characterized by a continuous positive pan-field visual disturbance resembling the view of a badly-tuned analogue television plus associated visual symptoms. For many patients VSS can be disabling. We present the 1st longitudinal study describing the long-term natural course of the disorder over 8 years.**Methods:** In total 78 Patients with confirmed VSS, including normal ophthalmologic exams, were followed from November 2011 to December 2019. The clinical course of the disorder was assessed in a semi-structured telephone interview.**Results:** 40 of 78 (51%) patients were reached for the follow up interview. Mean follow up time was 83.6±4.5 months. 2 of 40 (5%) reported the onset of additional visual symptoms, which were tunnel vision and light flashes. Compared to 2011, less patients rated visual snow itself as the most disturbing symptom (40% in 2019 vs 72.5% in 2011, p=0.001); instead, patients suffered more from floaters and palinopsia. New treatments were commenced in 14/40 (35%) patients. Of those, 6 (42%) were somewhat helpful: lamotrigine, diet/vitamin supplements/probiotics, lorazepam, cinnarizine, polarized glasses, chiropractic treatment. During follow up, 3 patients experienced new visual migraine aura without headache, and one had new migraine headache (total prevalence aura 35%, migraine 47.5%). There was no significant difference in anxiety and depression measured by the PHQ-8 and the GAD-7 questionnaire.**Conclusion:** In a group of patients with VSS, symptoms can persist over 8 years without spontaneous resolution. New visual symptoms can develop, but visual snow itself might get less bothersome.**Disclosure:** Nothing to disclose

EPR1104

Early Efficacy in Patients ≥60 Years of Age With Episodic or Chronic Migraine: Pooled Results of 3 Randomised, Double-blind, Placebo-controlled Phase 3 StudiesD. Holle-Lee¹, J.M. Cohen², X. Ning², L.J. Krasenbaum², R. Yang², P. Pozo-Rosich³¹West German Headache Center, University Hospital Essen, Department of Neurology, Essen, Germany, ²Teva Branded Pharmaceutical Products R&D, Inc., West Chester, PA, USA, ³Headache Unit, Neurology Department, Vall d'Hebron University Hospital, Barcelona, and Headache and Neurological Pain Research Group, Vall d'Hebron Institute of Research (VHIR), Universitat Autònoma de Barcelona, Barcelona, Spain**Background and aims:** Older patients with migraine often experience more frequent and severe side effects with migraine preventive medications. Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. This pooled analysis evaluated early efficacy of fremanezumab in patients ≥60 years of age.**Methods:** This analysis in patients ≥60 years of age with episodic migraine (EM) or chronic migraine (CM) included data from 3 double-blind phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to subcutaneous quarterly or monthly fremanezumab, or matched monthly placebo over 12 weeks. Reductions from baseline in weekly migraine days and monthly headache days of at least moderate severity, and proportions of patients achieving ≥50% reduction in monthly migraine days were evaluated during the 1st 4 weeks.**Results:** Reductions from baseline in weekly migraine days were significantly greater with fremanezumab (monthly and quarterly) versus placebo by Week 1 (P<0.05; Table). Reductions in monthly headache days of at least moderate severity were significantly greater with both fremanezumab regimens versus placebo at Week 4 (P<0.05; Table). The proportion of patients achieving ≥50% reduction in monthly migraine days at Week 4 was significantly greater with quarterly fremanezumab versus placebo (P<0.05; Table).**Table. Early Efficacy of Fremanezumab in Migraine Patients ≥60 Years of Age**

	Placebo (n=80)	Quarterly fremanezumab (n=74)	Monthly fremanezumab (n=92)
Change from BL in weekly average number of migraine days at Week 1			
LSM (SE)	-0.4 (0.20)	-1.1 (0.21)	-1.1 (0.19)
LSMD (SE) versus placebo	—	-0.7 (0.27)*	-0.7 (0.26)*
Change from BL in monthly average number of headache days of at least moderate severity at Month 1			
LSM (SE)	-1.7 (0.54)	-4.3 (0.56)	-4.0 (0.51)
LSMD (SE) versus placebo	—	-2.6 (0.70)*	-2.2 (0.66)*
≥50% reduction from BL in monthly average number of migraine days at Month 1			
Proportion of patients, n (%)	18 (23)	28 (38)	32 (35)
OR (95% CI) versus placebo	—	2.15 (1.06, 4.38)*	1.86 (0.94, 3.68)

BL, baseline; LSM, least-squares mean; SE, standard error; OR, odds ratio; CI, confidence interval.
*P<0.05 versus placebo.**Conclusion:** In this pooled analysis, fremanezumab treatment demonstrated early onset of efficacy in patients ≥60 years of age with EM or CM.**Disclosure:** This study was funded by Teva Pharmaceuticals.

EPR1105

Characterization of Treatment Emergent Adverse Events in Headache Pain-Free Patients after Lasmiditan Dosing for the Acute Treatment of a Single Migraine Attack

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Background and aims: Evaluate treatment emergent adverse events (TEAEs) of patients experiencing pain freedom, or experiencing no change/worsening of pain 2 hours after lasmiditan treatment.

Methods: Post-hoc analyses were completed using pooled data from 2 phase 3 studies, SAMURAI (2231 patients in almost 100 US-based centers) and SPARTAN (3005 patients in 125 centers in the US, UK, Germany). Migraine patients were randomized to receive placebo or lasmiditan (50 [SPARTAN only], 100, or 200mg). Fisher's exact test was used to compare overall adverse event rate of patients in each dose level group that responded at 2 hours versus corresponding group that stayed same or worsened.

Results: Top 5 TEAEs experienced by pain-free patients at 2 hours were dizziness, somnolence, paraesthesia, fatigue, hypoaesthesia. Among lasmiditan-treated patients, percentage of patients reporting ≥ 1 TEAE was higher in group experiencing pain freedom versus group who experienced no change/worsening of pain at 2 hours. A dose response in pain-free patients was observed, with greater percentages of patients reporting paraesthesia, fatigue, hypoaesthesia when treated with higher lasmiditan doses. However, only within lasmiditan 200mg-dose group, the overall adverse event rate in patients who experienced pain freedom at 2 hours was significantly higher versus the group that stayed same or got worse (44.5% vs 30.7%, $p=0.002$).

Conclusion: Lasmiditan-treated patients who experienced pain freedom reported TEAEs at a higher rate versus lasmiditan-treated patients who showed no improvement/worsening of pain. Additionally, patients treated with lasmiditan who achieved pain freedom had higher incidence of TEAEs with higher lasmiditan doses.

Disclosure: The SPARTAN and SAMURAI studies were sponsored by CoLucid Pharmaceuticals, a wholly owned subsidiary of Eli Lilly and Company, Indianapolis Indiana.

EPR1106

Healthcare Resource Utilization and Economic Burden of Migraine in the United Kingdom, France, and Spain: Results of a Real-world Study

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Background and aims: This longitudinal, retrospective study evaluated epidemiology, pharmacologic management, resource utilization, and treatment costs (medications/consultations/diagnostic tests) for patients with episodic migraine (EM; <15-days/month, last 3-months) and chronic migraine (CM) in the UK, France, and Spain.

Methods: The patient cohort, from a representative panel of electronic medical records, included adults with a record of migraine diagnosis or specific treatment from April 2016 to March 2017. Patients were stratified, with triptan usage as a surrogate for migraine, by migraine classification (EM/CM). Patients were followed for 1-year after 1st recorded migraine diagnosis or specific migraine treatment.

Results: This study included 42,439 patients in the UK (EM, 96%), 31,250 in France (EM, 88%), and 10,577 in Spain (EM, 82%). In the UK, France, and Spain, 15.7%, 10.1%, and 2.7% of all patients, respectively, received acute and preventive treatments. During follow-up, CM patients had more mean migraine-related consultations with general practitioners than EM patients in the UK (13.9 vs 4.6), Spain (15.0 vs 5.7), and France (4.2 vs 2.5); proportions with ≥ 1 migraine-related diagnostic test were higher for CM versus EM patients in the UK (12.1% vs 7.2%) and France (25.1% vs 18.7%), but not Spain (10.7% vs 9.8%). Mean quarterly treatment costs (payer's perspective) were higher in CM versus EM patients in the UK (434.3€ vs 104.3€), France (155.7€ vs 40.8€), and Spain (98.6€ vs 111.5€).

Conclusion: Migraine is associated with substantial healthcare and economic burden, with higher resource utilization and treatment costs among CM versus EM patients in the UK, France, and Spain.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPR1107

Pooled Analysis of Cardiovascular Safety With Fremanezumab Treatment in Patients With Migraine by Number of Cardiovascular or Cerebrovascular Risk Factors

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Background and aims: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for the preventive treatment of migraine in adults. Overall adverse events (AEs) and cardiovascular (CV) safety of fremanezumab were evaluated in a subgroup of patients with migraine and cardiovascular/cerebrovascular risk factors (CVRFs; eg, smoking, diabetes mellitus, hyperlipidemia, obesity, hypertension, birth control pill use) at baseline.

Methods: This pooled analysis included data from 3 phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to receive subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Overall AEs and cardiac and vascular disorder AEs (CVAEs) were evaluated by number of CVRFs at baseline and/or CV medical history. Patients with serious vascular diseases were excluded.

Results: In total, 499 out of 2,842 pooled patients had ≥ 2 CVRFs (0 CVRFs, n=1,350; ≥ 1 CVRF, n=1,492; ≥ 2 CVRFs, n=499; ≥ 3 CVRFs, n=183, ≥ 4 CVRFs, n=55). Of these patients, 66% had CV medical history. Common CV risk factors were hypertension, obesity, and use of hormonal birth control pills. Over 12 weeks of double-blind treatment, CVAEs were infrequent in patients with ≥ 2 or ≥ 3 CVRFs; no CVAEs were reported in patients with ≥ 4 CVRFs (Table). Incidences of CVAEs were similar in patients with and without CV medical history. No new CV safety signals were identified.

Conclusion: This pooled analysis demonstrates that fremanezumab treatment was well tolerated in migraine patients with ≥ 2 CVRFs and did not increase the risk of CVAEs compared with placebo.

Table. Overall AEs and Cardiac or Vascular Disorder AEs By Number of Cardiovascular or Cerebrovascular Risk Factors, n (%)

AEs, n (%)	Placebo (n=169)	Quarterly fremanezumab 675mg/placebo/placebo (n=174)	Monthly fremanezumab	
			675mg/225mg/225mg (n=95)	225mg/225mg/225mg (n=61)
≥ 2 CVRFs				
≥ 1 AE*	96 (57)	116 (67)	60 (63)	36 (59)
Cardiac disorders	3 (2)	1 (1)	1 (1)	0
Palpitations	0	0	1 (1)	0
Supraventricular tachycardia	0	1 (<1)	0	0
Atrial fibrillation	1 (<1)	0	0	0
Bradycardia	1 (<1)	0	0	0
Tachycardia	1 (<1)	0	0	0
Vascular disorders	1 (<1)	3 (2)	4 (4)	0
Hypertension	1 (<1)	3 (2)	1 (1)	0
Hypertensive crisis	0	0	1 (1)	0
Hypotension	0	0	1 (1)	0
Raynaud's phenomenon	0	0	1 (1)	0
≥ 3 CVRFs				
≥ 1 AE	36 (59)	48 (71)	26 (72)	7 (39)
Cardiac disorders	1 (2)	0	1 (3)	0
Palpitations	0	0	1 (3)	0
Tachycardia	1 (2)	0	0	0
Vascular disorders	1 (2)	2 (3)	2 (6)	0
Hypertension	1 (2)	2 (3)	1 (3)	0
Hypertensive crisis	0	0	1 (3)	0
≥ 4 CVRFs				
≥ 1 AE	10 (59)	14 (70)	9 (75)	2 (33)
Cardiac disorders				
Vascular disorders				
			None reported	None reported
			None reported	None reported

CVRFs, cardiovascular/cerebrovascular risk factors; AE, adverse event. *Overall AEs.

Disclosure: This study was funded by Teva Pharmaceuticals.

Motor neurone diseases

EPR1108

Gene Therapy in Spinal Muscular Atrophy Type 1 (SMA1): Long-Term Follow-Up (LTFU) From the Onasemnogene Abeparvovec Phase 1 Clinical Trial

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Background and aims: Onasemnogene abeparvovec (formerly AVXS-101), a 1-time intravenous gene therapy, delivers a fully functional copy of the human survival motor neuron (SMN) gene that addresses the genetic root cause of SMA. In the phase 1 trial (START; NCT02122952), SMA1 patients who received an onasemnogene abeparvovec infusion at the high dose (Cohort 2, n=12) demonstrated significantly improved outcomes vs untreated natural history. Here, we evaluate long-term safety and efficacy of high-dose onasemnogene abeparvovec in patients previously treated in START.

Methods: Patients in START could rollover into a LTFU study (Study LT-001; NCT03421977). Primary objective: long-term safety. Patients have annual visits (5 years) followed by annual phone contact (additional 10 years). Patient record transfers are requested. Safety assessments include medical history and record review, physical examination, clinical laboratory evaluation, and pulmonary assessments. Efficacy assessments include evaluation of developmental milestones maintenance.

Results: 13 patients (Cohort 1, n=3; Cohort 2, n=10) enrolled (31 May 2019). All Cohort 2 patients were surviving free of permanent ventilation (mean [range] age at last follow-up: 4.2 [3.7–5.0] years; mean [range] time since dosing: 3.9 [3.5–4.6] years). No developmental milestones were lost; 2 patients achieved standing with assistance. Of the 10 enrolled Cohort 2 patients, 6 require no regular, daily respiratory support and 7 are not receiving concomitant nusinersen. No new treatment-related serious adverse events occurred (8 March 2019).

Conclusion: 1-time intravenous administration of onasemnogene abeparvovec at the high dose in START continues to provide durable efficacy with milestone development in Study LT-001.

Disclosure: AveXis, Inc., a Novartis Company, sponsored this clinical trial.

EPR1109

Onasemnogene Abeparvovec-xioi Gene Therapy in Presymptomatic Spinal Muscular Atrophy (SMA): SPR1NT Study Update

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Background and aims: SMA is caused by biallelic SMN1 deletion/mutation. Copies of SMN2 modify disease severity. This study evaluates safety/efficacy of onasemnogene abeparvovec (formerly AVXS-101) in presymptomatic SMA patients.

Methods: SPR1NT is a multicentre, open-label, phase 3 study. Asymptomatic patients expected to develop SMA (2–3xSMN2, ≤6 weeks) receive a 1-time intravenous onasemnogene abeparvovec infusion and are assessed through 18/24 (2xSMN2/3xSMN2) months. Primary outcomes: sitting ≥30 seconds/standing unassisted (2xSMN2/3xSMN2). Exploratory outcomes include CHOP INTEND.

Results: As of 31 May 2019, 23 infants were dosed (8–43 days of age [mean: 24.7]; 2xSMN2/3xSMN2/4xSMN2, n=10/12/1). All patients are alive and none required ventilation support as of last visit. Among 2xSMN2 patients, 7 achieved a full/near full CHOP INTEND score of 60–64; 9 achieved head control; 6 achieved sitting (all within the

WHO 1st–99th percentile range [3.9–9.2 months]); 3 achieved standing with assistance (mean [range]: 10.1 [8.8–12.3] months). Among 3xSMN2 patients, 11 achieved head control; 2 sat (6.3–9.0 months); 1 crawled/stood with assistance (9.0 months). No patient is delayed in standing alone or independent sitting. All patients (2x–3xSMN2) with a 6-month evaluation (12/12) had normal swallowing. As of 8 March 2019, 13/18 patients experienced ≥ 1 TEAE; treatment-related TEAEs were reported in 7/18 patients; 4/18 patients experienced TEAEs of special interest.

Conclusion: Preliminary SPR1NT data show improvements in presymptomatic SMA patients dosed with onasemnogene abeparvovec vs SMA type 1 natural history, underscoring the importance of early treatment.

Disclosure: This study was sponsored by AveXis, Inc., a Novartis company.

EPR1110

FIREFISH Part 2: Efficacy and safety of risdiplam (RG7916) in infants with Type 1 spinal muscular atrophy (SMA)

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions and/or mutations of the SMN1 gene. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (RG7916) is an orally administered, centrally and peripherally distributed SMN2 pre-mRNA splicing modifier that increases the levels of functional SMN protein. Part 2 of the FIREFISH study (NCT02913482) aims to determine the efficacy and safety of risdiplam in infants with Type 1 SMA.

Methods: FIREFISH is an ongoing, multicentre, open-label study of risdiplam in infants aged 1–7 months at enrolment with Type 1 SMA and two SMN2 gene copies. Part 1 (n=21) assesses the safety, tolerability, pharmacokinetics and pharmacodynamics of different risdiplam dose levels (plus exploratory efficacy outcomes). The primary objective of confirmatory Part 2 (n=41) is to investigate the efficacy of risdiplam at the dose selected in Part 1. The primary efficacy endpoint is the proportion of infants sitting without support for 5 seconds after 12 months of treatment, as assessed by Item 22 of the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development, third edition. Additional secondary endpoints will also be measured.

Results: Here we will report safety and novel efficacy data from FIREFISH Part 2 in infants treated with risdiplam for a minimum of 12 months at the Part 1 selected dose.

Conclusion: FIREFISH Part 2 will provide important data on the efficacy and safety of risdiplam in Type 1 SMA.

Disclosure: Study sponsored by F. Hoffmann-La Roche AG, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media, UK, in accordance with Good Publication Practice (GPP3) guidelines.

EPR1111

C9orf72 ALS human neural organoids for the development of new therapeutics and disease modeling.

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease. C9orf72 repeat expansion is the most frequent genetic cause of ALS (C9ALS) in Europe and North America. Partially owing to an incomplete understanding of disease etiopathogenesis, disease-modifying therapies in C9ALS still lack. A better insight into C9ALS pathomechanisms in reliable models is fundamental for developing new therapeutics. Here, we aim to model C9ALS pathology in 3D human neural organoids.

Methods: We differentiated iPSCs from C9ALS patients and healthy controls' fibroblasts using a free-floating 3D-culture method. We generated early cerebral-like organoids (COs) using standard methods and ventral spinal cord-like organoids (vSCOs) with a modified protocol inducing neural caudalization and ventralization. Then, we treated C9ALS COs and vSCOs with morpholino antisense oligonucleotides (MO) against c9orf72 repeat expansion. Finally, we evaluated the differentiation of organoids at different time points with immunohistochemical and qPCR analysis.

Results: We obtained control and C9ALS COs and vSCOs organoids displaying different co-existing neuronal subpopulations. COs exhibited progenitor (SOX2), forebrain (PAX6) and immature post-mitotic neuronal markers (TUJ1); vSCOs expressed SOX2, TUJ1, ventro/caudal marker (HOXB4) and motor neuron marker (ISL1). C9ALS organoids dissociated into single cells showed pBRCA1 and γ H2AX foci, markers of DNA damage associated with c9orf72 expansion. Preliminary results on gene expression analysis using qPCR reported differential expression of genes involved in DNA damage response (GADD45A, CDKN1A) in MO treated C9ALS organoids.

Conclusion: Neural organoids represent an innovative in vitro system and a valuable platform for modelling aspects of C9ALS pathology, studying C9ALS pathomechanisms and potentially developing new treatments in vitro.

Disclosure: Nothing to disclose

EPR1112

Human Organoids to study and treat Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a neuromuscular disease and the 1st cause of genetic death in infancy. SMA results from mutations in the Survival Motor Neuron (SMN) gene encoding for SMN, a ubiquitously expressed protein with a fundamental role in RNA processing. The optimization of available therapies and the development of complementary therapeutic approaches to SMA requires a deeper understanding of SMN pathophysiology in reliable models. We herein present a new model of SMA pathology in 3D human neural organoids.

Methods: We generated induced pluripotent stem cells (iPSCs) from fibroblasts of SMA patients and healthy controls and developed cerebral organoids, exploiting an already established protocol. Using a novel modified differentiation method based on small molecules to promote caudalization and ventralization, we also derived ventral spinal cord-like organoids. We performed morphological and molecular analyses and single-cell RNAseq to evaluate the organoid differentiation state. Electrophysiological studies were also undertaken to study circuit function and activity. Ventral spinal cord-like organoids were also treated with a novel antisense oligonucleotides able to restore SMN protein levels through SMN2 splicing correction.

Results: SMA organoids exhibited a significant alteration in their neurofilament elongation and electrophysiological activity compared to those derived from healthy controls. Treatment of SMA ventral spinal cord-like organoids with a second-generation optimized anti-sense oligonucleotide rescued SMN levels and main pathological features.

Conclusion: Our data support the use of neural organoids as an innovative in vitro platform to investigate pathogenic mechanisms and test potential therapeutic strategies.

Disclosure: Nothing to disclose

EPR1113

Altered excitability in upper and lower motor neurons in Amyotrophic Lateral Sclerosis

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Background and aims: Corticomotoneuronal hyperexcitability via an anterograde trans-synaptic glutaminergic process has been proposed as an underlying mechanism for the processes underlying motor neuron degeneration in ALS. The initiation site of degeneration is still controversial. In this study we aim to explore the temporal pattern of excitability of upper and lower motor neurons over the disease course.

Methods: We examined 62 patients and 25 controls subjects. Multiple excitability measurements of median nerve were recorded from the abductor pollicis brevis muscle and upper motor neuron excitability was tested using transcranial magnetic stimulation of increasing intensity and recording of the same muscle.

Results: Our findings reveal that in ALS patients there is increased refractoriness, higher threshold changes in depolarizing threshold electrotonus at 90-100ms and higher superexcitability along with lower subexcitability of the recovery cycle. Regarding the peripheral excitability, our data demonstrate significant changes in the threshold of depolarizing electrotonus at 90-100ms at early stages of ALS. Furthermore, with respect to the cortical excitability, there is a positive correlation between the stage of ALS and the slope of the area of the motor evoked potentials (MEPs); the earlier the stage the greater the increase in MEPs. Finally, the excitability of lower and upper motor neurons was concurrently increased in our patients.

Conclusion: Central and peripheral excitabilities are increased in ALS and their measures can serve as prognostic factors for the disease.

Disclosure: Nothing to disclose

EPR1114

Clinical Development of SRK-015, a Fully Human Anti-proMyostatin Monoclonal Antibody, for the Treatment of Later Onset Spinal Muscular Atrophy

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Background and aims: SRK-015 is a fully human anti-proMyostatin monoclonal antibody (mAb) that selectively binds to pro-/latent myostatin with high affinity, inhibiting its activation. SRK-015 is being developed for the treatment of spinal muscular atrophy (SMA) with the aim of offering clinically meaningful improvements in motor function.

Methods: A Phase 1, adult healthy volunteer study demonstrated a favorable safety profile at all doses tested; a well-behaved pharmacokinetic profile and robust and durable target engagement. The ongoing Phase 2 study evaluates the safety and efficacy of SRK-015 dosed IV every four weeks over 52 weeks. 3 distinct and parallel cohorts were enrolled. Cohort 1 enrolled ambulatory Type 3 SMA patients treated with 20mg/kg of SRK-015 as monotherapy, or in conjunction with an approved SMN up-regulator therapy. Cohort 2 enrolled Type 2 or non-ambulatory Type 3 SMA patients, who were already treated with an approved SMN up-regulator therapy. Patients were treated with 20mg/kg of SRK-015. Cohort 3 enrolled Type 2 SMA patients, who initiated treatment with an approved SMN up-regulator therapy before turning 5; patients were randomized 1:1 to either 2mg/kg or 20mg/kg of SRK-015.

Results: The primary objectives of this study are safety and efficacy (including Revised Hammersmith Scale, Hammersmith Functional Motor Scale Expanded and other motor function outcome measures).

Conclusion: N/A

Disclosure: All authors of this abstract are employees of Scholar Rock, a biopharmaceutical company. At the time of this abstract submission, this data has not been presented at, nor accepted to, any other medical congress.

EPR1115

Facial Onset Sensory and Motor Neuronopathy (FOSMN): Aetiology, Pathophysiology and Natural History

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Background and aims: FOSMN Syndrome remains poorly characterised as only small number of cases have been described in the literature. Herein, we describe 6 novel cases and perform the 1st systematic review of the literature (SRL), thus elucidating the aetiology, pathophysiology and natural history of FOSMN.

Methods: Clinical examination, SRL, genetic testing, neuropathology.

Results: A total of 73 patients were identified. The mean age of onset was 53 for men and 56 for women. Facial sensory disturbance was the commonest sensory feature (93%), followed by an abnormal corneal reflex (56%) (Figure 1). The commonest motor features were facial weakness (71%), upper limb weakness (69%), dysphagia (67%) and dysarthria (54%) (Figure 2). Median survival was 6 years and bronchopneumonia was the most common cause of death (30%). There was no clear evidence of benefit from immunosuppressive therapy.

TDP43 inclusions were present in 2 of our patients (figure 3) and in 66% of patients in total. Genetic testing revealed missense variants in genes associated with motor neurone disease (MND) in 21% of cases.

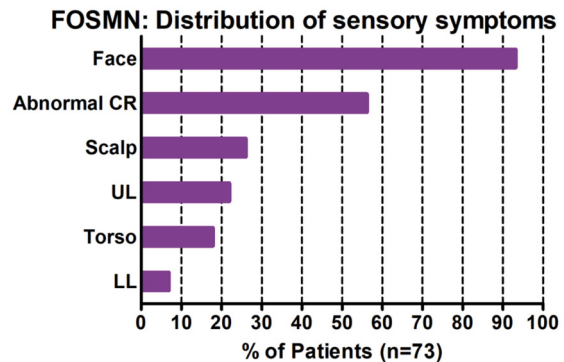


Figure 1: Sensory features of FOSMN. Facial sensory disturbance (93%) was present in almost all patients and an abnormal corneal reflex (CR) was also frequently present (56%).

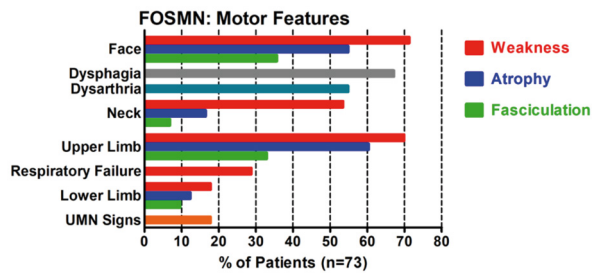


Figure 2: Motor features of FOSMN. Facial weakness (71%), upper limb (UL) weakness (69%), dysphagia (67%) and dysarthria (54%) were present in most patients.

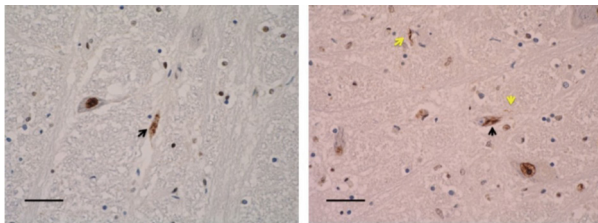


Figure 3: Representative images of histopathological examination of the medulla demonstrating TDP43 mislocalisation and aggregation in two patients diagnosed with FOSMN. The presence of neuronal intracytoplasmic inclusions (black arrows) and dystrophic neurites (yellow arrows) recapitulates the neuropathological hallmarks of MND. [Scale bar 50µm]

Conclusion: FOSMN starts with facial sensory disturbance. Deficits then spread rostro-caudally, in a similar pattern to bulbar-onset MND, albeit with longer median survival. Moreover, the clinical features, together with the emerging neuropathological and genetic data strongly support the suggestion that FOSMN is a rare variant of MND. Thus, patients with FOSMN should receive multidisciplinary care in the MND clinic and raise the scientific question of why, in these cases, sensory neurones are susceptible to neurodegeneration, which may provide further insight into the pathophysiology of MND.

Disclosure: I am appointed by the NIHR as an academic clinical lecturer in Neurology which has enabled me to take the lead in this research work.

EPR1116

A Phase 2 Study to Evaluate the Efficacy and Safety of SRK-015 in Patients with Later-Onset Spinal Muscular Atrophy (TOPAZ): An Introduction

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Background and aims: SRK-015 is a fully human anti-proMyostatin monoclonal antibody (mAb) that is being developed and investigated for the treatment of later-onset SMA. This Phase 2 study evaluates the safety and efficacy of SRK-015 on motor function in SMA patient Types 2 and 3.

Methods: All patients received SRK-015 every 4 weeks via intravenous infusion for 52 weeks. Patients in Cohorts 1 (N=20) and 2 (N=15) were treated with 20 mg/kg SRK-015 and patients in Cohort 3 (N=20) were randomized 1:1 in a double-blind manner to receive either 2 mg/kg or 20 mg/kg of SRK-015. Cohort 1 enrolled ambulatory Type 3 patients, aged 5-21, some of whom started an approved SMN up-regulator after the age of 5, and others who were not receiving an SMN up-regulator. Cohort 2 enrolled Type 2 and non-ambulatory Type 3 patients, aged 5-21, already receiving an approved SMN up-regulator that was started after the patient turned 5. Cohort 3 enrolled SMA Type 2 patients ages 2 and older, already receiving an approved SMN up-regulator that was started before the patient turned 5.

Results: Efficacy assessments include the Revised Hammersmith Scale (Cohort 1), Hammersmith Functional Scale Expanded (Cohorts 2 and 3) and other motor function outcome measures. Safety will be assessed throughout the trial. Pharmacokinetics, pharmacodynamics and immunogenicity of SRK-015 will also be evaluated. Demographic, baseline characteristics and preliminary PK/PD data will be presented.

Conclusion: N/A

Disclosure: All the authors of this abstract are employees of Scholar Rock, a biopharmaceutical company. At the time of this submission, this data has not been presented, nor accepted, at any other medical congresses.

EPR1117

Protease Activated Receptor 1 Pathway: A Therapeutic Target in the SOD1 Mouse Model of Amyotrophic Lateral Sclerosis

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Background and aims: Motor neuron degeneration in amyotrophic lateral sclerosis (ALS) involves interactions with glial cells, which can exert either supportive or toxic effects. Protease activated receptor 1 (PAR1) is activated by thrombin and is related to various central and peripheral nervous system pathologies. PAR1 is present on perisynaptic astrocytes, adjacent to large pyramidal motor neurons. PAR1 location and harmful effects suggests its involvement in ALS and therefore was studied in the superoxide dismutase 1 (SOD1) model.

Methods: Brain thrombin activity in SOD1 mice was measured using a fluorometric assay, and PAR1 levels by western blot. PAR1 was localized using immunohistochemistry staining. Treatment targeted PAR1 pathway on 3 levels; thrombin inhibitor TLCK (N-Tosyl-Lys-chloromethylketone), PAR1 antagonist SCH-79797 and the Ras intracellular inhibitor FTS (S-trans-trans-farnesylthiosalicylic acid). Mice were weighed weekly and assessed for motor function and survival.

Results: SOD1 Brain thrombin activity was increased ($p < 0.001$) particularly in the posterior frontal lobe ($p = 0.027$) and hindbrain ($p < 0.01$). PAR1 levels were decreased ($p < 0.001$). Immunohistochemistry showed decreased staining in the cerebellum and cortex. SOD1 mice lost weight (≥ 17 weeks, $p = 0.047$), and showed shorter rotarod time (≥ 14 weeks, $p < 0.01$). Treatment with FTS 40mg/kg significantly improved rotarod scores ($p < 0.001$). SOD1 mice survival improved with all treatments ($p < 0.01$ for all treatments). PAR1 antagonism was the most efficient, with a median survival improvement of 10 days ($p < 0.0001$).

Conclusion: Our results support PAR1 pathway involvement in ALS pathogenesis. Intervention in the PAR1 pathway improves SOD1 mice survival and motor function, marking it a novel therapeutic target for ALS.

Disclosure: JC has a registered patent "Non-malignant disease treatment with Ras antagonist" in which FTS is included.

EPR1118

Structural MRI outcomes and predictors of disease progression in amyotrophic lateral sclerosis

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Background and aims: This study aims to explore the progression of clinical and structural brain changes in patients with ALS, and to assess magnetic resonance imaging (MRI) measures of brain damage as predictors of subsequent functional decline.

Methods: 50 ALS patients underwent clinical evaluations and 3T MRI scans at regular intervals for a maximum of 2 years (total MRI scans=164). MRI measures of cortical thickness, as well as diffusion tensor (DT) metrics of microstructural damage along white matter (WM) tracts were obtained. Voxel-wise regression models and longitudinal mixed-effects models were used to test the relationship between clinical decline and baseline and longitudinal MRI features.

Results: The rate of decline of the ALS Functional Rating Scale revised (ALSFRS-r) was significantly associated with the rate of fractional anisotropy (FA) decrease in the body of the corpus callosum (CC). Damage to the corticospinal tract (CST) and CC-body had a faster progression in patients with higher baseline ALSFRS-r scores and greater CC-body damage at baseline. Lower FA of the cerebral peduncle was associated with faster subsequent clinical progression.

Conclusion: In this longitudinal study, we identified a significant association between measures of WM damage of the motor tracts and functional decline in ALS patients. Our data suggest that a multiparametric approach including DT MRI measures of brain damage would provide an optimal method for an accurate stratification of ALS patients into prognostic classes.

Disclosure: Supported by: Italian Ministry of Health (RF-2010-2313220; RF-2011-02351193).

EPR1119

Functional impairment and survival prediction in Amyotrophic Lateral Sclerosis patients: a probabilistic model of disease progression

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Background and aims: We aimed to develop a probabilistic model of progression in ALS.

Methods: Data from 6 International referral ALS centres were used (overall database, OD). A database including only data from Italian registries was created too (Italian database, ID).

ALSFRS-R scores from clinical evaluations were converted into MITOS score. Progression to positivity of each MITOS domain and to survival was considered.

Dynamic Bayesian Networks were used to predict progression. Each database was divided into a training dataset for developing the model and a test dataset to validate it.

The concordance of the real and the simulated progression was quantified as the difference between the percentages of patients having experienced each event in the 2 models at predefined intervals. Additionally, area under ROC curve (AUC) was computed at the same intervals.

Results: OD included 4,026 ALS patients and 24,960 visits. ID included 2,149 ALS patients and 15,767 visits.

The simulated model showed a median difference in percentage of 2.19 (IQ 1.78-3.49) and 1.4 (IQ 0.26-2.16) for the OD and the ID respectively; prediction of survival showed a median difference of 1.86 (IQ 0.59-2.9) and 2.64 (IQ 0.81-3.12) respectively. The AUC for simulated MITOS impairment and survival was in median 0.83 (IQ 0.81-0.84) and 0.85 (IQ 0.83-0.88) for OD and ID respectively.

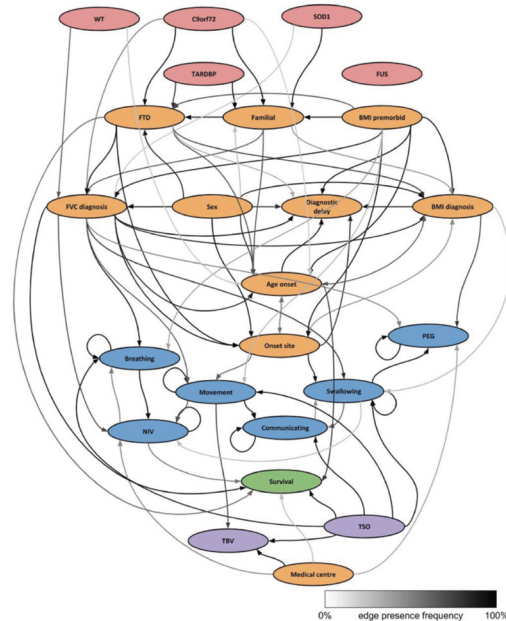


Fig1. Directed graph obtained on training set, representing the conditional dependencies among variables in ID. TBV=time between consecutive visits; TSO=time since ALS onset; Breat., Swallow., Commun., Mov.:MITOS domains. The node colour encodes the variable type: static=orange, genetic=pink, dynamic=blue, time-encoding=purple and survival=green.

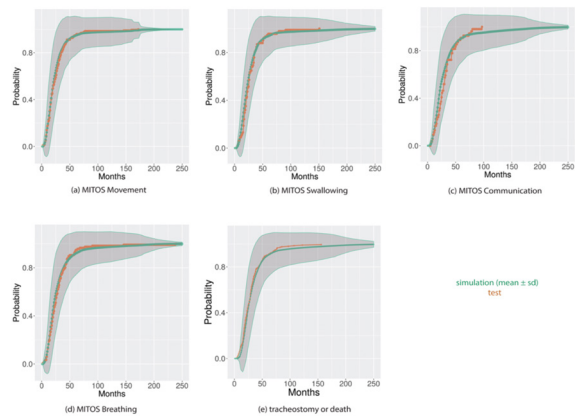


Figure 2. Cumulative probability of impairment in the four MITOS domains and of tracheostomy/death over time in the ID training dataset (orange line) and in the simulated population (green line: mean values over population; shaded region: standard deviation), based on probabilities modeled by the Dynamic Bayesian Networks.

Conclusion: We developed a model able to predict the loss of independence in four main motor domains and survival in ALS with a high accuracy.

Disclosure: This work was funded by the bilateral Italian-Israel project CompALS (Computational analysis of the clinical manifestations and predictive modeling of ALS), supported by the Italian Ministry of Foreign Affairs and International Cooperation and the Ministry of Science, Technology and Space of the State of Israel. The model is currently under patent evaluation.

EPR1120

Plateaus in Amyotrophic Lateral Sclerosis progression: results from a population-based cohort.

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Background and aims: To assess the frequency of plateaus in Amyotrophic Lateral Sclerosis (ALS) progression using a large population-based cohort.

Methods: Data from the Piedmont and Aosta Valley ALS register were used. Patients who were diagnosed between 2007 and 2014 were considered. Follow-up period was extended until December 31st 2018. Visits subsequent tracheostomy were not considered. A plateau was defined as a stable ALSFRSr revised score lasting at least 6, 12 or 18 months.

Results: Out of 1214 patients, 200 (16.5%), 93 (7.7%) and 52 (4.3%) showed at least one plateau lasting a minimum of 6, 12 and 18 months, respectively. Plateaus occurred mostly at high ALSFRSr scores and were more frequent during the initial phases of the disease course (fig. 1. e 2). Spinal onset (OR 1.83, 95% CI 1.16–2.95, p-value=0.01) and predominant upper motor neuron phenotype (OR 2.18, 95% CI 1.36–3.48, p-value=0.001) conferred a higher risk for the subsequent appearance of plateaus; conversely, older age at diagnosis (OR 0.25, 95% CI 0.1–0.54, p-value=0.002 for >75 age class) reduced the risk.

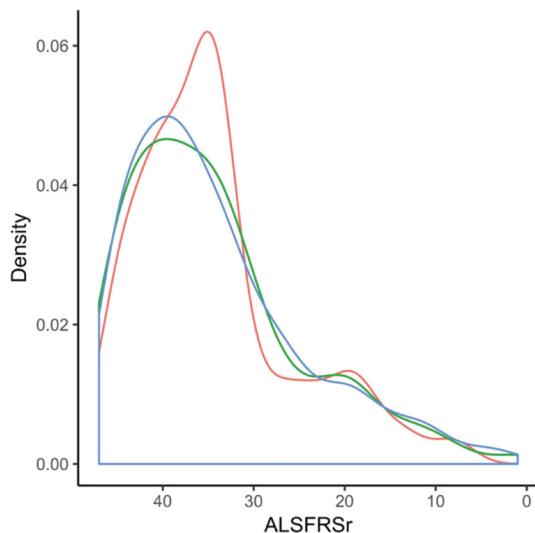


Figure 1. Kernel density estimation (KDE) of ALSFRSr total scores at which occurred plateaus lasting at least 6 months (blue), 12 months (green) and 18 months (red). KDE is a non-parametric estimation of a probability density function of a random variable allowing a smoothing of density curves.

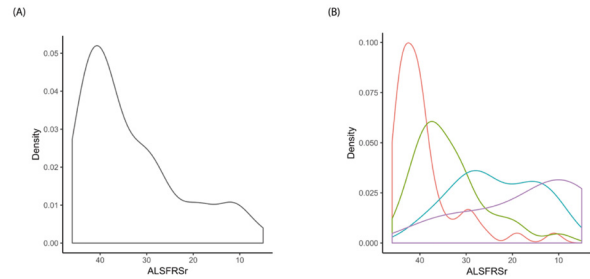


Figure 2. Kernel density estimation (KDE) of ALSFRSr total scores at which occurred 6-months plateaus of patients deceased during the follow-up: A) globally and B) divided by survival quarters (1st quarter=red; 2nd quarter=green; 3rd quarter=blue; 4th quarter=violet).

Conclusion: Plateaus in ALS progression lasting at least 6 months appear in about one out of 6 patients and could last even 12, 18 months or more in a smaller subgroup of patients. Plateaus occurrence should not necessarily suggest the neurologist to reconsider the ALS diagnosis and should be considered for future clinical trials design.

Disclosure: Nothing to disclose

Movement disorders 1

EPR1121

Glucocerebrosidase activity and atypical parkinsonism: a multi-centre exploratory study

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Background and aims: Glucocerebrosidase (GBA) mutations cause autosomal recessive Gaucher's disease (GD) due to enzyme deficiency. GBA heterozygous mutations are common in Parkinson's disease (PD), in Spain accounting for 9.8% of PD patients. GD1 (adult type) has only systemic features, but PD and exceptionally atypical parkinsonism (AP) resembling corticobasal syndrome (CBS) have been reported, with mild or absent systemic features of GD. We aimed to determine the frequency of GBA deficiency (subclinical GD1) in patients with AP with features of tauopathy (progressive supranuclear palsy-PSP and CBS).

Methods: Cross-sectional multicentre study of PSP and CBS patients, including demographic and clinical variables, beta-glucosidase and chitotriosidase serum activity in dried blood spots, and complete GBA gene sequencing whenever activity was low or dubious.

Results: 60 patients (55% male, mean age 74 years, 60-80) diagnosed with PSP (46), CBS (10) or mixed PSP/CBS (4) were included. Family history was positive for parkinsonism (PD/AP) in 13 (22%). Beta-glucosidase and chitotriosidase serum activity were normal in 53 but dubious in 7. 13 cases, including these 7, underwent complete GBA gene sequencing, which showed heterozygous mutations in 3 cases (23%) (c.1226A>G N370S; c.1093G>A and c.-15A>G); 2 had CBS and 1 mixed PSP/CBD phenotype.

Conclusion: Our study does not support an association among tauopathies and low GBA enzyme activity. However, GBA mutations were found in a higher than expected frequency, which could result from selection bias but warrants further research for clarification.

Disclosure: Shire (now Takeda Pharmaceutical Company) supported dried blood spot enzymatic tests and gene sequencing.

EPR1122

Impulse Control Behaviours in People with Parkinson's Disease: Findings from the Parkinson's Disease Real-World Impact Assessment (PRISM) Study

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Background and aims: Impulse control disorders are part of behavioural disturbances in people with Parkinson's disease (PwP) and may result in serious financial and psychosocial consequences [1,2]. Impulse control behaviour (ICB) was assessed in PRISM, a European survey of PwP and their care-partners.

Methods: PRISM was a descriptive, exploratory, observational study with cross-sectional design fielded through an online survey developed in collaboration with The Cure Parkinson's Trust (UK-based advocacy group) and an international scientific committee. Collecting data through online channels may limit results interpretation. ICBs were collected based on yes/no answers to the question "are any of the behaviours listed an issue for you, or do others think that you have an issue?". Behaviours included pathological gambling, hypersexuality, compulsive shopping, binge-eating, overuse of antiparkinsonian medications and hobbyism. Data were assessed in relation to patient characteristics, including dopamine agonist (DA) use and presence of comorbid depression/anxiety.

Results: Between April-July 2019, data were collected from 861PwP from 6 European countries. Overall, approximately 45% of PwP reported at least one ICB (Figure 1). All ICBs were more frequently reported in PwP currently taking DA versus those who had never taken DA (Figure 1). PwP diagnosed with comorbid depression (22%) or anxiety (16%) were more likely than other PwP to report ICBs relating to eating, shopping, overuse of antiparkinsonian medications and hobbyism (Figure 2).

Figure 1. Impulse control behaviours reported by total PwP and according to DA use. DA, dopamine agonist; PD meds, overuse of Parkinson's disease medications; PwP, people with Parkinson's disease. n/N, affected subjects/total number of replies

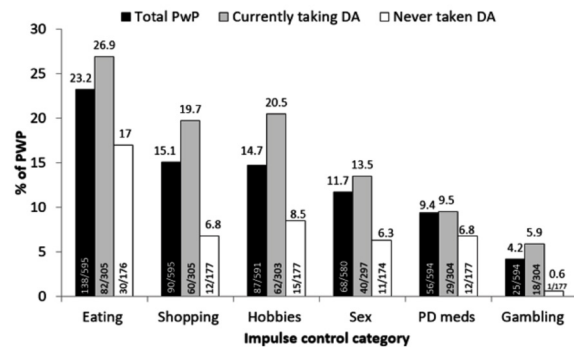


Figure 1

Figure 2. Impulse control behaviours reported by PwP, according to diagnosis of comorbid depression or anxiety. PD meds, overuse of Parkinson's disease medications; PwP, people with Parkinson's disease. n/N, affected subjects/total number of replies

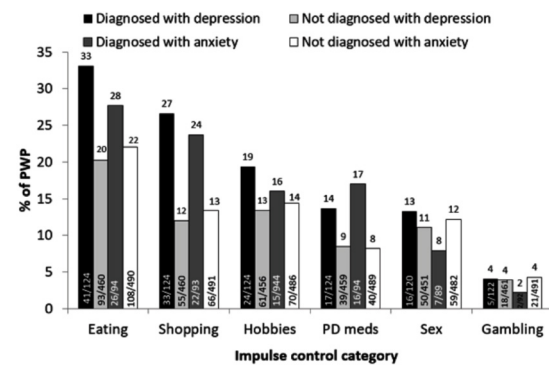


Figure 2

Conclusion: PRISM highlights relevance and range of ICBs in PwP and reinforces its association with DA use, mood and anxiety.

1. Gatto EM, Aldinio V. *Front Neurol*.2019;10:351.
2. Rodríguez-Violante M, Antonini A. *Front Neurol*. 2019;10:972.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPR1123

Brain connectivity and music in Parkinson's disease

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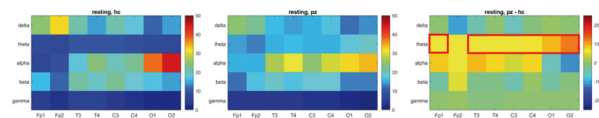
Background and aims: The study of brain activity and functional connectivity is of increasing interest in neurodegenerative diseases, including Parkinson's disease (PD). In this study, PD patients and healthy controls (HC) were compared in terms of EEG spectral power and effective connectivity, both at rest and during exposure to music tracks.

Methods: We enrolled 14 non-demented PD patients and 12 healthy controls. EEG recordings were obtained during resting-state condition and while listening to music. Fast Fourier Transform (FFT) was used to calculate the relative power spectral density (PSD) in the theta and alpha bands. Directional interactions among EEG channels were examined through Granger Causality Analysis (GCA). FFT and GCA parameters were compared between patients and HC using Wilcoxon rank sum tests.

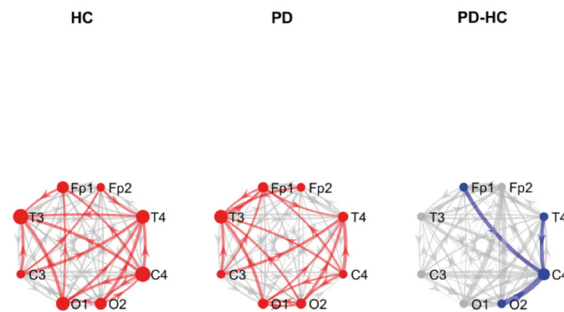
Results: Resting state PSD displayed diffuse higher theta power in PD, a pattern predictive of cognitive impairment development according to literature. Effectively, patients showed a sensitive decrease in Montreal cognitive assessment (MoCA) test scores after three years of follow-up.

During music listening, patients exhibited no occipital theta enhancement as found in HC.

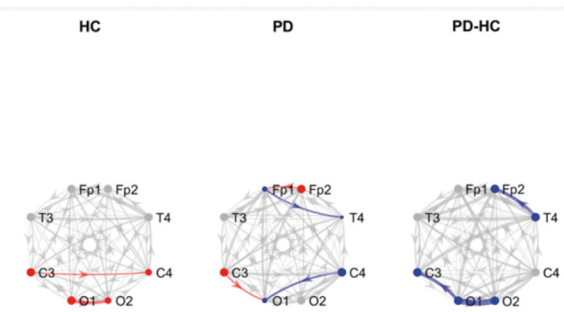
GCA showed that PD patients have much less theta and alfa information entering the right sensorimotor area; this pattern was maintained during both resting state and music. Music listening modulated differently brain connectivity in PD patients compared to HC, as result of altered neuronal synchronization.



Resting state PSD as measured in healthy controls and patients



Topographical maps showing resting state GCA alpha band analysis in HC, patients and their statistically significant differences



Topographical maps showing GCA alpha band percent change during Bach listening in HC, patients and their statistically significant differences

Conclusion: We highlighted brain activity and connectivity alterations in PD, predominantly involving the right sensorimotor cortex. This happened regardless of the mainly involved side and can be considered an expression of an increased risk of cognitive impairment development.

Disclosure: Nothing to disclose

EPR1124

Risk of Parkinson's disease in GBA mutation carriers: results from a Kin-cohort study in unselected Parkinson patients

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Background and aims: Biallelic glucocerebrosidase (GBA) mutations cause Gaucher Disease (GD), while monoallelic heterozygous GBA mutations are considered the most important known genetic risk factor for Parkinson Disease (PD). The estimated risk of PD in heterozygous GBA mutations-carriers is highly variable, ranging between 10 and 30%. This risk is age specific and depends other genetic and non-genetic factors. The aim of this study was to assess the penetrance of GBA mutations in PD in a cohort of unselected PD patients using the Kin-cohort method.

Methods: 123 PD patients with GBA mutations were previously identified in a series of 2843 unrelated consecutive PD patients. Proband pedigrees were used in the Kin-cohort analysis. Mutations were divided in mild (p. N370S) and severe (p.L444P, p.G377S, splicing mutations).

Results: Data on family history was available for 63 out of 123 PD GBA mutations-carriers; 381 1st-degree relatives were analysed. The risk to develop PD was significantly different among relatives of GBA mutation-

Table. Percent penetrance estimates (95% CI) according to age.

First-degree relatives of:	N.	N.PD	60 y	70 y	80 y	p*
GBA-PD	381	20	10.0 % (5-17)	16.0 % (9-24)	19.4 % (12-28)	0.0069
GBA-PD Severe mutations	189	11	13.5 % (5-23)	18.2 % (9-29)	18.2 % (9-29)	0.014
GBA-PD Mild mutations	192	9	6.7 % (1-15)	13.6 % (3-27)	22.4 % (9-40)	0.011
Non-carriers	257	3	0.6 (0-22)	0.6 (0-21)	3.0 (0-7)	

N. = number of subjects (first degree relatives) considered in the Kin-cohort analysis.
N.PD = number of relatives affected by PD.
y= years of age.
* p value is calculated comparing the carrier group to the non-carrier.
The Relative Risk of each age-group was calculated comparing the carrier group to the non-carrier: for the whole GBA carrier at 60y was 17.26 (3.46-1.87-), at 70y was 27.40 (5.99-2.26), at 80y was 6.73 (2.17-inf); for the GBA-severe at 60y was 22.32 (4.53 -inf), at 70 y was 30.34 (6.82-inf), at 80y was 6.93 (2.36-inf); for the GBA-Mild at 60y was 11.28 (0.61-inf), at 70y was 22.45 (3.31-inf), at 80y was 6.93 (1.74-inf).

Table. Percent penetrance estimates (95% CI) according to age.

Conclusion: The estimated prevalence in this study is higher than the one estimated in GD cohorts and lower than the one estimated in familial PD cohorts. Our study was performed on unselected PD patients, avoiding the over or under estimation of penetrance that can occur in studies performed preferably on subjects with a positive family history of PD or GD. It is important that neurologists and genetic counsellors consider a possible ascertainment bias in their counselling.

Disclosure: Nothing to disclose

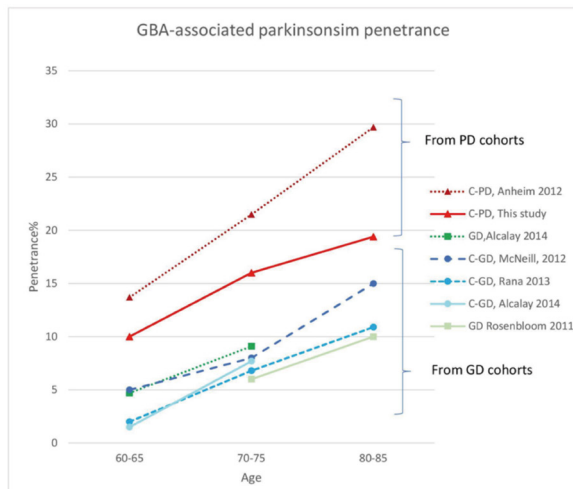


Figure: GBA-associated parkinsonism penetrance in previous studies.

GD= Gaucher Disease (symbol=■), C-GD= Carriers from GD cohorts (symbol=●), C-PD= Carriers from PD cohort (symbol=▲). Anheim et al., 2012: patients with GBA- PD from familial cases and their first-degree relatives(C-PD); Alcalay et al., 2014: GD patients and their parents (C-GD); McNeil et al., 2012: parents of GD patients (C-GD); Rana et al., 2013: GD patients and their parents (C-GD); Rosenbloom et al., 2011: GD patients

Figure: GBA-associated parkinsonism penetrance in previous studies.

EPR1125

Refractory tremor: is perampanel a potentially useful therapy?

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Background and aims: Up to 40% of patients with essential (ET) or dystonic (DT) tremor are refractory. An increase in excitatory neurotransmitters has been hypothesized. Perampanel, an antiepileptic drug with AMPA receptor antagonist effect, may thus be potentially useful.

Methods: Retrospective analysis of the electronic records of patients with refractory ET or DT of our movement disorders unit along a 2-year period.

Results: 11 patients (7 women, mean age 72±8 years) who were prescribed perampanel due to insufficient tremor control were analysed. 4 were diagnosed with ET and 7 with DT, most of them with cephalic, vocal and upper limbs involvement, and mean previous follow-up of 7.6±4.0 years. Previous/concomitant treatments included propranolol (mean dose 70mg, range 20-120), primidone (250mg, 125-375), clonazepam (1mg, 0.5-2), and cervical botulinum toxin (4 cases). Mean perampanel dose was 4mg (2-8mg) qid, with a slow titration along several weeks, and follow-up 2.4±1.3 months. 4 patients improved, 2 were diagnosed with DT (Clinical Global Impression-Improvement, CGI-I, scale score of 1) and 2 with ET (CGI-I score 2). 5 patients (3 in monotherapy) reported mild-moderate adverse events (dizziness, sleep disturbances) at a mean dose of 3.2mg (range 2-4mg), and 1 patient was admitted due to ataxia and confusion at 8mg qid, overall leading to discontinuation in 5.

Conclusion: Perampanel may be effective in some patients with refractory tremor, albeit blinded randomized controlled trials are warranted to confirm this hypothesis. Poor tolerability may hinder dose escalation in a subset of patients.

Disclosure: Nothing to disclose

EPR1126

The association of early caudate involvement and REM sleep disorder behaviour could influence disease progression in Parkinson's Disease: A PPMI study.

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Background and aims: We investigated the occurrence of dopaminergic caudate dysfunction in patients with and without REM sleep behaviour disorder (RBD) in the early stages of Parkinson's Disease (PD) using 123I-FP-CIT SPECT, to determine whether this had an effect on clinical outcomes.

Methods: PD patients and healthy controls who had completed the RBD questionnaire were identified from the Parkinson's Progressive Markers Initiative database. Scores ≥5 were defined as 'RBD-positive' and those with a score <5 as 'RBD-negative'. Cohorts were then subdivided based on the presence of significant caudate dysfunction on 123I-FP-CIT binding from age-corrected z-scores, with abnormal scores <-2 SDs from normal mean. Statistical interrogation between groups was used to compare dopaminergic, clinical and cerebrospinal fluid (CSF) parameters.

Results: At baseline, 40.6% of our PD population had abnormal caudate function, with 37.5% of these being RBD-positive. There was no significant difference at baseline regarding caudate involvement and the presence of RBD (p=0.361), however the relationship was significant at 4-year follow-up (p=0.044), with a significant difference in the progression of caudate degeneration between cohorts (p=0.03).

At baseline, in the RBD-positive cohort patients with caudate involvement had greater UPDRS-scores (p=0.007) and lower alpha-synuclein CSF concentrations (p=0.017). There were no significant differences in the RBD-negative subjects relating to caudate involvement. At 36 months, there were significant differences regarding UPDRS score (p=0.02), cognitive scores (p=0.001) and alpha-synuclein sampling (p=0.048) comparing the abnormal caudate/RBD-positive group with the abnormal caudate/RBD-negative group.

Conclusion: Our findings suggest that co-existent early caudate dysfunction and presence of RBD is predictive of worse clinical outcomes in PD.

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EPR1127

Intrinsic brain functional connectivity predicts treatment-related motor complications in early Parkinson's disease patients

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Background and aims: Fluctuations in the symptoms of Parkinson's disease (PD) may be related to duration and dosage of levodopa, age at onset as well as pharmacokinetic and pharmacodynamics mechanisms. Using resting-state functional MRI, we investigated intrinsic brain networks connectivity at baseline in a cohort of drug-naïve PD patients which successively developed treatment-related motor complications (PD-Fluct) over a 4-years follow-up period compared with patients who did not (PD-no-Fluct)

Methods: Baseline 3Tesla MRI images of 88 drug-naïve PD patients and 20 matched healthy controls (HC) were analyzed. Single-subject and group-level independent component analysis was used to investigate functional connectivity differences within the major resting state networks. Additionally, a region-of-interest analysis was performed within the basal ganglia. After the baseline assessments, all patients started a dopaminergic replacement therapy and were followed for an observation period lasting a maximum of 4 years, with a clinical assessment every 6 months. Regression analyses were used to investigate baseline predictors of motor complications development.

Results: At baseline, an increased connectivity within the default mode and the frontoparietal networks as well as within the basal ganglia were detected in PD-Fluct patients compared with PD-no-Fluct. Functional connectivity changes at baseline showed to be an independent predictor of motor complications at 4-year follow-up.

Conclusion: Our findings demonstrated that sensorimotor and neurocognitive functional connectivity changes may characterize drug-naïve PD patients more prone to develop treatment-related complications. We hypothesize that these findings may reflect the presence of early dopaminergic pathways differences and might predict development of motor complications over time.

Disclosure: Nothing to disclose

EPR1128

Clonidine GH stimulation test to differentiate MSA from idiopathic late onset cerebellar ataxia: a prospective, controlled study.

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Background and aims: Despite the consensus criteria for multiple system atrophy (MSA), the diagnosis of MSA of cerebellar type (MSA-C) is difficult in the early stage of the disease. There are several differential diagnoses including idiopathic late-onset cerebellar ataxias (ILOCA) and it is often necessary to wait for clinical worsening so that the criteria can be met. Our aim was to assess the efficacy of clonidine growth hormone test (CGH test) to distinguish MSA-C from ILOCA in the early stage of the disease.

Methods: Within our cohort of late-onset sporadic, progressive cerebellar ataxia, the group of patients meeting the criteria for MSA was compared to the ILOCA group. Clinical and paraclinical examination including CGH test were repeated during the prospective follow-up.

Results: 86 patients were recruited, including 42 patients in the MSA group and 44 ILOCA patients with a mean follow up of 33 months. At the inclusion visit, CHG test was pathological for 31% MSA of patients and 18.2% of ILOCA (p=0.35). During the follow-up, 52.4% of MSA-C had a pathological CGH test, while only 20.5% of ILOCA (p<0.01). CGH test had a sensitivity of 69.1% and a specificity of 68.2%, (p<0.001) for MSA-C patients; CGH test allows in ¾ of cases, if negative, to rule out a probable MSA-C (negative predictive value of 75%, p=0.0014).

Conclusion: This prospective, controlled study showed that CGH test could be helpful in clinical practice to differentiate MSA-C from ILOCA in the early stage of the disease.

Disclosure: Nothing to disclose

EPR1129

Pathophysiology of Parkinson's disease: Investigating the protein alpha-synuclein bound to ubiquitin, dopamine, proteasomal and lysosomal system dysfunction with theoretical nuclear physics methods

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Background and aims: Parkinson's disease (PD) results from the death of dopamine-producing neurons in the substantia nigra and is characterized by an abnormal accumulation of protein alpha-synuclein. This study aims to identify, investigate and analyze the protein alpha-synuclein bound to ubiquitin, dopamine, proteasomal and lysosomal system dysfunction with theoretical nuclear physics methods.

Methods: Structural properties of protein alpha-synuclein bound to ubiquitin and dopamine have been determined using both density-based and wave-function-based electronic structure methods in order to assess the ability of ab initio "force fields" to retain the properties described by experimental structures measured with crystallography or nuclear magnetic resonance. Using Molecular Dynamics (MD) and Monte-Carlo simulations, the proteasomal and lysosomal system dysfunction in pathophysiology of Parkinson's disease were analyzed. The computational simulations and analyzes of this scientific work were elaborated with the use of software: ACD/ChemSketch, Swiss-PdbViewer, ABCpred, BepiPred-2.0, ElliPro, DEseq, GOseq, FunRich, Cytoscape, BiNGO, PepSurf, AxonDeepSeg, AxonSeg, PyMol, ICM-Browser, LAMMPS, Gaussian, Visual Molecular Dynamics (VMD), Cell Illustrator, GENESIS, NEURON, NeuronStudio and ChemDraw.

Results: Protein alpha-synuclein bound to ubiquitin accumulates inside neurones and this accumulation impairs cell function. Local phi (ϕ) and psi (ψ) torsion angle fluctuations of the alpha-synuclein indicates that disturbances in protein synthesis and deformations in amphipathic N-terminal, central hydrophobic and a highly acidic and proline-rich region of this protein can interfere in the biosynthetic and metabolic pathway in dopamine. Dopamine degradation and synaptic problems can be triggered by alpha-synuclein conformation disorders.

Conclusion: Understanding the pathological mechanisms should help developing new therapeutic tools to treat this disease and other movement disorders.

Disclosure: Nothing to disclose

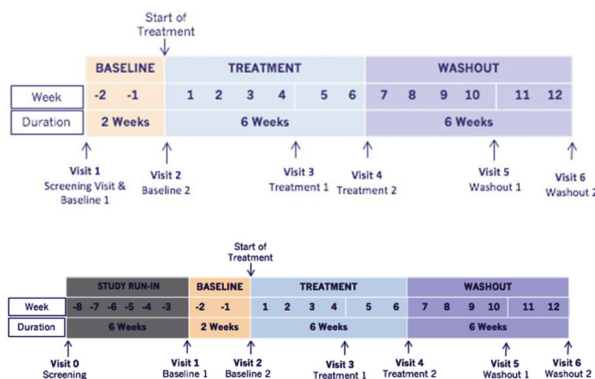
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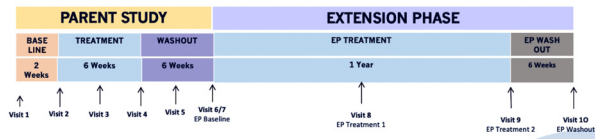
N-Acetyl-L-Leucine for Niemann-Pick Disease, Type C, GM2-Gangliosidosis and Ataxia telangiectasia: Three multinational, multicenter, open-label, rater-blinded phase II clinical trials

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Background and aims: Phase II trials are investigating the effects of N-Acetyl-L-Leucine (IB1001/ALL) in 3 ultra-rare, autosomal-recessive, neurodegenerative disorders: Niemann-Pick disease, type C (NPC), Ataxia-telangiectasia (A-T) and GM2-Gangliosidosis (GM2). Owing to their overlapping phenotypes, and the mechanism of action of ALL, a single master protocol was developed, implementing both an innovative trial design and a novel primary endpoint, better suited to these small, inhomogeneous patient populations.

Methods: The IB1001 studies investigate the symptomatic and disease-modifying effects of ALL. Screening of patients ≥ 6 years (Europe) AND ≥ 18 years (USA) occurs at 12 centers across Germany, Spain, Slovakia, UK, and USA. Patients who have completed the Parent Study (Fig. 1 and 2) may be included into an Extension Phase (Fig. 3) The dosage varies from 2 to 4g/day, based on patients' age/weight. A novel primary endpoint, the Clinical Impression of Change in Severity (CI-CS), was developed, based on two independent, blinded raters comparison of videos of the patient's change in performance from baseline to the end of treatment, and the end of treatment to the end of the washout on either the 8 Meter Walk Test (8MWT) or the 9 Hole Peg Test, Dominant Hand (9HPT-D).





Results: Recruitment is ongoing for all 3 studies. Approximately 39 patients per study will be screened. As of 15 January 2020, 29 NPC, 13 GM2, and 1 A-T patients have been enrolled.

Conclusion: A novel primary endpoint is being implemented to better demonstrate the clinically meaningful effect of ALL treatment in three ultra-rare neurodegenerative diseases with overlapping phenotypes.

Disclosure: The IB1001 Clinical Trials are sponsored and paid for by IntraBio Ltd.

EPR1131

Acetyl-Leucine slows disease progression in lysosomal storage disorders

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Background and aims: Acetyl-DL-leucine (ADLL) is a derivative of the branched amino acid leucine. In observational clinical studies ADLL improved symptoms of ataxia in patients with the lysosomal storage disorder (LSD) Niemann-Pick disease type C (NPC). We investigated ADLL and its enantiomers acetyl-D-leucine (ADL) and acetyl-L-leucine (ALL) in *Npc1*^{-/-} mice.

Methods: Affected mice (*Npc1*^{-/-}, *Hexb*^{-/-}) and controls (*Npc1*^{+/+}, *Hexb*^{+/+}) were included. Behavioral tests were performed (gait analysis, motor function assessment, incl. strength and coordination). Biochemical analyses (Western blot, ADP/ATP and NAD/NADH, sphingoid base, glycosphingolipid, cholesterol) were performed. Moreover, lysotracker green staining, filipin staining as well as immunohistochemistry were conducted. Clinical observational studies of 13 adult NPC (12 on miglustat) and 3 GM2-gangliosidosis patients treated with ADLL were included.

Results: ADLL, ADL and ALL in symptomatic *Npc1*^{-/-} mice all improved ataxia. When ADLL and ALL were administered pre-symptomatically to *Npc1*^{-/-} mice, they both delayed disease progression and resulted in a modest extension to life span, whereas ADL did not. These data are consistent with ALL being the active neuroprotective enantiomer. Altered energy metabolism was implicated as a potential mechanism of action of the active L enantiomer in *Npc1*^{-/-} mice. When miglustat and ADLL were used in combination significant synergy resulted. Disease progression rates were slowed after 12 months of treatment. A neuroprotective effect of ADLL was also observed in a mouse model, and clinical benefit observed in GM2 gangliosidosis patients in observational clinical studies.

Conclusion: Taken together, we have identified an unanticipated neuroprotective effect of ALL, supporting its further evaluation in clinical trials in LSD.

Disclosure: Nothing to disclose

EPR1132

A reliable measure of rigidity with a novel robotic device

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Background and aims: Rigidity is 1 of the cardinal symptoms of Parkinson's disease (PD), which responds best to dopamine, but the pathogenesis is not yet understood. The assessment remains subjective depending on the examiner, and tremor may interfere with the assessment. A reliable measure of rigidity will allow determine more precisely the dopamine response and its interaction with bradykinesia for a better understanding of the pathophysiology of PD. The objective of our study was to objectively measure the rigidity in PD patients, using a recently validated robotic device

Methods: We studied 35 PD patients with (n=20) and without tremor (n=15), and 10 healthy subjects (HS). All participants underwent clinical evaluation including MD-UPDRS. The rigidity was assessed with the device, which measures the resistance of passive wrist flexion and extension movements at different speeds. PD patients with tremor underwent an additional tremor recording with surface EMG, inertial monitors and a writing tablet.

Results: Preliminary results show that the device records a hysteresis-shaped rigidity profile consistent with the literature, which differentiates PD patients from HS and correlates significantly with the UPDRS scores for rigidity. In PD patients with tremor, the device detects the tremor frequency, which correlates with the conventional tremor recording.

Conclusion: This device provides a reliable measure of rigidity for clinical studies and practice.

Disclosure: Nothing to disclose

Movement disorders 2

EPR1133

Association of the number of lost teeth with new-onset Parkinson’s disease; nationwide retrospective cohort study

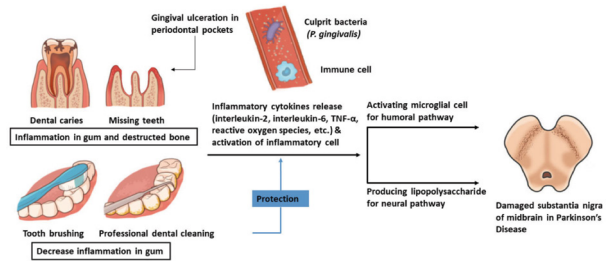
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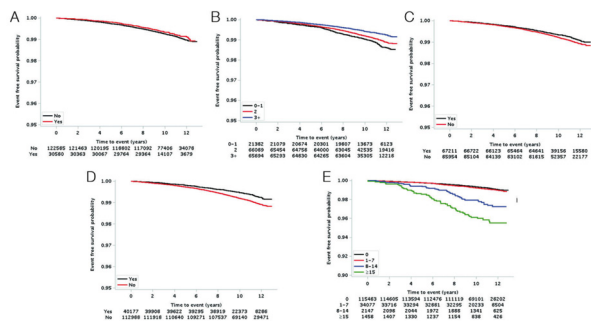
Background and aims: Lost teeth is representative of poor oral hygiene. Poor oral hygiene can provoke transient bacteremia and systemic inflammation. Systemic inflammatory reaction may be related to the degeneration of dopamine neurons in the substantia nigra. We hypothesized that lost teeth would be associated with increased risk of new-onset Parkinson’s disease.

Methods: Between 2003 and 2006, we included 153,165 participants from the national health insurance system-health screening cohort in Korea without missing data for demographics, laboratory findings, comorbidities, and oral hygiene indicators (periodontal disease, dental clinic visit for any reasons, professional dental care, frequent tooth brushings, and number of lost teeth). The incidence of new-onset Parkinson’s disease was defined as International Classification of Diseases-10 code “G20” accompanying the prescription records for any anti-parkinson medication.

Results: Approximately 19.9% of the included participants had periodontal disease. After a median follow-up of 10.4 years, 1,227 (0.8%) new-onset Parkinson’s disease cases were noted. The number of lost teeth was positively associated with an increased risk of new-onset Parkinson’s disease. In contrast, frequent tooth brushings, dental clinic visit for any reasons, and professional dental care were negatively related to the occurrence of new-onset Parkinson’s disease. In multivariable analysis, number of lost teeth (≥ 15) remained positively related to occurrence of new-onset Parkinson’s disease (hazard ratio: 1.38, 95% confidence interval (1.03-1.85), $p=0.029$, p for trend=0.043).



Disclosure: Nothing to disclose



Conclusion: Increased number of lost teeth may be an augmenting factor for the risk of new-onset Parkinson’s disease.

EPR1134

Midbrain MRI morphometric measurements and MCI in Parkinson's disease: the PACOS study.

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Background and aims: Mechanisms that lead Parkinson's disease (PD) patients to develop Mild Cognitive Impairment (MCI) are still poorly understood. Evidence from MRI studies have highlighted the progressive atrophy of several cortical areas involved especially in cognitive function. Nevertheless, data about subcortical structures, such as the midbrain and pons, that have an important role in cognitive functions, are often conflicting.

Methods: From the sample of the PACOS study, we selected patients with an available MRI and who underwent the morphometric measurements of midbrain and pons areas, Medium Cerebellar Peduncle (MCP) and Superior Cerebellar Peduncle (SCP) width and the midbrain anteroposterior diameter. MCI was diagnosed according to the MDS level II criteria. Univariate and multivariate logistic regression analysis have been performed for each of the measured structures.

Results: Morphometric measurements were available for 168 subjects. Among them 67 (39.9%) were diagnosed as PD-MCI. The mean age of the sample was 64.2±9.8 and 84 (50%) were men with a mean disease duration of 5.2±5.4 and a mean UPDRS-III of 32.1±12.9. At the univariate and multivariate analysis, after adjusting for age, sex, education and disease duration, MCI was associated with midbrain area (OR 0.98;95%CI 0.96-0.99; p=0.048) and with a midbrain anteroposterior diameter <16.4mm (OR 2.56;95%CI 1.22-5.33; p=0.012).

Conclusion: Midbrain atrophy is not a typical feature of PD, however a mild midbrain atrophy may represent a hallmark of PD-MCI, considering the cortical projections of the midbrain nuclei and their influence on executive and attentive functions.

Disclosure: Nothing to disclose

EPR1135

Does peripheral neuropathy affect gait and balance in Parkinson's disease?

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Background: Parkinson's disease (PD) is a chronic neurodegenerative disorder. Peripheral neuropathy (PN) is often observed in PD patients than in non-PD subjects, with a prevalence between 10-40% (1-8% in non-PD subjects). We aimed in a prospective observational study to determine PN in a consecutive series of PD patients, identify the etiology and evaluate the functional impact on gait and balance.

Methods: A group of PD patients from Centro Hospitalar do Porto (CHUP) underwent clinical (Neuropathy Impairment Score; modified Toronto Clinically Neuropathy Score questionnaires), neurophysiological (nerve conduction studies; Quantitative Sensory Testing) and neuropathological (intraepidermal nerve fiber density in skin biopsies punches) examinations. Gait and balance were characterized using 3 wearable sensors (Hasomed, Germany) during ON and OFF states.

Results: We evaluated 98 patients, with a mean age of 67.1 (±9) ys and a mean disease duration of 6.6 (±5) ys. PN was present in 31 patients (31.6%). 8 patients showed axonal sensory polyneuropathy, 18 presented small fiber neuropathy and 5 had both large and small nerve involvement. The PN-PD group had lower straight walking velocity (p=0.01) and turning duration (p<0.05) during both medication states. During OFF state, PN-PD had higher JERK values, compared to non-PN-PD patients (P<0.05).

Conclusion: The prevalence of PN in our cohort is similar to previous reports. Preliminary analysis of gait and balance parameters suggest that peripheral nervous system involvement influences gait and balance parameters as measured with mobile digital technology during ON and OFF states. Ongoing research is focusing on better understanding of reasons for this phenomenon.

Disclosure: Nothing to disclose

EPR1136

A novel SGCE variant is associated with myoclonus dystonia in a Spanish family

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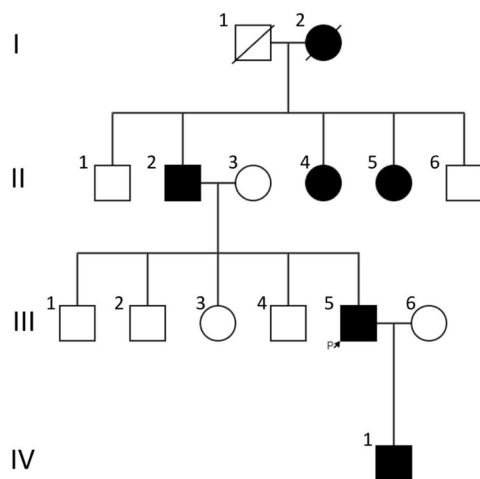
Background and aims: Hereditary myoclonus dystonia (DYT 11) associated with SGCE variants was described in 2001. We report a novel pathogenic nonsense mutation in SGCE found in a large Spanish family with multiple individuals affected.

Methods: A 58-year-old man presented to the emergency room with persistent diarrhea. In addition, the patient referred a history of abnormal posture and generalized jerks since childhood. No evidence of pregnancy abnormalities or developmental delays was noted. He denied intellectual impairment. He had earned a university degree and worked as a public server. He had never consulted with a neurologist. On examination, he showed severe cervical dystonia and spasmodic dysphonia. Moderate spontaneous myoclonus affecting the neck, arms, and trunk that worsened with activity was seen. Family history was positive for jerky movements in his father, 2 paternal aunts, his paternal grandmother and his son (figure 1). Only his son was available for examination, showing a much milder clinical picture that had started at the age of 3. Mild spontaneous myoclonus that affected trunk and proximal arms were seen. He was an industrial engineer and practiced several sports. None of them noted alcohol responsiveness.

Results: Next Generation Sequencing analysis of the entire SGCE gene coding region revealed a previously unreported heterozygous nonsense mutation in exon 7, c.904A>T (p.Lys302Ter). The mutation was found (by Sanger) in the proband's son and was absent in a non-affected brother.

Conclusion: We report a novel nonsense mutation in exon 7 of the SGCE gene in a Spanish family with myoclonus dystonia and intrafamilial phenotypic variability.

Disclosure: Nothing to disclose



Family pedigree

EPR1137

Technology-based diagnostic, therapy-response and prognostic biomarkers in Parkinson's disease

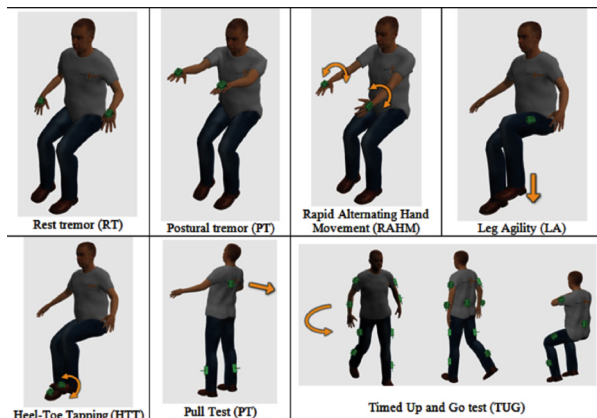
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Background and aims: One major unmet need in Parkinson's disease (PD) is the availability of non-invasive, early and reliable biomarkers, for diagnosis, prognosis and therapy response evaluation. Technology-based Objective Measures (TOMs) recently gained relevance in this field.

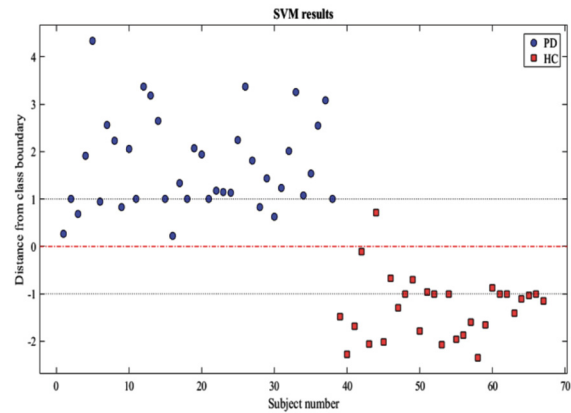
Our aim is to prospectively evaluate motor performances with technology-based objective measures (TOMs) in a cohort of Parkinson's disease patients in order to identify diagnostic, therapy response and progression biomarkers.

Methods: We enrolled 40 consecutive drug free PD patients and evaluated them clinically and with a set of wearable inertial sensors, during 7 motor tasks (tremor, four-limbs bradykinesia, timed-up-and-go test and pull test) at T0 and after 1 year. we followed them up for at least 2 years. we also enrolled 30 healthy subjects who underwent the kinematic assessment. Mann-Whitney test was performed between PD and HC features at T0, PD patients features at T0 and T1 and between T0 features of responder and non-responder patients.

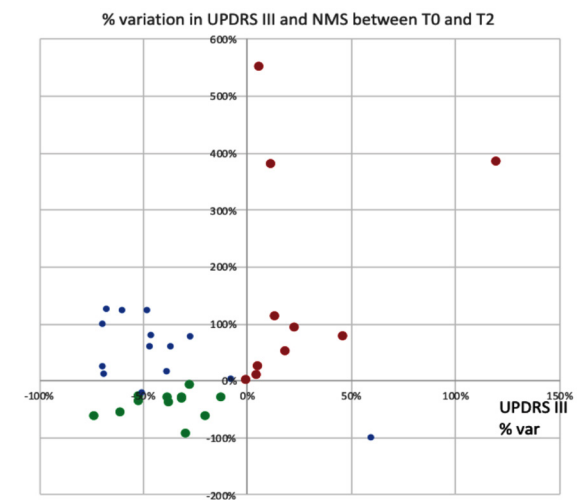


Sensors positioning during the 7 motor tasks evaluated (rest tremor, postural tremor, rapid alternating hand movement, leg agility, heel to toe test, pull test, timed-up-and-go test)

Results: 36 patients completed the study. We identified an algorithm able to discriminate HC from PD subjects with 97% accuracy. Then, among all kinematic features, at T1 at least one per task was significantly improved. Interestingly, many features from TUG test and PT ameliorated, even if they were scored as normal in UPDRS. In addition, one feature from upper limb bradykinesia and 6 features from TUG were significantly different between responder and non-responders at T0.



PD-HC classification



% variation of UPDRS and NMS after 24 months of dopaminergic therapy and identification of responder and non-responder patients

Conclusion: Our results demonstrate the possibility to objectively measure the efficacy of a therapeutic intervention in PD and identify candidates for early, technology-based prognostic and diagnostic biomarkers.

Disclosure: Nothing to disclose

EPR1138

Longitudinal clinical and neuroanatomical changes of PD-MCI Reverters

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Background and aims: To investigate baseline and longitudinal clinical and neuroanatomical features of patients with Parkinson's disease who experienced mild cognitive impairment, but reverted to normal cognition overtime (PD-MCIr) compared to PD with normal cognition (PD-CN), stable MCI (PD-MCIs), and patients who converted to MCI (PD-MCIc) or dementia (PD-Dc).

Methods: We recruited 154 patients with known cognitive-outcome after 4 years: 12 PD-MCIr, 55 PD-CN, 37 PD-MCIc, 26 PD-MCIs, and 24 PD-Dc. All visits included neuropsychological/clinical assessments and MRI scans. Regional cortical thickness (CT) progression overtime was investigated within and between groups.

Results: At baseline, compared to PD-MCIc, PD-MCIs and PD-Dc, PD-MCIr patients had younger age, lower treatment dose, shorter disease duration, less motor and non-motor disturbances, and greater CT in the parieto-temporal cortices and subcortical regions. On the other hand, compared to PD-CN, PD-MCIr patients had lower education, performed worse in cognition, and experienced more gastrointestinal symptoms. Overtime, PD-MCIr patients showed a global worsening of motor and non-motor symptoms, and decreased CT in fronto-temporal regions, in a way similar to that of the PD-CN group. At the last visit, compared to PD-MCIc, PD-MCIs and PD-Dc cases, PD-MCIr patients still showed a better motor and non-motor condition, and thicker cortical structures.

Conclusion: PD-MCIr is associated to a mild phenotype and a relatively preserved brain structure relative to patients with a progressive cognitive decline. The PD-MCIr cognitive vulnerability seems to be independent of the progression of motor and (other) non-motor disturbances.

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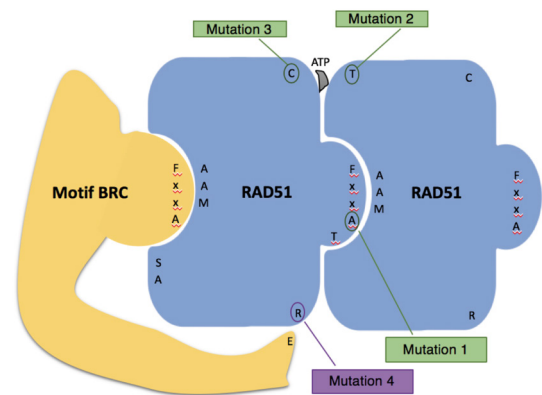
EPR1139

Biochemical consequences of RAD51 mutations involved in congenital mirror movement disorder

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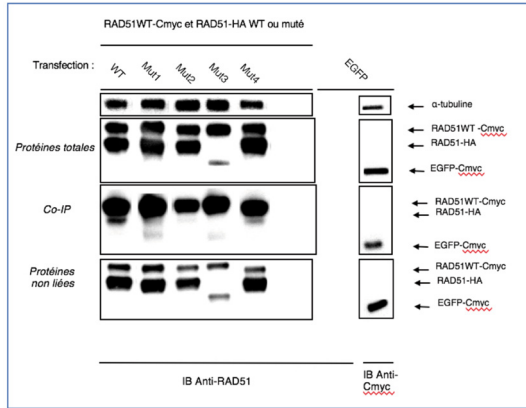
Background and aims: Congenital mirror movement disorder (CMM) is a rare genetic disorder characterized by involuntary movements of 1 hand that mirror voluntary movements of the other hand. Developmental abnormalities of the cortico-spinal tract (CST) is the most striking associated anatomical abnormality. 4 mutations in the RAD51 gene have been identified in CMM patients. RAD51 is known for its nuclear function in DNA repair but, in cortico-spinal neurons, it is mainly detected in the cytoplasm. We hypothesized that performing its cytoplasmic function during the CST development would require properties similar to those needed to exert its nuclear role in DNA repair.



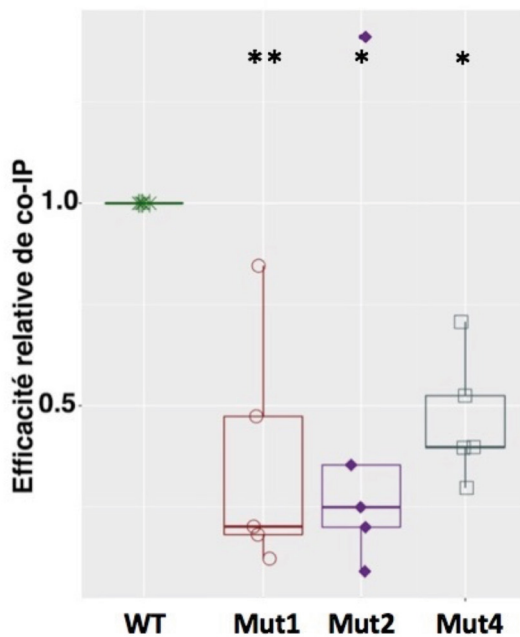
Schematic representation of the RAD51-RAD51 and RAD51-BRC interaction, and position of the 4 mutations responsible for CMM on the RAD51 protein.

Methods: We studied the biochemical properties of the various mutated RAD51 proteins by transfection of HEK 293 cells, co-immunoprecipitation of RAD51 proteins, pull-down with BRC peptides, and western-blot analysis. The wild-type protein was used as a control.

Results: We showed that 3 of the 4 mutations disturb the dimerization of RAD51, through alteration of RAD51/RAD51 interaction. Regarding the interaction with BRC peptides, no impact of the mutations could be highlighted.



Study of the RAD51-RAD51 interaction by co-immunoprecipitation of RAD51WT-Cmyc and RAD51-HA WT/mutant in immunoblot. Immunoblots made with an anti-RAD51 antibody. Right EGFP-Cmyc track revealed by an anti-Cmyc antibody. The α -tubulin is revealed by an anti- α -tubulin antibody and makes it possible to verify the homogeneity of the protein deposit



Statistical analysis of the co-IP of RAD51WT-cmyc with RAD51-HA WT or mutant. Quantification of the relative efficiency of co-IP expressed as a percentage of the RAD51WT condition for each independent experiment. ANOVA, $F(5,24) = 4.64$; $p=0.004$ followed by a post-hoc Dunnett test, $* = p < 0.05$, $** = p < 0.01$.

Conclusion: As the dimerization defects of RAD51 results in defective oligomerization in the nucleus, our findings suggest that CMM mutations of RAD51 would likewise result in altered oligomerization of RAD51 in the cytoplasm. More studies are needed to further investigate the intracellular consequences of CMM RAD51 mutations and the exact role of RAD51 in the development of the CST.

Disclosure: Nothing to disclose

EPR1140

When and how to stop subthalamic deep brain stimulation in late stage Parkinson's disease

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Background and aims: Subthalamic-deep brain stimulation (STN-DBS) effects may decrease with Parkinson's disease (PD) progression. There is currently no clear indication on how and when to consider the interruption of DBS treatment in late stage (LS) PD.

Our aim was to investigate the percentage of "poor stimulation responders" among LSPD patients in order to elaborate an algorithm to decide whether DBS interruption may be considered.

Methods: LSPD patients (Schwab and England ADL Scale < 50 and Hoehn Yahr Stage > 3 in Med On/Stim On) treated with STN-DBS for at least 5 years underwent a cross-over double-blind randomized evaluation of acute effects of stimulation. Physicians, caregivers and patients were blinded to stimulation conditions. Poor stimulation responders (Δ MDS-UPDRS part III < 10% Stim On/Med Off vs. Stim Off/Med Off) maintained the Stim Off/Med On condition during one month for open label assessment.

Results: 36 patients were included (Table 1). The acute effect of stimulation was significant (17% improvement at the MDS-UPDRS part III Stim On/Med Off vs. Stim Off/Med Off). 7 patients (20%) were classified as "poor stimulation responders" (Table 2). After 1 month, 4 switched stimulation back "On" due to worsening of parkinsonism, dysphagia and scialorrea, with a variable time delay (up to 10 days) (Figure 1). No serious adverse effects occurred.

EPR1141

Opicapone as First-Line Adjunctive Levodopa Treatment in Parkinson's Disease Patients with Motor Fluctuations: Findings from BIPARK-I and II Combined Post-Hoc Analysis

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Background and aims: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved effective in treating motor fluctuations in Parkinson's Disease (PD) patients in 2 large multinational trials (BIPARK-I and II) [1,2]. This exploratory post-hoc analysis evaluated the efficacy and safety of OPC as 1st-line adjunctive therapy in levodopa/DOPA decarboxylase inhibitors-treated PD patients with end-of-dose motor fluctuations.

Methods: Data from matching treatment arms in BIPARK-I and II were combined in placebo (PLC) and OPC 50mg groups for patients treated with levodopa-only at baseline (i.e. without dopamine agonists [DAs] or monoamine oxidase-B inhibitors [MAOIBs]). Studies had similar designs and eligibility criteria [1,2]. Statistical analysis of efficacy was performed using analysis of covariance.

Results: At baseline, 59 and 68 were treated with levodopa-only in the PLC and OPC 50mg groups, respectively (Table 1). Changes from baseline in absolute OFF- and ON-time were significantly greater for OPC 50mg versus PLC (p=0.0161 and p=0.0049, respectively; Table 2). The most frequently reported at least possibly related treatment-emergent adverse events (TEAEs) (≥5% patients) were dyskinesia, constipation and nausea (Table 3). The incidence of at least possibly related TEAEs leading to discontinuation was similar in both arms (Table 3).

Parameter	n = 36
Age (yr)	71.1 (7.2)
Women (%)	14 (38.9)
BMI (kg/m ²)	24.1 (4.8)
Age at disease onset (yr)	44.3 (8.7)
Disease duration (yr)	27.2 (8.7)
Age at DBS (yr)	58.4 (7.4)
Years after DBS	14.1 (8.3)
Stimulation Voltage	
R_STN_L STN	2.3 (0.1) / 2.4 (0.7)
LEDD before surgery (µg)	1004 (174)
LEDD after surgery (µg)	728 (148)
SAE	28 (77.8)
HY	4 (11.1)
HY V. at 1yr	18 (50.0)
MMSE	28 (7.3)
MMSE V. at 1yr	26 (7.4)
Interim/total on Chg	4 (11.1)
PG-I (yr)	0
MDI-UPDRS I total score	17.4 (7.4)
Score, mean (SD) / # of patients scoring positive in the item (%)	
Cognition	12 (33.3)
Habitual/episodic depression	18 (50.0)
Depressed mood	28 (77.8)
Anxiety mood	26 (72.2)
Apathy	24 (66.7)
EDS	4 (11.1)
DYS	20 (55.6)
Sleep problems	20 (55.6)
Dietary changes	20 (55.6)
Pain	21 (58.3)
Urinary problems	20 (55.6)
Constipation problems	27 (75.0)
Light headiness	17 (47.2)
Fatigue	20 (55.6)
MDI-UPDRS II	14.7 (8.1)
MDI-UPDRS IV	3.9 (4.3)
L-Alpha-Raclopride Motor complications (%)	26 (72.2)
Motor fluctuations (%)	27 (75.0)
Tremulousness motor fluctuations (%)	9 (25.0)
Dyskinesias (%)	14 (38.9)
Tremulousness dyskinesias (%)	4 (11.1)
Paradoxical dyskinesias (%)	9 (25.0)
EQ-5D VAS patients	61.5 (11.1)
EQ-5D VAS caregivers	68.2 (19.2)
ZDRS	32 (88.9)

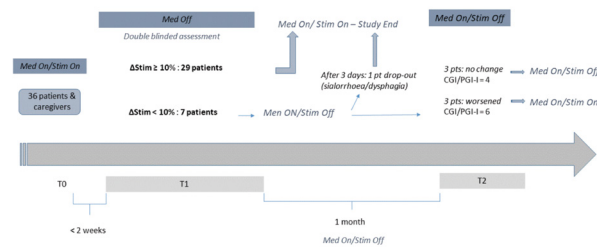
Table 1. Demographic and clinical characteristics of LSPD patients. Values are presented as mean (SD) if an otherwise specified. HY: Hoehn-Yahr Stage; SAE: Schwab and English score; LEDD: levodopa equivalent daily dose; BMI: Body mass index; MMSE: Mini-Mental State Examination; EQ-5D VAS: Visual Analogue Scale of the Euro-QoL-5D; ZDRS: Zaitsev Caregiver Burden Inventory. At MDI-UPDRS part I a patient was considered as having a "positive" score for the item if score was ≥1; at MDI-UPDRS part IV motor complications and dyskinesias have been considered " troublesome" if item was ≥2.

Table 1. Demographic and clinical characteristics of LSPD patients.

	All patients (n=36)		Placebo responders (n=7)		Post-stimulation responders (n=29)	
	Med Off/Time On	p-value	Med Off/Time On	p-value	Med Off/Time On	p-value
MDI-UPDRS III	71.3 (19.3)	29.7 (11.1)	<0.001	66.3 (12.0)	66.3 (12.1)	0.3
Speech	3.0 (9)	2.7 (8.7)	0.071	2.8 (8.9)	2.7 (8.9)	0.3
Epiglot	9.3 (7.7)	6.7 (5.3)	<0.001	9.2 (8.9)	8.4 (7.4)	0.4
Breathlessness	27.4 (8.6)	24.8 (9.7)	0.003	27 (9.1)	29 (7.2)	0.1
Rest tremor	3.2 (4.3)	0.6 (1.0)	<0.001	0.1 (0.2)	0.1 (0.2)	1
Arising from chair	3.4 (8.9)	3.3 (11.1)	0.24	3.8 (8.3)	3.8 (8.5)	1
Feeling of gut	3.3 (8.9)	3.3 (11.1)	0.934	3.5 (8.5)	3.3 (8.5)	1
Paradoxical inhibition	3.7 (8.6)	3.5 (8.7)	0.803	3.8 (8.7)	3.7 (8.4)	0.3
Pain	2.4 (8.7)	2.4 (8.8)	0.99	2.8 (8.8)	2.8 (8.8)	1
Const	3.4 (8.5)	3.4 (8.7)	0.99	3.5 (8.7)	3.4 (8.7)	0.3
GI	4.7 (8.4)	4.7 (8.5)	0.99	4.5 (8.5)	4.5 (8.5)	0.3
CGI*	5.1 (1.1)	/	/	4.0 (8)	/	/
PGI2†	5 (8)	/	/	4 (8.7)	/	/

Table 2. Stimulation challenge test: double-blinded assessment. Values are presented as mean (SD) if an otherwise specified. * one included patient did not perform the stimulation challenge test as the PD was not in the OFF state. HY: Hoehn-Yahr Stage. The following mean of sum of the MDI-UPDRS part III have been considered: Speech (item 11), Epiglot (item 12), breathlessness (item 13), rest tremor (item 14), arising from chair (item 15), and feeling of gut (item 16). † Post-stimulation responders (n=29) were considered: Speech (item 11), arising from chair (item 15), and feeling of gut (item 16). PGI2: Patient's Global Impression Scale; CGI: Clinical Global Impression Scale; CGI: change from baseline. 1: 1 (no change), 2: 2 (worse), 3: 3 (better), 4: 4 (worse), 5: 5 (better), 6: 6 (worse), 7: 7 (worse), 8: 8 (better), 9: 9 (worse), 10: 10 (better), 11: 11 (worse), 12: 12 (better), 13: 13 (worse), 14: 14 (better), 15: 15 (worse), 16: 16 (better).

Table 2. Stimulation challenge test: double-blinded assessment.



Study algorithm and follow-up

Conclusion: The majority (92%) of LSPD patients still respond to STN-DBS. Effects of stimulation may take days to disappear after its interruption. We present a safe and effective decisional algorithm that could guide physicians and caregivers in taking challenging therapeutic decisions in late stage PD.

Disclosure: Nothing to disclose

Table 1. Baseline characteristics (Safety Set)

Characteristic	PLC N=59	OPC 50 mg N=68
Male gender, n (%)	36 (61.0)	42 (61.8)
Age, mean (SD) years	64.4 (9.8)	65.6 (9.2)
Disease duration, mean (SD) years	6.2 (2.8)	7.0 (4.3)
Daily OFF-time, mean (SD) hours	6.6 (2.3)	6.6 (2.3)
Levodopa dose, mean (SD) mg/day	718.3 (359.1)	730.3 (347.0)

OPC, opicapone; PLC, placebo; SD, standard deviation

Table 1

Table 2. Changes from baseline in absolute OFF- and ON-time (Full Analysis Set)

Characteristic	PLC N=59	OPC 50 mg N=67
Absolute OFF-time		
LS mean (SE; 95% CI) change from baseline, min	-40.3 (20.6; -80.7, 0.0)	-109.2 (19.8; -147.9, -70.4)
LS mean (SE; 95% CI) absolute difference, min	-68.8 (28.5; -124.8, -12.8)	
p-value		0.0161
Absolute ON-time		
LS mean (SE; 95% CI) change from baseline, min	16.9 (20.5; -23.3, 57.0)	96.7 (19.7; 58.1, 135.3)
LS mean (SE; 95% CI) absolute difference, min	79.8 (28.3; 24.3, 135.4)	
p-value		0.0049

CI, confidence interval; OPC, opicapone; LS, least squares; PLC, placebo; SE, standard error

Table 2

Characteristic	PLC	OPC 50 mg
	N=59	N=68
Patients with at least possibly related ^a TEAEs, n (%)	13 (22.0)	30 (44.1)
Most frequently reported ^b at least possibly related ^a TEAEs, n (%)		
Dyskinesia	1 (1.7)	8 (11.8)
Constipation	0	4 (5.9)
Nausea	4 (6.8)	1 (1.5)
Patients with at least possibly related ^a TEAEs leading to discontinuation, n (%)	5 (8.5)	5 (7.4)

^aRelationship to study medication reported as 'possible', 'probable', 'definite' or missing; ^b≥5% of patients in either group
OPC, opicapone; PLC, placebo; TEAE, treatment-emergent adverse event

Table 3

Conclusion: OPC 50mg demonstrated efficacy and was generally well tolerated in PD patients treated with levodopa-only, suggesting that OPC is a viable option as a first-line adjunctive therapy in levodopa-treated PD patients with motor fluctuations.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.

2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

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EPR1142

Prediction of the effect of deep brain stimulation on gait freezing of Parkinson's disease

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Background and aims: The response of freezing to deep brain stimulation of the subthalamic nucleus (STN-DBS) is controversial and obviously depending very much on factors which are poorly controlled. On the other hand, a clinical predictor for the individual patient is needed to counsel the patient regarding this symptom.

Methods: A cohort of 124 patients undergoing STN-DBS has been evaluated based on the video-documented Levodopa test at baseline and the outcome in the worst and best condition 1 year postoperatively. We compared the freezing item of the Unified Parkinson's disease rating scale (#14), the UPDRS total score, and a severity rating of 4 freezing subtypes with regard to its predictive value.

Results: We found 'freezing during the turning task' to be the best predictor with a ROC-value of 0.857 compared to 0.603 for the UPDRS Item 14 and 0.583 for the total UPDRS III. An improvement of 1 or 2 grades of the turning item during the preoperative levodopa test predicts an improvement during the worst condition postoperatively of 1 grade or more with an 80% probability.

Conclusion: This freezing prediction test is simple and clinically useful. The test needs to be studied in a prospective study.

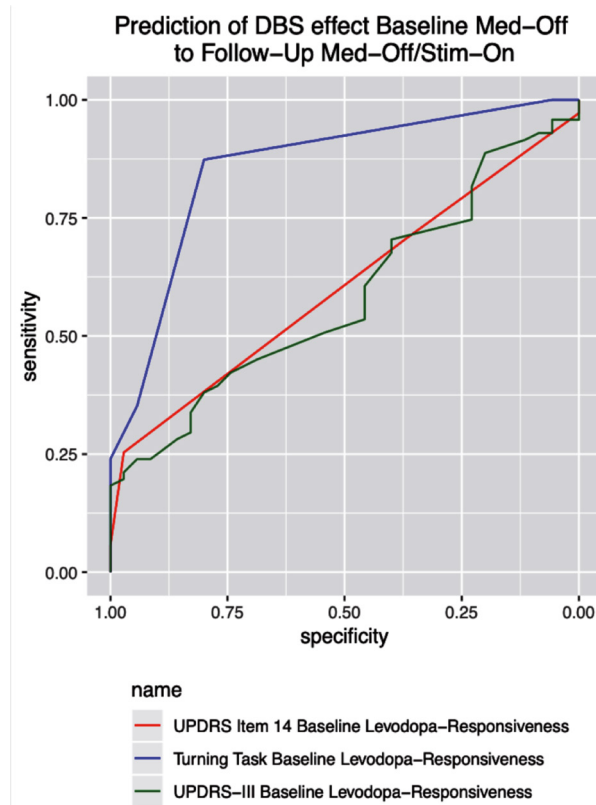


Figure 1. Prediction of DBS effect baseline Med-OFF to follow-up Med-Off/Stim-On.

Disclosure: Nothing to disclose

EPR1143

Unusual Complications related to LCIG treatment-The Cretan Parkinson Disease Cohort-A ten years prospective observational study.

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Background and aims: Enterally administered Levodopa/Carbidopa Intestinal Gel (LCIG) is a device-aided treatment for the management of intractable motor complications that characterize the advanced stages of Parkinson's disease (PD). Although considered safe, LCIG treatment can be associated with short- and long-term complications. Its safety has been studied in retrospective and prospective studies of relatively short duration. The aim of our study was to report unusual complications related to the LCIG treatment over a course of 10 years.

Methods: A prospective observational cohort study on the safety of LCIG treatment in advanced PD patients was conducted from 2009 to 2019.

Results: 40 patients received LCIG treatment during the study period. 3 patients (7.5%) discontinued the LCIG treatment due to treatment-related side effects. 1 patient developed double gastric ulcer and intestinal perforation with dislocation of the intestinal tube to the jejunum and another 1 developed severe psychosis. 33 patients (82.5%) remained on LCIG treatment and were followed regularly. 5 of them (15%) developed buried-bumper syndrome which was efficiently managed surgically without discontinuing treatment. 3 patients (9%) lost their teeth. 9 patients (27%) suffered bone fractures due to falls. 1 patient (3%) on LCIG monotherapy developed impulse control disorder and another 1 (3%) fecal incontinence. 3 patients (9%) required significant levodopa dose reduction due to psychotic symptoms.

Conclusion: LCIG treatment is a life-changing device-aided treatment for advanced PD patients. Complications are not uncommon. Most of them are easily managed. Severe treatment-related adverse events that require LCIG treatment discontinuation can occur but are rare.

Disclosure: Nothing to disclose

EPR1144

Changes in brain network topology as a function of a cognitively engaged lifestyle in Huntington's disease: a longitudinal resting-state fmri and diffusion tensor imaging study

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Background and aims: Huntington's disease (HD) is an inherited neurodegenerative disorder which affects the cortico-striatal network leading to highly individual differences of motor, cognitive and psychiatric symptoms. Understanding the sources of this variability is crucial to be able to develop preventive strategies that may change the progression of the symptoms. In terms of protecting against cognitive impairment, a cognitively engaged lifestyle (CEL) has been shown to ameliorate cognitive decline, however, the underlying neurobiological basis remains largely unknown. Network analysis provides a new perspective for understanding how CEL may modulate brain changes. In this study, we aimed to explore the relationship between CEL and the longitudinal changes in brain structural and functional topology, using graph analysis.

Methods: Thirty-three HD individuals were scanned longitudinally and evaluated for CEL using the Cognitive reserve questionnaire. Topological organization of whole-brain structural and functional network was calculated using diffusion and resting state MRI. Then, correlation analysis was performed between changes in topological measures and CEL.

Results: CEL showed a negative correlation with longitudinal change of mean functional and structural betweenness, modularity and average shortest path length, suggesting that HD individuals with higher CEL scores are better able to cope with the effects of pathology. These findings indicate that despite the burden of pathology, they have a higher ability for processing and distributing specialised information across the network and less vulnerability to disruption in highly connected nodes.

Conclusion: Our study suggests that a CEL may promote brain maintenance by modulating the topological and dynamical brain network's properties and conferring protection against neurodegeneration.

Disclosure: Nothing to disclose

MS and related disorders 1

EPR1145

Motor disability assessment in the Google Maps era: a feasibility study to test a digital tool

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Background and aims: Ambulation score (As) plays a major role in the final EDSS scoring. Aim of our study is to evaluate whether the use of Google Maps application in calculating the As in clinical practice may improve the accuracy of EDSS scoring in MS patients.

Methods: 243 MS patients were recruited. We evaluated: 1) the As based on the Maximum Walking Distance (MWD) referred by the patients (pAS), 2) the As based on MWD identified on Google Maps (gmAs), 3) the agreement between these 2 measurements. We evaluated whether demographic and clinical data might have influenced the belonging to the group of MS patients with pEDSS congruent with gmEDSS (unchanged group) or MS patients with pEDSS different from gmEDSS (changed group). Finally, in a subgroup of patients we tested the consistency among these 2 measurements and the As objectively measured (actAS). For statistical analysis Spearman correlation test and Intraclass Correlation Coefficient (ICC) were used.

Results: One third of MS patients of our sample reported a pAS different from the gmAS. Progressive phenotype were more likely to belong to the changed group as well as fatigued or depressed patients. Considering the subgroup in which the As was objectively measured, in 45.3% of patients the pAS corresponded to actAS while the degree of concordance increased to 60% when considering gmAS and actAS.

Table 1 – Whole population; demographic and clinical features

	Total (n=243)		EDSS <=3.5 (n=142)		EDSS >=4 (n=101)		P
	n	%	n	%	N	%	
Sex							
Female	173	71.19	97	68.31	76	75.25	
Male	70	28.81	45	31.69	25	24.75	0.239
Age							
Mean, sd							
Median (Q1-Q3)							
Disease type							
CIS	1	0.41	1	0.70	0	0.00	
RR	210	86.78	140	98.59	70	69.31	
SP	22	9.09	1	0.70	21	20.79	
PP	9	3.72		0.00	9	8.91	<0.001
Disease duration							
mean, sd	9.60	7.83	7.75	6.39	12.2	8.9	<0.001
median (Q1-Q3)	7	3-13	6	3-11.3	10	5.5-17	
Ongoing therapy							
Copaxone	19	7.82	13	9.15	6	5.94	
INF	51	20.99	35	24.65	16	15.84	
DMF	52	21.4	35	24.65	17	16.83	
Terifunomide	16	6.58	5	3.52	11	10.89	
Fingolimod	46	18.93	26	18.31	20	19.80	
Natalizumab	36	14.81	20	14.08	16	15.84	
Alemtuzumab/Altro	10	4.12	2	1.41	8	7.92	
Nessuna	13	5.35	6	4.23	7	6.93	

Table 2 – Whole population; clinical scores

	Totale n=243		EDSS <=3.5 n=142		EDSS >=4 n=101		p
	mean, sd	median (Q1-Q3)	mean, sd	median (Q1-Q3)	mean, sd	median (Q1-Q3)	
FSStot	30.63	16.09	24.27	13.94	39.56	14.65	<0.001
PHQ91	7.52	6.07	5.6	5.22	10.22	6.17	<0.001
ASp	1.20	1.71	0.11	0.49	2.74	1.62	
EDSSp	3.24	1.67	1.97	0.7	5.03	0.73	
ASgm	1.11	1.70	0.23	0.74	2.35	1.9	
EDSSgm	3.24	1.65	2.15	1.03	4.77	1.05	

Abbreviations: pAS = perceived Ambulation Score; pEDSS = perceived Expanded Disability Status Scale; gmAS = Google Maps Ambulation Score; gmEDSS = Google Maps Expanded Disability Status Scale; actAS = actual (objective) Ambulation Score; actEDSS = actual (objective) Expanded Disability Status Scale; FSS = Fatigue Severity Scale; PHQ-9 = Patient Health Questionnaire-9.

Table 3 - Multinomial logistic model – Factors influencing the belonging to the changed group (CG) or unchanged group (UG)

Variables	ODDS RATIO (OR)	95 % Confidence Interval (95% CI)		P value	
Intercept	0.02			<.0001	
Disease type	PP/SP vs RR	2.8	1.1	7.11	0.03
age, years		1.02	0.99	1.06	0.164
Level of education, years		0.95	0.86	1.05	0.321
disease duration, years		1.03	0.98	1.07	0.208
FSS		1.03	1.01	1.06	0.01
PHQ-9		1.1	1.04	1.17	0.002

Abbreviations: PP = Primary Progressive Multiple Sclerosis; SP = Secondary Progressive Multiple Sclerosis; RR = Relapsing-Remitting Multiple Sclerosis; FSS = Fatigue Severity Scale; PHQ-9 = Patient Health Questionnaire-9.

Conclusion: Google Maps technology is a feasible tool that could permit to measure MWD increasing the concordance with actual measure especially in pwMS with moderate disability, where MWD heavily influences the final EDSS score.

Disclosure: Nothing to disclose

EPR1146

Long-term follow-up of three-times-weekly glatiramer acetate: 7-year results of the Glatiramer Acetate Low-Frequency Administration (GALA) open-label extension study

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Background and aims: The 1-year GALA study showed that glatiramer acetate (GA) 40mg/mL (GA40) reduced annualized relapse rate (ARR) and MRI activity versus placebo in patients with relapsing multiple sclerosis. Here, we describe effects of early start (ES) and delayed start (DS) GA40 treatment for up to 7 years.

Methods: Clinical evaluations occurred every 6 months. ARR was the primary endpoint; additional endpoints were exploratory or post hoc analyses.

Results: 1404 patients randomized to GA (N=943) or placebo (N=461); 834 (88.4%) ES and 419 (90.9%) DS patients continued into open-label (OL). ARR was 0.26 for ES and 0.31 for DS (RR: 0.83; 95% CI: 0.700, 0.993; P=0.0409). Percent of patients without relapse was 48.1% ES and 44.0% DS, and during only the OL was 60.7% ES and 65.9% DS. ES prolonged median time to relapse (4.9 years) versus DS (4.3 years; hazard ratio [HR]: 0.82; 95% CI: 0.693, 0.959; P=0.0135). Percent of patients without 6-month CDP was 81.9% ES and 81.3% DS, and HR for time to 6-month CDP of ES versus DS was HR=0.89; 95% CI 0.688, 1.157; P=0.3898. 49.3% of ES and 46.2% of DS patients were free of clinical disease activity. The most common adverse events (AEs), injection-site reactions and immediate post-injection reactions, were generally mild and consistent with the GA safety profile.

Conclusion: No new AEs emerged in patients receiving GA40 for up to 7 years. Treatment with GA40 was associated with low ARR and CDP in patients continuing on GA40 and those switching from placebo.

Disclosure: Funded by Teva Pharmaceutical Industries, Petach Tikva, Israel.

EPR1147

Evidence for Improved Myelination in Patients Treated with Siponimod: Results from the Phase 3 EXPAND MRI Substudy

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Background and aims: Changes in magnetisation transfer ratio (MTR) are widely used as a marker of changes in myelin density in brain. In preclinical studies, siponimod showed evidence of remyelinating effects. This exploratory analysis assessed the effect of siponimod on MTR versus placebo in different brain regions, and MTR recovery within lesions.

Methods: This prospective, MTR EXPAND substudy included 633 2ndary progressive multiple sclerosis (SPMS; siponimod [n=409]; placebo [n=224]) patients. MTR was analysed in normal-appearing brain tissue, cortical grey matter and normal-appearing white matter at baseline, Month (M)12 and M24. MTR was normalised to reduce MTR variability across scanners. Median absolute normalised MTR (nMTR) change from baseline expressed in percent units was derived from mixed models for repeated measures. MTR recovery metrics were assessed in new MTR lesions comparing nMTR decrease from pre- to post-lesion timepoints for siponimod versus placebo.

Results: Siponimod reduced median nMTR decrease from baseline to M12 and M24 versus placebo across brain tissues. Decrease was lower with siponimod at M24 across tissues by -55% to -98% (p<0.05; Table). In normal-appearing white matter, siponimod appeared to have fully prevented a decrease in nMTR. Lesion MTR recovery favoured siponimod (-1.321) versus placebo (-1.506; difference, 0.185 [0.056; 0.314]; p=0.005).

Table. Absolute change from baseline in median normalised MTR (percent unit) by brain tissue

Brain tissue	Adjusted means		% Reduction; p-value
	Siponimod (N=409) (N=327)	Placebo (N=224) (N=180)	
Normal-appearing brain tissue			
M12	-0.016	-0.024	-38%; p=0.3178
M24	-0.022	-0.056	-61%; p=0.0187
Cortical grey matter			
M12	-0.019	-0.026	-27%; p=0.4236
M24	-0.025	-0.056	-55%; p=0.0468
Normal-appearing white matter			
M12	0.002	-0.019	-105%; p=0.0209
M24	-0.001	-0.045	-98%; P=0.0018

N, number of patients included in the MTR sub-study (with any MTR data)
 N', number of patients included in the analysis (i.e. with at least one result post-baseline)
 Absolute median normalised MTR change from baseline was derived from mixed models for repeated measures adjusted for treatment, region, age, visit, baseline median normalised MTR of the respective brain tissue, baseline number of gadolinium-enhancing T1 lesions, baseline T2 lesion volume and treatment by visit and baseline median normalized MTR by visit interactions as covariates
 M, month; MTR, magnetisation transfer ratio

Table. Absolute change from baseline in median normalised MTR (percent unit) by brain tissue

Conclusion: Siponimod demonstrated a consistent and significant effect on the MTR decrease over time in normal-appearing white matter and cortical grey matter versus placebo, and improved MTR recovery in newly formed lesions. These data are consistent with observations in preclinical models and support potential beneficial effects of siponimod on remyelination in SPMS patients.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

EPR1148

Inflammatory markers for predicting progression in Multiple Sclerosis: An Indian story

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Background and aims: Cytokines have been widely studied as potential inflammatory markers in Multiple Sclerosis (MS) though no data from South Asia is available to contribute to this concept. We studied the cytokine profiles in treatment naïve and off-treatment Multiple Sclerosis patients in order to establish a marker panel for early prediction of progression.

Methods: Paired CSF (Cerebrospinal fluid) and serum samples were collected from N=47 treatment naïve RRMS, N=20 treatment naïve or on no DMT (Disease-modifying treatment) for last one-year SPMS patients [Inclusion criteria: Age 18-65years, EDSS <6.5, having no recent history of long term infection] and N=50 matched healthy controls. 27 cytokines were analysed by BIORAD Bio-plex ProTM human cytokine standard 27 plex kit. The reference point of comparison was taken as Healthy control levels. Only the statistically significant (p<0.05) and showing similar trends in both blood and CSF were considered.

Results: Described in detail in Figure 1.

Results:

N=67 total MS patients were taken amongst which N=47 were RR and N=20 were SP. The mean age at diagnosis for both groups combined were 27±9.5 and the female:male ratio was 1.5:1. In the RR group, the most common first symptoms at presentation was Brainstem-cerebellum (43.7%) whereas in SP was spinal cord and optic (53%). The mean baseline EDSS was 1.8± 1.2 in RR and 4.7± 2.23 in SP. The median duration of disease in the RR group 1.3 ±0.34 and 8.01± 0.4 for SP. Baseline median annualized relapse rates (ARR) were 1.76 ±1.2 and 0.76 ±0.26 for RR and SP groups, respectively. In the SPMS population, pro-inflammatory cytokines TNF alpha, IFNg, IL9, MIP1a, MIP1b, IL2, IL7 were observed to be upregulated (p<0.05). VEGF was downregulated (p<0.05) whereas RANTES was only observed in CSF. The anti-inflammatory cytokines IL1ra, IL13, FGFb were also upregulated in SPMS samples whereas GCSF was lower in as compared to the RR group (p<0.05). IL10 was observed only in CSF with an upregulation in SPMS. The sensitivity and specificity of these markers combined for the SPMS patients compared to RRMS were 94.8%. The upregulated pro-inflammatory cytokines were associated with disease severity defined by increased annualised relapse rates and with an increase in EDSS in the RR group (12.7%) directing towards these patients inclination to move to early progression. Levels of all cytokines were significantly higher in both MS groups compared to the healthy controls (specificity=98.3%).

Figure 1: Result summary

Conclusion: The upregulation of both kinds of cytokines was consistent with the neuronal tissue damage. Specifically, the increased levels of most anti-inflammatory cytokines bear testimony to the non-relapsing progressive nature observed in the SPMS phase. It can be well stated that the above set of reported cytokines (TNF alpha, IFNg, IL9, MIP1a, MIP1b, IL2, IL7, VEGF, RANTES, IL1ra, IL13, FGFb, IL10) holds potential as a panel for prediction of progression although validation in a larger cohort is necessary with real-time long term follow-ups of patients moving to the progressive phase to further find correlations with other clinical and imaging findings.

Disclosure: The research project was supported by the home Institution PGIMER, Chandigarh as part of the Intramural project scheme.

EPR1149

B-cells, T-cells and inflammatory CSF biomarkers in primary progressive MS and relapsing MS in the OBOE (Ocrelizumab Biomarker Outcome Evaluation) trial

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Background and aims: Ocrelizumab is an anti-CD20 molecule that reduces progression in MS. Less is known about biomarkers and anti-CD20 mechanisms of action in primary progressive MS (PPMS) than relapsing MS (RMS). Presence of T1 gadolinium-enhancing lesions have been associated with higher baseline cerebrospinal fluid (CSF) neurofilament light (NfL) and serum NfL (sNfL) levels in PPMS and RMS and significant treatment-related sNfL reductions in PPMS (ORATORIO). We assessed longitudinal changes in B-cells, T-cells, NfL and soluble inflammatory markers in patients from the OBOE study.

Methods: 28 patients with PPMS received ocrelizumab 600mg every 24 weeks. Blood and CSF samples were assessed for NfL, CXCL13, CCL19 and CSF B- and T-cells. Data were compared with previously reported RMS data.

Results: Baseline CSF B-cells, T-cells and CCL19 levels were indistinguishable between patients with PPMS and RMS, whereas CSF NfL ($p=0.012$) and CXCL13 ($p=0.020$) levels were decreased in PPMS. PPMS CSF B-cell ($n=15$; median percent change, -100 [IQR $-100, -91.4$]; $p<0.001$) and T-cell ($n=17$; -63.69 [IQR $-80.5, -12.9$]; $p=0.051$) counts were reduced at 52 weeks post-treatment. Neither CSF NfL nor sNfL levels were decreased at 52 weeks; however, NfL trended lower in 7 patients with PPMS with baseline T1 gadolinium-enhancing lesions vs those without.

PPMS CSF CXCL13 levels were reduced following ocrelizumab treatment, but this was nonsignificant.

Conclusion: Baseline CSF B-cell, T-cell and inflammatory biomarker levels were similar in PPMS and RMS. CSF B-cell, T-cell and CXCL13 levels were reduced following ocrelizumab treatment in PPMS and RMS.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; editorial assistance was provided by Health Interactions, USA.

EPR1150

Blood neurofilament light levels are reduced following ocrelizumab treatment in patients with relapsing and primary progressive multiple sclerosis

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Background and aims: Neurofilament light (NfL) is a marker of neuroaxonal injury. Ocrelizumab (OCR) reduced disease activity and progression in patients with relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS) from the OPERA and ORATORIO trials. Here, we investigated blood NfL levels and changes over time following OCR initiation.

Methods: Patients with RMS (OPERA: OCR, n=368; interferon β -1a, n=347) and PPMS (ORATORIO: OCR, n=347; placebo, n=169) were included. Blood NfL was measured with the Quanterix Advantage kit. Baseline NfL levels were compared between groups using serum samples; longitudinal assessments were conducted using serum from patients with RMS and EDTA plasma from patients with PPMS. Findings were compared to an age-matched cohort of 118 healthy donors (HD) with median (10th to 90th percentile) serum and plasma NfL concentrations of 7.2 (4.2–12.2) pg/mL and 5.9 (3.1–9.4) pg/mL, respectively.

Results: At baseline, median (range) serum NfL levels were 10.6 (2.74–339) pg/mL and 10.8 (2.74–199) pg/mL in patients with RMS and PPMS, respectively. In OCR-treated patients with RMS, median (10th to 90th percentile) serum NfL decreased from 10.8 (5.25–32.5) to 6.7 (3.9–11.5) pg/mL over 96 weeks; in OCR-treated patients with PPMS, plasma NfL decreased from 10.6 (6.0–22.4) to 8.8 (5.4–16.6) pg/mL. Among OCR-treated patients with elevated NfL, the majority (RMS, 93.7%; PPMS, 61.5%) reached levels below the 90th percentile of HD.

Conclusion: Ocrelizumab lowered elevated blood NfL levels in the majority of patients with RMS and PPMS to below the 90th percentile of HD.

Disclosure: Sponsored by Hoffmann-La Roche Ltd; editorial assistance was provided by Health Interactions, USA.

EPR1151

PM2.5 exposure is a risk factor of multiple sclerosis. An ecological study with a Bayesian mapping approach

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Background and aims: Some environmental factors have been associated to the increased risk of multiple sclerosis (MS). Air pollution might also play a relevant role. The aim of the study was to investigate the association of the air pollutant particulate matter PM2.5 with MS prevalence in the province of Pavia, which is one of the most polluted area in Europe.

Methods: A total of 927 MS cases (315 M, 612 F) resident in the province of Pavia (547,251 inhabitants) were identified. Spatial emission data regarding PM2.5 were gathered from the European Monitoring and Evaluation Programme database. Gridded data of winter ground-level PM2.5 concentrations subdivided into 188 municipalities were extracted for the period 2010–2017. Municipalities were stratified into 3 groups by tertiles according to PM2.5 concentrations. Ecological regression and Bayesian statistics were used to analyse the association between PM2.5 concentrations, urbanisation degree, deprivation index and MS risk.

Results: The overall MS prevalence in the province of Pavia was 169.4 per 100,000 inhabitants (95% CI: 158.8–180.6). MS risk was significantly higher among those persons living in areas with PM2.5 concentration higher than the European threshold limit (25 microgram/m³). The Bayesian map revealed consistent clusters of MS high risk.

Conclusion: The study found a relationship between MS risk and PM2.5 suggesting that air pollution may be one of the environmental risk factors for MS. The detection of high-risk clusters with an excess number of MS cases encourages analytical studies in those areas to analyse multiple environmental factors related to the different distribution of the MS.

Disclosure: Nothing to disclose

EPR1152

Siponimod in the Central Nervous System (CNS): Translational Evidence on its Penetration and Distribution

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Background and aims: Mechanism of action of siponimod is believed to involve, at low nM range, both sphingosine 1-phosphate (S1P) receptor subtype-1 (S1P1)-dependent anti-inflammatory effects on pathogenic lymphocytes and glial cells in the CNS, and S1P receptor subtype-5 (S1P5)-dependent pro-myelination effects on oligodendrocytes. This study consolidates translational evidence to establish penetration and distribution of siponimod in the CNS.

Methods: Siponimod CNS penetration/distribution was explored in Xenopus tadpoles, mice, rats, non-human primates (NHPs) and SPMS patients from the EXPAND study (Figure).

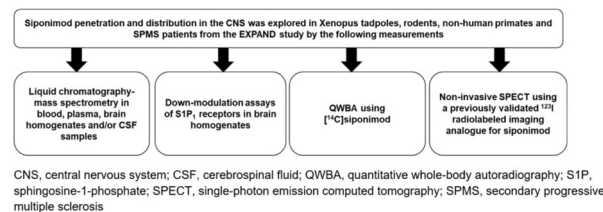


Figure. Study Methodology

Results: In tadpoles exposed to siponimod in swimming water, a dose-proportional increase in siponimod levels was obtained in brain homogenates. In mice, 10 days of siponimod-loaded diet produced dose-proportional steady-state blood siponimod levels, concomitant with 6- to 8-fold higher levels in brain-homogenates. Findings were similar in siponimod-treated rats (oral gavage, 7 days). In addition, siponimod cerebrospinal fluid (CSF)/plasma concentration ratio was 0.0025 and S1P1 protein levels in brain-homogenates indicated a dose-dependent down-modulation of brain S1P1 receptors. Quantitative whole-body autoradiography analysis in rats revealed highest siponimod-related radioactivity concentrations in the spinal cord, cerebellum (white matter), choroid plexus, medulla oblongata and corpus callosum. In NHPs, single photon emission computed tomography monitoring revealed siponimod distribution in the CNS with a brain/blood ratio of 6–8 as in mice. Of the EXPAND population (N=1,651), nine patients (five siponimod-treated) consented to CSF sampling at the end of treatment. Siponimod was detected in CSF of all siponimod-treated patients (sub-nM range).

Conclusion: Translational evidence from animal models and SPMS patients suggests penetration and distribution of siponimod in the CNS across species.

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EPR1153

Long-term Follow-Up After Autologous Haematopoietic Stem Cell Transplantation: The Italian Multiple Sclerosis Cohort

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Background and aims: Despite active treatment, long-term neurological progression is common in multiple sclerosis (MS). Autologous haematopoietic stem cells transplantation (aHSCT) has been extensively explored as a treatment strategy for aggressive MS. However, it's unknown whether aHSCT is able to prevent long-term disability progression.

Aim: To report long-term outcomes of the Italian multi-center experience of the use of aHSCT in MS.

Methods: Retrospective cohort study including aHSCT treated MS patients from 1998 to 2019 in Italy, evaluating long term (i) 3-months confirmed disability progression; (ii) occurrence of relapses; (iii) MRI activity and (iv) treatment-related mortality (TRM).

Results: 206 patients were included in the study. Median (interquartile range) follow-up was 4 (10-2) years (35 and 7 patients had at least 10 and 15 years of follow-up respectively). 69% of patients were free of confirmed neurological progression 10 years after aHSCT. Progressive MS patients had a significantly higher risk of EDSS progression than relapsing-remitting (RR) MS patients (75%vs58%; log-rank p=0.004). 50% of RRMS and 18% of progressive MS patients maintained an EDSS improvement for 5 years. Over 10 years, 71% of patients were free of

relapses and 18%. BEAM+ATG based conditioning regimen was associated with a reduced risk of relapses (24% vs 82%; log rank test $p < 0.0001$) compared with Cy+ATG and Thiohepa+Cy based conditioning regimens. TRM was 1.5% in the entire cohort [mean time(SD)=41.3 (25) days after transplant]. No deaths occurred after 2007.

Conclusion: In most patients, aHSCT is able to prevent disability progression for up to 20 years. RRMS patients are those who benefit the most from aHSCT.

Disclosure: Nothing to disclose

EPR1154

Cognitive Dysfunction in Treatment-naïve Patients with Multiple Sclerosis

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Introduction: Cognitive dysfunction is a common feature of Multiple sclerosis (MS). Studies have shown that 50-70% of patients with MS are unemployed after 10 years of disease onset. It is considered that one of the main reasons for early retirement is cognitive impairment. There is increasing evidence that disease-modifying therapy (DMT) has a positive effect on cognitive function in MS patients.

Aim: The study aimed to identify the prevalence and features of cognitive dysfunction in patients with multiple sclerosis who never received disease-modifying therapy.

Methods: 54 patients with a diagnosis of MS based on the 2017 McDonald criteria were included in the study. All patients underwent neuropsychological evaluation with Brief International Cognitive Assessment for MS battery (BICAMS) and Montreal Cognitive Assessment (MoCA). Demographics, Medical history details and Expanded Disability Status Scale (EDSS) scores were recorded. 32 patients in the study population were treated with immunomodulatory drugs. 22 patients never received DMT (8 out of them had disease duration of one year).

Results: Patients with treatment naïve multiple sclerosis performed worse on MoCA, California Verbal Learning Test II (CVLT-II) and Symbol Digit Modality Test (SDMT). They obtained significantly lower scores on SDMT.

	Patients receiving DMT n 32	Treatment-naïve patients n 22
Age, y	40 ± 9.4 (24-57)	40.6 ± 11.6 (25-65)
Women/men	23/9	17/5
Disease duration, y	8 ± 4.6 (2-22)	5.3 ± 5 (1-17)
RRMS	24 (75%)	16 (73%)
SPMS	8 (25%)	2 (9%)
PPMS	-	4 (18%)
Education	13.7 ± 4.2	14.7 ± 2.0
EDSS	3.1 ± 1.6 (1.5-6.5)	3.4 ± 1.4 (1.5-7.0)
SDMT	40 ± 12.3 (16-68)	29 ± 8.9 (5-44)
CVLT	53 ± 11.3 (30-76)	49 ± 8.4 (32-65)
BVMT-R	21 ± 7.1 (6-31)	22 ± 6.8 (6-36)
MoCA	23.4 ± 2.9 (17-28)	22.3 ± 3.8 (12-27)

Table 1. Difference in means for all measure

Conclusion: Our study demonstrates that disease-modifying therapy has a definite beneficial effect on cognitive function of patients with multiple sclerosis.

Disclosure: Nothing to disclose

EPR1155

Rationale, design and feasibility assessment of the Phase IV CLASSIC-MS study evaluating long-term efficacy for patients with multiple sclerosis treated with cladribine tablets

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Background and aims: Cladribine tablets 10mg (CT; cumulative dose 3.5mg/kg over 2 years) demonstrated efficacy versus placebo over 2 years in CLARITY, CLARITY Extension and ORACLE-MS, showing sustained efficacy without further active treatment in CLARITY Extension. CLASSIC-MS will explore long-term efficacy and real-world treatment patterns in these trial patients. Long-term safety in this population has been assessed in the PREMIERE registry.

Methods: CLASSIC-MS is an exploratory, low-interventional, multicentre, ambispective, Phase IV study of patients with MS, or those with a 1st clinical demyelinating event enrolled into the Phase III trials and who received ≥1 course of CT or placebo (N=1946). Following pre-baseline screening and assessment for eligibility, long-term retrospective data will be obtained from medical records at Study Visit 1; prospective data collected at Study Visits 1 and 2 (Figure 1). Patients will be enrolled for 17 months (Q3 2019-Q4 2020). Last Patient Last Visit is expected in Q1 2021. Primary objective: evaluation of long-term mobility after treatment with CT or placebo. Table 1 lists primary, secondary and tertiary key objectives.

Figure 1. CLASSIC-MS study design

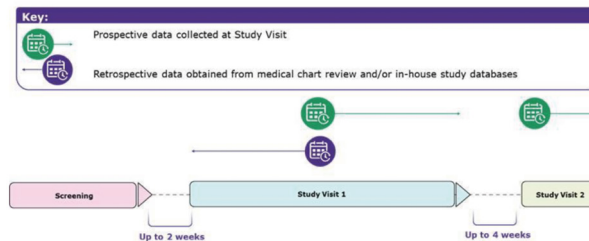


Table 1. Key exploratory objectives in CLASSIC-MS

Primary	Evaluation of long-term mobility
Secondary	Differences in clinical and MRI characteristics between long-term responders* and non-responders Real world treatment patterns Durability of clinical outcomes, quality of life and cognitive outcomes after treatment with IMP
Tertiary	Durability of outcome on brain imaging after treatment with IMP High-disease activity influencing long-term response Differences in genetics between long-term responders* and study participants who are not
* Study participants who did not demonstrate any evidence of disease reactivation based on Investigator assessment of clinical and imaging outcomes until Year 4 or later following their last dose of IMP and who did not receive disease modifying treatment until Year 4 or later following their last dose of IMP	
IMP, investigational medicinal product (cladribine tablets or placebo)	

Results: In 2018, a second feasibility survey was sent to 225 centres; 110 centres provided positive responses and were included, representing 48% of sites originally enrolled in the Phase III studies. In total 115 centres were not included (81 were not willing to participate; 13 were dropped; 16 were non-responders; 5 were rejected).

Conclusion: CLASSIC-MS will provide valuable information on the long-term efficacy of patients with MS treated with CT.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW). The authors and Merck acknowledge the involvement of Kristin Gabriel for their role in study design, data interpretation and publication concept.

MS and related disorders 2

EPR1156

Fingolimod and dimethyl-fumarate derived lymphopenia is not associated with short-term treatment response and risk of infections in a real-life MS population

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Background and aims: The association between treatment related lymphopenia in multiple sclerosis (MS), drug efficacy and risk of infections is not yet fully understood. To assess whether lymphopenia is associated with short-term treatment response and infections rate in a real-life MS population treated with Fingolimod (FTY) and Dimethyl-fumarate (DMF).

Methods: We analyzed the associations between absolute lymphocyte count (ALC) at baseline, 6 and 12 months and mean percentage decrease (MPD) at 6 and 12 months with treatment response and the occurrence of infections over a 12 months period.

Results: 137 and 75 patients treated with FTY and DMF respectively were included. FTY patients had lower ALC and higher MPD (63.5%) at 12 months ($p < 0.001$, $\chi^2=94$; $p < 0.001$, $U=540$). Higher number of previous therapies and lower baseline ALC were predictors of lymphopenia at 6 months ($p=0.047$, $OR=1.60$ and $p=0.014$, $OR=1.1$) and 12 months ($p=0.003$, $OR=1.97$ and $p=0.023$, $OR=1.1$). In FTY patients only, female sex and higher EDSS were predictors of lymphopenia at 12 months ($p=0.006$, $OR=7.58$ and $p=0.03$, $OR=1.56$). No significant changes in mean ALC, MPD at 6 and 12 months were found between patients with and without disease control and in those experiencing infections in both treatment groups.

Conclusion: Peripheral blood lymphocytes changes are not associated with short-term treatment response and with the rate of infections during FTY and DMF treatment in real-world patients. Careful monitoring of infectious adverse events is required even in the absence of lymphopenia.

Disclosure: Nothing to disclose

EPR1157

Artificial Intelligence on Conventional Magnetic Resonance Images for the Diagnosis of Neuromyelitis Optica Spectrum Disorders

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Background and aims: Diagnostic criteria of neuromyelitis optica spectrum disorders (NMOSD) exclude seronegative patients suffering limited forms of the disease, as they are usually considered prodromal phases of multiple sclerosis (MS). Using MRI data, a great effort is ongoing to allow an automatic and reliable diagnosis of MS-mimicking diseases. Deep-learning-based imaging diagnostics could go beyond conventional MRI and clinical evaluation and contribute to provide objective data-driven classification of these patients.

Methods: The model structure was based on 4 consecutive 3D convolutional neural network layers, followed by a fully dense layer after the extraction of features and was trained on conventional brain T2- and T1-weighted MRI scans from seropositive NMOSD patients ($n=55$) and early MS patients ($n=65$). After validation on an independent set of 30 NMOSD and 30 MS, the final algorithm was applied to a group of seronegative patients ($n=46$) to evaluate their classification as NMOSD or MS with deep-learning-based diagnostics.

Results: In the validation sample, the final algorithm showed a classification accuracy of 0.98. Of seronegative patients, 17 were recurrent myelitis (36.9%), 17 recurrent optic neuritis (RON, 36.9%) and 12 NMOSD (26.2%). In this dataset, the deep-learning algorithm classified 45/46 (97.8%) patients as NMOSD. The patient classified as MS was a Caucasian female with RON (disease duration 4.5 years), without oligoclonal bands in the cerebrospinal fluid.

Conclusion: Deep-learning evaluation suggests that a large majority of seronegative patients is likely to belong to the NMOSD spectrum. A longitudinal evaluation is required to confirm the diagnostic accuracy of this approach.

Disclosure: Nothing to disclose

EPR1158

Durvalumab and Multiple Sclerosis: a causal link or simple unmasking?

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Background and aims: Immune checkpoint inhibitors (ICIs) treatment is revolutionizing the immune-oncology therapy. Durvalumab is a monoclonal antibody blocking programmed cell death ligand-1 (PDL-1). Its toxicity on Central Nervous System (CNS) is not well established and its impact on demyelinating diseases is not clear.

Methods: A Caucasian 46-year-old man was diagnosed with lung adenocarcinoma in 2018 for which he was treated with Durvalumab 120mg endovenously following chemoradiotherapy. After 10 infusions, restaging whole-body computed tomography showed a right peritrigonal contrast enhancing (CE+) lesion, and brain magnetic resonance imaging (MRI) revealed other sovratentorial white matter lesions. Durvalumab was discontinued and the patient received a standard course of methylprednisolone with reduction of CE+. Therefore, he was admitted to our Neurology Department to rule out a demyelinating disorder. Brief fluctuating episodes of paraesthesia of right limbs were reported since 2013. All clinical and laboratory tests were normal, but the cerebrospinal fluid analysis showed twenty-three oligoclonal bands.

Results: Therefore, a diagnosis of Multiple Sclerosis (MS) was made according to 2017 Mc Donald criteria and treatment with glatiramer acetate was started.

Conclusion: This case report indicates that PDL-1 is an immunological checkpoint triggering MRI brain activity in a patient previously not diagnosed with MS. ICIs can exacerbate or unmask demyelinating diseases but it is unknown if they can be responsible of de novo inflammatory demyelinating pathology. It is hypothesized that epitope spreading and a broader T-cell response determined by ICIs may cause demyelinating events. It is crucial to be aware of the role of the new biodrugs in neurological inflammatory disease.

Disclosure: Nothing to disclose

EPR1159

Brainstem monoaminergic functional and structural connectivity is altered in multiple sclerosis and associated to cognitive fatigue

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Background and aims: Monoamines play a role in multiple sclerosis (MS) pathogenesis and alterations in monoaminergic pathways have been linked to fatigue [1]. We evaluated brainstem monoaminergic nuclei (BrMn) functional (Fc) and structural (Sc) connectivity in a group of MS patients and controls, and assessed possible associations with fatigue.

Methods: 68 relapsing-remitting-MS patients and 39 controls underwent brain-MRI. BrMn Fc with the rest of the brain was evaluated by resting-state-functional-MRI[2], while Sc was investigated by fixel-based-analysis and compared by means of fibre-density/cross-section[3] in the 2 groups. Selected tracts of interest projecting from BrMn were derived from Fc analyses. Correlations of Fc/Sc with fatigue status were evaluated in MS.

Results: Controls displayed positive Fc between dopaminergic-BrMn and the default-mode network (DMN), serotonergic-BrMn and both DMN and cerebellar cortex, noradrenergic-BrMn and the executive control network. BrMn Fc with these functional networks was reduced in MS, as compared to controls. Fixel-based-analysis displayed structural disconnection between BrMn and cortical targets in MS patients, due to white matter (WM) abnormalities. Correlations between cognitive fatigue and structural integrity within the mesocorticolimbic tracts were found in MS, as well as within the noradrenergic-prefrontal cortex projections.

Conclusion: Our study revealed functional disconnections between BrMn and crucial brain networks in MS, that can be – at least partially – explained by structural alterations in the WM tracts projecting from BrMn, and support the hypothesis of a contribution of monoaminergic systems to cognitive fatigue in MS. These findings add new information about the role of monoaminergic systems in MS pathogenesis and suggest new therapeutic targets.

Disclosure: Nothing to disclose

EPR1160

Safety, Patient Reported Outcomes, and Clinical Assessment on Walking Ability of Prolonged-Release Fampridine Treatment in Routine Clinical Practice: Results of the LIBERATE Study

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Background and aims: Prolonged-release fampridine (PR-FAM) 10mg tablet twice-daily is the only approved treatment in the world for improvement of walking ability in adults with multiple sclerosis (MS) with walking disability (EDSS 4-7). LIBERATE, a post-authorization, prospective, multicenter, observational study, assessed the safety and effectiveness of PR-FAM in the real-world setting.

Methods: LIBERATE recruited MS patients newly prescribed PR-FAM at 201 sites in 13 countries. Demographic/safety data were collected at enrolment through 12 months. Multiple Sclerosis Impact Scale-29 (MSIS-29) and physician-rated Clinical Global Impression of Improvement (CGI-I) scores for walking ability, were assessed.

Results: The safety analysis included 4646 patients with 3534.8 patient-years of exposure. Median (range) age was 52.6 (21–85) years, 65.7% were female; 24.9% (n=1158) of patients discontinued treatment due to lack of efficacy. Treatment-emergent AEs (TEAEs) were reported in 52.7% of patients, and serious TEAEs in 6.0%. TEAEs of special interest occurred in 38.7%, and serious TEAEs of special interest in 2.8% (Table 1). MSIS-29 physical impact score improved significantly for patients on-treatment for 12 months vs those who discontinued (mean change from baseline to 12 months: 9.99 vs -0.34 points; p<0.001). Results were similar for MSIS-29 psychological impact. At 12 months, a greater proportion of patients on treatment had improvement in CGI-I for walking ability vs those who discontinued (61% vs 11%; p<0.001).

Table 1. Overall Adverse Events and Adverse Events of Special Interest

Preferred Term	European Countries (N = 4439)	Non-European Countries (N = 207)	Total (N = 4646)
Any TEAE, n (%)	2407 (54.2)	41 (19.8)	2448 (52.7)
Serious TEAEs, n (%)	277 (6.2)	2 (1.0)	279 (6.0)
TEAEs of special interest, n (%)	1767 (39.8)	32 (15.5)	1799 (38.7)
Serious TEAEs of special interest, n (%)	127 (2.9)	1 (0.5)	128 (2.8)
Seizure-related TEAEs, n (%)	17 (0.4)	0 (0.0)	17 (0.4)
Incidence rate/ 100 person-years (95% CI)	0.5 (0.3, 0.8)	0 (0.0)	0.5 (0.3, 0.8)
Serious hypersensitivity-related TEAEs, n (%)	1 (<0.1)	0 (0.0)	1 (<0.1)
Incidence rate/ 100 person-years (95% CI)	<0.1 (0, 0.2)	0 (0.0)	<0.1 (0, 0.2)
Urinary tract infection-related TEAEs, n (%)	399 (9.0)	7 (3.4)	406 (8.7)
Incidence rate/ 100 person-years (95% CI)	14.9 (13.6, 16.3)	5.5 (2.4, 10.8)	14.5 (13.3, 15.8)
Severe infections other than UTI-related TEAEs, n (%)	148 (3.3)	0 (0.0)	148 (3.2)
Incidence rate/ 100 person-years (95% CI)	5.1 (4.4, 6.0)	0 (0.0)	4.9 (4.2, 5.7)
Depression and suicide-related TEAEs, n (%)	59 (1.3)	0 (0.0)	59 (1.3)
Incidence rate/ 100 person-years (95% CI)	1.8 (1.4, 2.3)	0 (0.0)	1.7 (1.3, 2.2)
Anxiety-related TEAEs, n (%)	68 (1.5)	1 (0.5)	69 (1.5)
Incidence rate/ 100 person-years (95% CI)	2.1 (1.6, 2.6)	0.7 (0, 3.8)	2.0 (1.6, 2.5)
TEAEs suggestive of central nervous system stimulation related TEAEs, n (%)	1382 (31.1)	26 (12.6)	1408 (30.3)
Incidence rate/ 100 person-years (95% CI)	58.3 (55.7, 60.9)	20.6 (13.9, 29.4)	56.7 (54.3, 59.3)
Cardiovascular-related TEAEs, n (%)	80 (1.8)	1 (0.5)	81 (1.7)
Incidence rate/ 100 person-years (95% CI)	2.5 (2.0, 3.1)	0.7 (0, 3.8)	2.5 (2.0, 3.0)
Clinically significant haematological abnormality-related TEAEs, n (%)	26 (0.6)	0 (0.0)	26 (0.6)
Incidence rate/ 100 person-years (95% CI)	1.1 (0.7, 1.5)	0 (0.0)	1.0 (0.7, 1.4)

AE = adverse event; N = number of patients overall; n = number of patients in a category; TEAE = treatment-emergent adverse event; CI = confidence interval.
 Note: Percentages are calculated using the total number of patients (N) as the denominator.
 All recorded AE verbatim terms were coded using MedDRA version 18.1.
 TEAE is defined as any AE with an onset date that is on or after the first dose of Fampridine and within 28 days after the last dose or any pre-existing condition that has worsened in severity after the first dose of Fampridine. For overall AE in the study, the period is relative from the first dose of treatment and within 28 days after the last dose in the extension study.
 TEAEs of special interest in this study were those related to seizure, hypersensitivity reactions, urinary tract infections (UTI) and urinary symptoms, depression and suicide attempt, cardiovascular disorders, severe infections other than UTI, anxiety, central nervous system stimulation, and clinically significant haematological abnormalities.

Table 1. Overall Adverse Events and Adverse Events of Special Interest

Conclusion: MSIS-29 and CGI-I scores after long-term PR-FAM treatment show clinical benefits consistent with those previously reported. No new safety signals were identified in this real-world study suggesting that routine risk minimization measures are effective.

Support: Biogen

Disclosure: Supported by Biogen

EPR1161

Relationship between retinal layers' thickness and disability worsening in relapsing and progressive multiple sclerosis

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Background and aims: Data regarding the predictive value of macula-derived measures are lacking, especially in progressive-MS (PMS). We aimed at investigating whether a single optical coherence tomography (OCT) assessment including automated intra-retinal layer segmentation can predict risk of disability worsening in both relapsing-remitting-MS (RRMS) and PMS.

Methods: Baseline thickness of macula-derived measures was assessed in 180 patients (101 RRMS and 79 PMS, Table 1) who underwent Spectral-Domain-OCT. All patients had at least 1 Expanded Disability Status Scale (EDSS) measurement during the subsequent follow-up (FU). Differences in terms of OCT metrics and their association with FU-disability were assessed by ANCOVA and linear regression models, respectively.

	RRMS (n=101)	PMS (n=79)	p-values*
Demographics			
PPMS, no (%)	-	61 (77%)	-
Age, mean (SD), y	39 (10.3)	49 (10.7)	<0.0001
Female, no (%)	75 (74%)	37 (47%)	<0.0001
Disease duration, mean (SD), y	8.4 (6.5)	11.8 (8.1)	0.002
EDSS score at baseline, median (range)	2 (0-6)	5 (1.5-7.5)	<0.0001
EDSS score at follow-up, median (range)	2.5 (0-6)	5.5 (1.5-8)	<0.0001
OCT metrics			
pRNFL, mean (SD)	96.2 (13.7)	90.7 (12.1)	0.02
narRNFL, mean (SD)	19.3 (1.9)	19.8 (3.1)	n.s.
GCIPL, mean (SD)	81.1 (10.4)	76.5 (12.1)	0.003
INL, mean (SD)	37.2 (3.4)	37.5 (3.6)	n.s.
OPL, mean (SD)	33.3 (5.3)	34.1 (4.3)	n.s.
ONL, mean (SD)	73.8 (15.2)	72.6 (8.5)	n.s.

Table 1

Results: Mean FU was 2 years (range 1-5.5). Baseline pRNFL and GCIPL were thinner in PMS compared to RRMS (p=0.02 and p=0.003, respectively; Table 1). Multivariable models showed that GCIPL was significantly associated with subsequent disability (0.04 increase in EDSS for each 1-µm decrease in GCIPL, 95% CI: 0.006-0.08; p=0.02; Figure 1) in RRMS. Baseline GCIPL was thinner in patients with FU-EDSS>4 compared to those with FU-EDSS≤4, and individuals in the highest baseline

GCIPL tertile had a significantly lower FU-EDSS score compared to those in the middle and lowest tertile (p=0.01 and p=0.001, respectively). These findings were confirmed in analyses restricted to RRMS but not PMS patients.

Fig. 1: Association between baseline GCIPL thickness and EDSS score at the end of follow-up period in RRMS and PMS patients

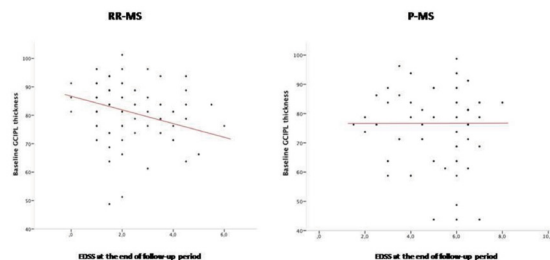


Figure 1

Conclusion: Among OCT-derived metrics, GCIPL thickness had the strongest association with short-medium term disability. However, such association was statistically significant only in RRMS patients. Future studies will have to investigate GCIPL predictive value in the longer term, especially in PMS patients.

Disclosure: Nothing to disclose

EPR1162

Multiple sclerosis fatigue and energy metabolites- Hints from Phosphorus Magnetic Resonance Spectroscopy

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Background and aims: Fatigue related to multiple sclerosis (MS) is usually perceived as 1 of the most annoying complaints. Hints towards its underlying mechanisms could be provided by various magnetic resonance (MRI) modalities including conventional MRI and phosphorous magnetic resonance spectroscopy (31P-MRS). The latter could offer valuable knowledge regarding the energetic status of different brain areas. Thus, the aim of this work was to assess the relationship that would exist between energetic metabolites and fatigue scores.

Methods: 30 patients suffering from progressive MS were recruited. Sociodemographic and clinical data were collected. Fatigue was assessed using Fatigue Severity Scale (FSS). 31P-MRS spectrum was obtained from two regions: (i) bilateral frontoparietal area and (ii) normal appearing white matter (NAWM) of the centrum semiovale. Percentages of PCr and β -ATP (β -ATP%) were calculated.

Results: Direct correlation was found between FSS scores and frontoparietal β -ATP% ($p < 0.05$). No correlation was found between FSS and NAWM energy metabolites, or between FSS and clinical and sociodemographic data.

Conclusion: These data hint towards a link between the accumulation of ATP metabolites and the exacerbation of fatigue. In fact, an energy relationship seems to exist between glial cells and neurons in a way that astrocytes are considered the production cells of ATP that is essential for neuronal depolarization and action potential propagation. In MS, the extent of axonal degeneration would lead to a decrease in ATP utilization and an accumulation of its metabolites (i.e., β -ATP). This may aggravate fatigue perception.

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EPR1163

Multiple sclerosis incidence and prevalence in Ukraine over the last two decades

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Background and aims: Multiple sclerosis (MS) epidemiological trends are a matter of a special attention due to a growing significance of this disease, so the aim was to reveal such trends in Ukraine.

Methods: Data of the official general and public health statistics on regions of Ukraine since 2000 were examined and used for the calculations.

Results: In 2000, the MS prevalence in Ukraine was 35.63 cases per 100,000 (middle-risk area) (Figure 1), but 5 regions were in a MS high-risk area (50-100 cases per 100,000) (Figure 2A). Ten years later, MS prevalence in Ukraine has grown to 42.29 per 100,000 and 19 (70.1%) regions of 27 ones were in the MS high-risk area (Figure 2B). In 2017, overall MS prevalence in Ukraine approached to a high-risk threshold (49.16 per 100,000). During the last two decades in Ukraine, with an average MS incidence of 2.60 ± 0.18 cases per 100,000, there is an upward trend in MS prevalence for Western and Central regions (Figure 2C). Medical check-up had risen from 83.9% to 92.0% in this period.

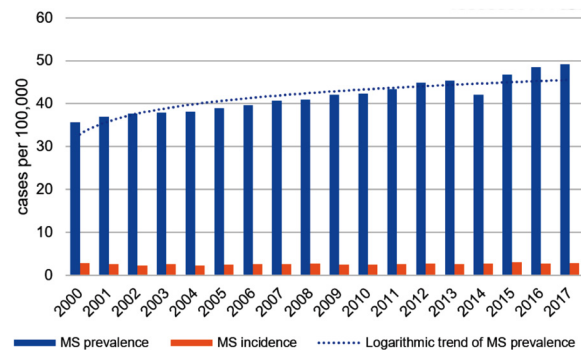


Figure 1. MS prevalence and incidence in Ukraine by year

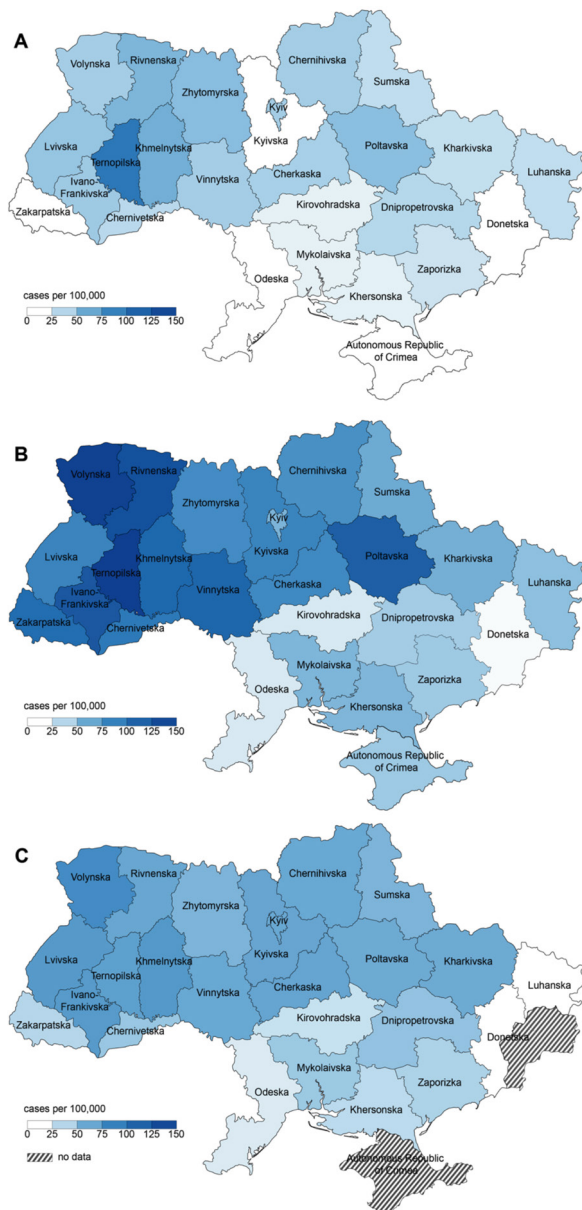


Figure 2. MS prevalence in regions of Ukraine: (A) in 2000; (B) in 2010; (C) in 2017

Conclusion: An increasing of MS prevalence and incidence in 2000-2010 was partly due to improvement of diagnostic tools and physicians' vigilance concerning MS diagnosis. A slower-than-expected according to MS incidence growth of MS prevalence in Ukraine resulted from migration processes first of all. It should be taking into account also that the statistical data since 2014 were under influence of a number of factors not related to MS, particularly sociopolitical ones.

Disclosure: Nothing to disclose

EPR1164

Serum Neurofilaments Light Chains Predict Visual Recovery and Neuroaxonal Degeneration After Acute Optic Neuritis

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Background and aims: Neuroaxonal degeneration after optic neuritis (ON) can be measured with Optical Coherence Tomography (OCT). Although the visual prognosis of typical optic neuritis is generally favourable, the degree of visual recovery and neurodegeneration associated with a single episode varies considerably. Neurofilament light chain (NfL) is part of the axonal cytoskeletal neurofilaments and is released upon immune-mediated axonal damage, such as multiple sclerosis (MS) relapses. We explored the usefulness of NfL levels at ON onset in predicting neuroretinal degeneration and visual outcome.

Methods: 31 patients (mean age 37.3 years, SD 8.7, 71% females) with an acute optic neuritis between October 2014 and August 2017 underwent serum NfL dosing at baseline (Simoa HD-1; Quanterix) and high- and low-contrast visual acuity and OCT at baseline and after a mean follow-up of 27.6 ± 12.3 months. Changes in inter-ocular difference in visual acuity and RNFL peripapillary thickness were measured, and multilevel mixed effect models were used to assess the prognostic factor of baseline NfL levels.

Results: At follow-up, inter-ocular visual acuity difference improved ($2.8/10 \pm 1.2$) with respect to baseline ($2.1/10 \pm 1.5$, $p < 0.05$), while inter-ocular RNFL thickness difference worsened (3.2 ± 10.2 vs 12.7 ± 15.2 microns). Baseline NfL levels above 75 percentile were significantly associated with worse inter-ocular visual acuity (B 0.05 SE 0.02, $p < 0.01$) and inter-ocular RNFL thickness difference at follow-up (B 0.64 SE 0.20, $p < 0.01$).

Conclusion: Serum NfL light chain could be a promising biomarker for prediction of visual outcome after ON and for the implementation of neuroprotective or regenerative strategies.

Disclosure: Part of this study was supported by a Merck research grant to L. Leocani. R.Furlan e L.Leocani: equal contribution

EPR1165

Early clinical and MRI predictors of long-term disability in pediatric onset multiple sclerosis patients: a 10 year longitudinal study

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Background and aims: The main clinical and MRI features driving clinician choices are not as clear for pediatric onset multiple sclerosis patients (POMS) as for adult ones. We aimed at assessing early predictors of long-term clinically-relevant outcomes in a large cohort of POMS.

Methods: A cohort of POMS (n=135) was retrospectively analyzed. Clinical and MRI assessment was obtained at disease onset and after 1, 2 and 3 years. The longest clinical follow-up (mean 9.33±6.45 years) was considered for clinically-relevant outcomes. Cox models were used to assess predictors of time to 1st relapse, while multivariable logistic and linear regression models identified clinical and MRI predictors of long-term outcomes. Disease-modifying treatments were not considered, since the reverse causation involved in selecting patients for treatment.

Results: Across baseline features, optic nerve involvement predicted shorter time to first relapse (HR=2.31, p=0.02). Baseline Expanded Disability Status Scale (EDSS) scores ($\beta=3.42$, p<0.001) and presence of brainstem lesions ($\beta=2.24$, p=0.01) were significantly associated with long-term EDSS. The detection of at least 2 new lesions at year-1 (OR=27.53, p=0.002) or at year-2 (OR=9.70, p=0.04) and EDSS changes (year-1: OR=22.84; year-2: OR=62.31; year-3: OR=2.02; p<0.001) were associated with long-term EDSS worsening. EDSS changes (year-1: $\beta=2.88$; year-2: $\beta=5.30$; year-3: $\beta=3.62$; p<0.001) were also associated with long-term EDSS score.

Conclusion: In POMS, baseline optic nerve involvement suggested a more active disease, while baseline brainstem involvement predicted worse prognosis. Accurate clinical and MRI monitoring during the 1st 2 years of disease might be a powerful tool for counselling patients about long-term prognosis, and personalizing treatment plans.

Disclosure: Nothing to disclose

EPR1166

Towards personalized medicine: assessing early predictors of treatment response in pediatric MS patients.

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Background and aims: No evidence of disease activity (NEDA) is increasingly considered an important treatment goal, but it has never been tested for pediatric multiple sclerosis patients (ped-MS). We assessed 1-year NEDA and its subcomponents as well as MRI activity as early predictors of response to interferon- β therapy.

Methods: 72 ped-MS on interferon- β treatment were included. 1 year after treatment start, clinical and MRI assessments were performed. The longest clinical follow-up (11.33±6.29 years) was included for outcome variables. Multivariate regression models were used to identify predictors of treatment failure (defined as treatment switch for inefficacy) and EDSS worsening.

Results: No significant association was found between 1-year NEDA status or traditionally-defined MRI activity [new T2-hyperintense lesions or at least 1 gadolinium-enhancing (Gd)-lesion] and clinical outcomes. However, significant increase of treatment failure was associated with 2 or more relapses [hazard ratio (HR)=7.14, p=0.03] and more than 1 Gd-lesions (HR=3.18, p=0.05). According to these results, risk levels were grouped into 3 classes: group-1 (<2 relapses, no Gd-lesions), group-2 (either 2 or more relapses or 1 or more Gd-lesions), group-3 (2 or more relapses and 1 or more Gd-lesions). Group-2 patients had an intermediate risk of treatment failure (HR=2.93, p=0.002) and EDSS worsening (HR=2.85, p=0.002). Group-3 patients had highest risk of treatment failure (HR=7.89, p=0.002) and EDSS worsening (HR=8.26, p=0.001).

Conclusion: One-year NEDA and traditionally-defined MRI activity were not predictors of treatment failure in ped-MS. Clinical activity and ongoing MRI activity during the first year of interferon- β treatment indicated significant long-term risk of treatment failure and EDSS worsening.

Disclosure: Nothing to disclose

MS and related disorders 3

EPR1167

Body mass Index influence CD20 dynamics in MS patients treated with Ocrelizumab

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Background and aims: Kinetic of B-cells repopulation after depletion therapy with Ocrelizumab (OCR) shows great intra and inter-individual variance. Several evidence revealed a link between B-cell activity and adipose tissue. The aim of this study was to explore the influence of Body Mass Index (BMI) on kinetic of B-cell repopulation after treatment with OCR and on the treatment efficacy.

Methods: 108 MS patients were enrolled at the time of the 1st administration of OCR and followed-up prospectively. Clinical and instrumental activity and disability progression were analyzed to determine the treatment effectiveness. B-cell count was collected before the 1st dose administration and every 6 months. Based on B-cells count, patients were divided into 2 groups: with faster (FR) and e with slower repopulation rate (SR). The correlation between BMI, repopulation rate and treatment effectiveness was evaluated.

Results: After 1 year, reduction of annualized relapse rate and T1 gd-enhancing lesions were observed ($p < 0.001$) with higher percentage of NEDA (72%) and NEPAD (45.45%). Results disclosed that FR patients had higher BMI compared to patients with a lower BMI ($p < 0.001$). Contrariwise no correlation was disclosed between repopulation rate and treatment effectiveness.

Conclusion: Patients with higher BMI had faster repopulation rate; therefore further studies to verify the long-term efficacy of OCR in FR and SR in correlation to BMI and to evaluate the best administration schedule are sought after.

Disclosure: Nothing to disclose

EPR1168

Longitudinal study with optical coherence tomography (OCT) in treated patients with relapsing-remitting Multiple Sclerosis.

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Background and aims: Loss of retinal nerve fiber layer (RNFL) thickness in patients with Relapsing-remitting Multiple Sclerosis (RRMS) correlates with clinical and paraclinical parameters due to axonal and neuronal degeneration. We studied the treatment response in RRMS patients using OCT.

Methods: We retrospectively analyzed RNFL thickness by OCT at year 1 and 5 in patients treated or with fingolimod or dimethylfumarate (DMF). Demographic features, optic neuritis (ON) and annualize relapse rate (ARR) during treatment were also analyzed.

Results: We analyzed 24 patients with a mean age of onset of 31y (15-48y), 75% women and a medium follow-up of 10y from diagnosis. After 5 years, RNFL thickness was increased in 7 patients, 6 treated with Fingolimod with an increase of 5.4 μm and 1 patient with DMF with an increase of 0.5 μm . Also, 14 eyes improved in patients treated with Fingolimod vs 2 with DMF (table 1).

There were 19 patients without relapses during the 1st year, in these patients: RNFL increased in 5/9 Fingolimod vs 1/10 BG12. (table 2).

After 5 years of follow-up, 13 patients presented no relapses, in this group: RNFL increased in 4/7 patients treated with Fingolimod and 1/6 with DMF.

On other hand 75% of the patients with ≥ 1 relapse during the 5 years follow-up showed a RNFL decrease (table 3).

Table 1. RNFL results at year 0 and 5 of follow-up.

Thickness	Fingolimod	BG12	Total
	n ^o (median μm)	n ^o (median μm)	
Increase	14 (X: 5,0 \pm 3,7)	2 (1)	16
Decrease	7 (X: 5,5 \pm 4,7)	18 (X: 4,2 \pm 2,4)	25
Estable	3	4	7

Table 2. Fingolimod and BG12 RNFL in patients with ARR of 0 at year 1 and 5.

RNFL thickness	ARR 0 at year 1		ARR 0 at year 5	
	Fingolimod n=9 (median μm)	BG12 n=10 (median μm)	Fingolimod n=7 (median μm)	BG12 n=6 (median μm)
Increase	5 (X: 4,8 \pm 3,1)	1 (X: 0,5)	4 (X: 5,8 \pm 2,6)	1 (X: 0,5)
Decrease	4 (X: 2,6 \pm 1,9)	9 (X: 3,3 \pm 1,5)	3 (X: 2,0 \pm 1,8)	5 (X: 3,2 \pm 1,7)

Table 3. RNFL in patient with relapse at first years and during 5 years of follow-up

RNFL thickness	ARR ≥ 1 at year 1		ARR ≥ 1 over 5 years	
	Fingolimod n=3 (median μm)	BG12 n=1 (median μm)	Fingolimod n=5 (median μm)	BG12 n=6 (median μm)
Increase	1 (X: 8,5)	0	2 (X: 4,8)	0
Decrease	2 (X: 3)	1 (X: 7,0)	3 (X: 3,5)	5 (X: 4,2)
Estable	0	0	0	1

Conclusion: After 5 years of follow-up 50% of patients treated with fingolimod increase RNFL vs 10% of BG12. Most of patients with relapses over 5 years have a decrease of RNFL. OCT could be used as a response biomarker.

Disclosure: Nothing to disclose

EPR1169

Neuromyelitis optica spectrum disorders associated with aquaporin-4 antibodies and MOG antibodies: a nationwide Portuguese registry

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Introduction: Neuromyelitis optica spectrum disorders (NMOSD) are rare and heterogeneous immune-mediated CNS conditions. Accurate diagnosis is fundamental once early treatment has impact on prognosis and quality of life. Their epidemiological, clinical and laboratory characteristics in the Portuguese population were unknown.

Objective: To identify the Portuguese patients with seropositive NMOSD and study their epidemiological-

demographic and clinical-serological characteristics.

Methods: National study. 24 adult centres and 3 neuropediatric units included all NMOSD patients that met the Wingerchuk 2015 criteria.

Results: We identified 145 seropositive NMOSD. 77 AQP4-Ab and 68 MOG-Ab positive. Portuguese population in 2018 was 10.276.617. We established prevalence for seropositive NMOSD of 1.41/100.000 (0.75/100.000 for AQP4-Ab; 0.66/100.000 for MOG-Ab). In 2018 there were 24 new seropositive NMOSD cases (9AQP4-Ab and 15MOG-Ab). Estimated incidence was 0.23/100.000 (0.09/100.000 for AQP4-Ab and 0.15/100.000 for MOG-Ab). Females predominated in AQP4-Ab compared to MOG-Ab subgroups (F:M ratio of 8.6:1 vs 1.6:1). Onset-age was higher in AQP4-Ab than MOG-Ab patients (40.7yo vs 34.8yo). Non-Caucasians predominated in the AQP4-Ab subgroup (10.4% vs 2.9%). Other autoimmune diseases were more frequent in AQP4-Ab than in MOG-Ab disease (23.4% vs 4.4%). Myelitis was the most frequently reported presenting syndrome (42.9%) in AQP4-Ab and optic neuritis in MOG-Ab (42.6%).

Conclusion: Discussion: Epidemiological, demographic and clinical characteristics of NMOSD in Portugal are similar to other published series, including European, which confirms the quality of the clinical and laboratory diagnosis of NMOSD throughout the country.

Disclosure: This project received a grant from Roche.

EPR1170

Assessing the contribution of genetic factors on brain MRI lesion load and volumetric measures in multiple sclerosis patients.

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Background and aims: Genetic determinants of heterogeneous disease expression are partially investigated in multiple sclerosis (MS). We aimed at identifying genetic factors influencing quantitative neuroimaging outcomes in two cohorts of Relapsing Remitting (RRMS) and Progressive (PMS) subjects.

Methods: 214 RRMS and 99 PMS patients underwent a brain MRI using a 3T scanner. 9 MRI metrics were obtained, spanning from conventional T1/T2 lesion to cortical lesion load and deep grey-matter volume measurements. A knowledge-driven candidate pathway strategy was adopted; brain cell-specific sets of enriched expressed genes were also tested. A self-contained gene set analysis was carried out, using Adaptive Rank Truncated Product method and adjusting for relevant confounders, followed by single SNP regression analysis.

Results: We tested seventeen KEGG pathways, 42 GO terms and 5 cell-specific enriched gene sets, encompassing ~189k SNPs. Gene set analysis revealed a differential pattern of association between the 2 disease subtypes, with processes related to Iron and Leukocyte Migration associated in PMS ($p < 0.01$), whereas inflammatory-related themes like Adaptive Immune Response and T-cell Differentiation appeared to be implicated in RRMS ($p < 0.01$). As of SNPs, we found evidence of association between white matter volume and rs740948 mapping to SEMA3A gene ($\beta = 2.2 \times 10^4$, $p = 5.5 \times 10^{-6}$) in RRMS, while rs7104613 mapping to SPON1 gene revealed to be significantly associated to reduced deep grey matter and thalamus volumes ($\beta = -731.9$, $p = 3.2 \times 10^{-7}$) in the PMS.

Conclusion: These data suggest a different pattern of association between neuroimaging metrics and functional processes across the two disease courses. A replication step in larger cohorts is warranted to validate these preliminary findings.

Disclosure: Nothing to disclose

EPR1171

Clinical outcomes of lymphoablative autologous hematopoietic stem cell transplantation (AHSCT) in multiple sclerosis (MS) patients

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Background and aims: We aimed to study if the reduced intensity regimen based on BEAM is safe and effective in MS patients.

Methods: A total of 135 patients were enrolled in the study: mean age – 34 (range-17-54) y.o; male/female – 53/82; mean EDSS-3.5 (range-1,5-8,5). Relapsing-remitting MS (RRMS) – 60 patients, 75 patients – progressive MS. Reduced-intensity BEAM-like conditioning was used (BCNU 300mg/m², etoposide 100mg/m², Ara-C 100mg/m² and melphalan 100mg/m²). Median follow-up was 24 months. Efficacy was evaluated based on EDSS and MRI changes.

Results: No transplant related deaths were observed. The mobilization and transplantation procedures were well tolerated. Estimated event-free survival at median follow-up of 48.9 months was 80%: 83.3% for relapsing-remitting MS versus 75.5% for progressive MS. EDSS scores improved significantly from a pretransplant median of 3.5 to 2.0 at 18 months after AHSCT; positive EDSS changes preserved at 36 months follow-up. Results of MRI scans at long-term follow-up were available in 55 patients. 15 patients (27%) had active lesions at baseline and all turned to inactive status except one case. Of the 40 patients without active lesions pre-transplant 39 remained inactive, whereas 1 patient showed disease activity at 6 months posttransplant. At long-term follow-up no active, new or enlarging lesions were registered in patients without disease progression/relapse. In total, no negative changes on MRI scans were registered in 93% patients.

Conclusion: The results of study support the feasibility of reduced-intensity condition regimen based on BEAM. AHSCT with reduced-intensity condition regimen may be beneficial for patients with various types of MS.

Disclosure: Nothing to disclose

EPR1172

Assessment of clinical, genetic and immune repertoire data to predict disease activity and progression in relapsing-remitting Multiple Sclerosis patients

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Background and aims: Multiple Sclerosis (MS) has a highly heterogeneous clinical course and, given the broad spectrum of approved therapies, there is a strong need to identify parameters that can guide treatment choice. The present study investigates clinical, genetic and immunological parameters associated with MS severity.

Methods: An “Extended” cohort of ~1,000 patients that started a 1st-line drug, with available clinical and genetic data, and a “Core” dataset of ~200 patients with genetic and immune repertoire information obtained before 1st-line treatment were enrolled. The following outcomes were considered at the 4-year follow-up: NEDA-3 criterion, time to first relapse (TFR), EDSS and MS Severity Score (MSSS). A regression analysis was performed on both cohorts and results were meta-analyzed.

Results: A younger age at onset (AAO) and a shorter disease duration strongly correlate with higher inflammatory activity; a higher baseline EDSS and AAO are the best prognostic markers of disability increase. The genetic study identified some interesting signals with suggestive association: rs6925307 was associated with NEDA (OR 0.55, p:1.53e-06) and has an eQTL effect on CLVS2 gene, required for normal morphology of endosomes and lysosomes in neurons. Rs9264731, an intronic variant in the HLA-C gene, was associated with TFR (HR 1.49, p:4.11e-06). T-cell receptor (TCR) sequencing is ongoing and immune repertoire data are already available for 61 patients with >4.000.000 clonotypes identified.

Conclusion: We confirmed the association of clinical parameters with disease severity and we identified some interesting genetic markers whose association need to be replicated. TCR data are being generated and will be integrated in a predictive model of disease activity.

Disclosure: This study was funded by the Italian Ministry of Health, project code: GR-2016-02363997

EPR1173

Depression and Anxiety in Multiple Sclerosis Patients: the role of genetic variability of Interleukin 1-beta

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Background and aims: Mood disorders, as depression and anxiety, are frequent in Multiple Sclerosis (MS) patients. High pro-inflammatory cytokine levels (e.g. IL-1beta) have been reported in depressed individuals. The aim of this study was to investigate whether rs16944 (-511C>T) polymorphism, a modulator of IL-1beta expression, contributes to depression and anxiety susceptibility in MS patients.

Methods: Hospital Anxiety and Depression Scale (HADS) was initially (T1) applied to 393 MS patients (63.6% female, 39±11 years of age, 10±8 disease duration, EDSS 2.9±2.2; 318 relapsing-remitting, 38 2ndary progressive, and 37 primary progressive). HADS cut-off scores for depression and anxiety were respectively ≥8 and ≥11. The HADS was applied four years later (T2) to 176 MS patients. The rs16944 polymorphism was genotyped by allelic-specific Taqman probes.

Results: Depression was identified in 29.5% of patients at T1 and 34.7% at T2, whereas anxiety was found in 27% at T1 and 16.5% at T2. Persistent depression and anxiety (T1 and T2) were observed in 19.9% and 11.9% of MS patients, respectively. MS patients who were carriers of rs16944C allele exhibited lower predisposition to depression and anxiety at T1 and at T2 (pD1=0.001 and pA1=0.005; pD2<0.001 and pA2=0.027). This association was also observed with persistent psychopathological indices, even when taking into account clinical and demographical characteristics (pD=0.001 and pA=0.019).

Conclusion: The study results support the protective role of rs16944C allele in depression and anxiety in MS patients and reinforce the role of inflammation in the development of psychopathology.

Disclosure: Nothing to disclose

EPR1174

Baseline characteristics of multiple sclerosis patients enrolled in NOVA, a multicentre, randomised trial to assess the efficacy of natalizumab every-6-weeks dosing

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Background and aims: Natalizumab is associated with increased progressive multifocal leukoencephalopathy (PML) risk. Extended interval dosing (EID) is associated with significantly lower PML risk in anti-JC virus (JCV) antibody-positive patients, but the efficacy of EID has not been established in a randomised, controlled trial. NOVA is the 1st prospective, interventional, controlled, randomised study to assess efficacy of natalizumab every-6-weeks (Q6W) dosing compared with every-4-weeks (Q4W) dosing (ClinicalTrials.gov NCT03689972). The primary study endpoint is the number of new/newly enlarging T2 lesions at 72 weeks. Key 2ndary endpoints include number of new gadolinium-enhancing lesions, time to 1st relapse, annualized relapse rate, and adverse events.

Methods: Relapsing-remitting MS patients stable on natalizumab 300mg Q4W dosing for ≥ 1 year were randomised 1:1 to remain on Q4W or switch to Q6W dosing. Baseline characteristics were assessed using summary statistics.

Results: As of November 2019, NOVA was fully enrolled; 487 patients were randomised (244 Q6W, 243 Q4W). Treatment groups were well-balanced with respect to key demographic and disease characteristics, including age, weight, time since MS diagnosis, number of relapses in the year before natalizumab initiation, and duration of natalizumab exposure (Table). The majority of patients were anti-JCV antibody-negative at the start of the study (Q6W=78.3%; Q4W=80.7%); median anti-JCV antibody index values were identical for the 2 treatment groups (Table).

Category	Q6W (n=244)	Q4W (n=243)	Overall (N=487)
Age, years			
n	244	242	486
Mean (SD)	41.1 (9.7)	40.3 (10.0)	40.7 (9.8)
Female, n (%)	172 (70.5)	176 (72.4)	348 (71.5)
Weight, kg			
n	243	242	485
Mean (SD)	79.8 (19.6)	78.4 (20.2)	79.1 (19.9)
Natalizumab exposure, years			
n	239	236	475
Mean (SD)	4.7 (3.0)	4.7 (2.8)	4.7 (2.9)
EDSS score			
n	239	240	479
Mean (SD)	2.35 (1.30)	2.31 (1.31)	2.33 (1.30)
Time since MS diagnosis, years			
n	237	231	468
Mean (SD)	9.5 (6.2)	9.2 (6.1)	9.3 (6.1)
Relapses in year prior to natalizumab initiation			
n	233	227	460
Mean (SD)	1.1 (1.1)	1.0 (0.9)	1.0 (1.0)
Anti-JCV serostatus			
Anti-JCV antibody-negative, n/N (%)	191/242 (78.9)	196/242 (81.0)	387/484 (80.0)
Anti-JCV antibody-positive, n/N (%)	51/242 (21.1)	46/242 (19.0)	97/484 (20.0)
JCV index			
n	239	237	476
Median (Q1, Q3)	0.15 (0.11, 0.27)	0.15 (0.11, 0.22)	0.15 (0.11, 0.25)

Table. Baseline characteristics of RRMS patients enrolled in NOVA. EDSS=Expanded Disability Status Scale; Q1, Q3=quartile 1, quartile 3; RRMS=relapsing-remitting MS; SD=standard deviation.

Conclusion: Baseline characteristics of Q6W and Q4W NOVA patients were well-matched. Efficacy results from NOVA (expected June 2021), combined with the prior TOUCH database PML risk assessment, will help define the benefit/risk profile of natalizumab Q6W.

Disclosure: This study is supported by Biogen. Detailed disclosures of each author will be included in the e-poster/oral presentation.

EPR1175

Reversibility of Clinical Abnormalities Associated with Ponesimod: Results from Randomised Phase II Core and Extension Studies in Relapsing Remitting Multiple Sclerosis

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Background and aims: Ponesimod, an orally active, selective sphingosine 1-phosphate receptor-1 (S1P1) modulator, showed benefits in clinical and MRI outcomes in patients with relapsing-remitting multiple sclerosis (RRMS) in a double-blind, placebo-controlled, phase-2b Study. Patients could then roll-over into an ongoing Extension Study.

Objective: Characterise reversibility of ponesimod-mediated changes in lymphocyte count, pulmonary function, and blood pressure (BP).

Methods: 435 patients with RRMS received ≥ 1 dose of ponesimod (10/20/40mg/day) during Core and/or the Extension Study. The 40mg and 10mg doses were subsequently discontinued during Treatment Period-1 (TP1) and TP2 of Extension Study. All patients received 10mg or 20mg during TP2, followed by open-label 20mg in TP3. Changes from baseline in lymphocyte count, pulmonary function tests (PFT; FEV1 and FVC), systolic and diastolic BP (SBP and DBP) were assessed 7-, 30- and 90-days after discontinuation of ponesimod.

Results: Treatment was ongoing in 214 patients as of 31-March-2019; results cover patients who prematurely discontinued from ponesimod at any time during the studies. With 20mg treatment at last-on-treatment visit, mean baseline lymphocyte count was reduced by 61.7% and returned to near-baseline at follow-up Days 7 (-17%) and 30 (-7.9%); with no evidence of rebound (Table_1). For all groups, mean changes from baseline in SBP/DBP observed after stopping ponesimod treatment returned to near-baseline values by follow-up Days 7 and 30. Similarly, mean FVC/FEV1 declined on treatment, partially recovered at follow-up Day-7 and remained stable at Day-30 (Table_2).

Table 1: Change from baseline in lymphocyte count, systolic and diastolic blood pressure over time

Mean (SD) change from baseline	Ponesimod		
	10 mg (n=42)	20 mg (n=54)	40 mg (n=66)
Lymphocyte count, % change			
Last on-treatment Visit	-51.3 (16.50)	-61.7 (19.20)	-65.6 (16.70)
Follow-up Day 7	-6.5 (35.71)	-17.7 (29.01)	-19.0 (30.24)
Follow-up Day 30	0.7 (31.05)	-7.9 (27.66)	-8.9 (32.60)
Follow-up Day 90	20.2 (67.34)	-12.1 (21.79)	-14.7 (23.97)
Last follow-up	5.4 (44.89)	-5.6 (27.14)	-6.1 (30.34)
	n=44	n=53	n=65
Systolic Blood Pressure (absolute change, mmHg)			
Last on-treatment Visit	2.5 (15.9)	4.1 (13.9)	5.3 (13.0)
Follow-up Day 7	2.3 (12.4)	3.7 (15.4)	5.6 (11.8)
Follow-up Day 30	-0.4 (10.5)	0.4 (13.1)	3.2 (11.5)
Follow-up Day 90	3.1 (11.3)	-2.4 (17.2)	2.1 (12.5)
Last follow-up	0.8 (10.5)	0.1 (14.6)	3.5 (11.6)
Diastolic Blood Pressure (absolute change, mmHg)			
Last on-treatment Visit	-0.5 (12.9)	1.7 (8.8)	1.7 (11.8)
Follow-up Day 7	2.4 (11.7)	1.5 (10.2)	0.5 (8.5)
Follow-up Day 30	0.1 (10.1)	0.8 (11.1)	0.0 (9.7)
Follow-up Day 90	1.7 (11.4)	-0.0 (8.8)	-1.6 (9.9)
Last follow-up	-0.1 (10.2)	0.5 (10.2)	-1.1 (10.3)

Data presented here are from subset of patients who prematurely discontinued from ponesimod treatment at any time during the Core or Extension study

Table 2. Change from baseline in pulmonary function test parameters over time

Mean (SD) change from baseline	Ponesimod		
	10 mg (n=43)	20 mg (n=52)	40 mg (n=65)
Forced Expiratory Volume in 1 Second (FEV₁) (% change)			
Last on-treatment Visit	-8.1 (8.77)	-8.8 (12.94)	-13.7 (11.03)
Follow-up Day 7	-4.7 (11.25)	-6.0 (13.63)	-6.7 (8.61)
Follow-up Day 30	-4.3 (8.95)	-5.5 (10.84)	-4.5 (8.66)
Follow-up Day 90	-6.8 (11.33)	-6.0 (10.65)	-7.5 (7.35)
Last follow-up	-3.8 (9.81)	-5.6 (10.56)	-4.9 (8.95)
Forced Vital Capacity (FVC) (% change)			
Last on-treatment Visit	-1.7 (12.33)	-2.3 (11.99)	-6.9 (8.63)
Follow-up Day 7	0.4 (12.82)	-1.1 (11.49)	-4.5 (10.28)
Follow-up Day 30	0.4 (12.57)	-1.3 (12.13)	-1.1 (14.68)
Follow-up Day 90	0.9 (17.52)	-1.4 (13.01)	-4.5 (9.88)
Last follow-up	0.8 (11.62)	-1.1 (11.16)	-1.8 (14.24)

Data presented here are from subset of patients who prematurely discontinued from ponesimod treatment at any time during the Core or Extension study

Conclusion: Changes observed in lymphocytes and BP during ponesimod treatment were rapidly reversible following treatment discontinuation, with partial recovery in PFT.

Disclosure: Funding was provided by Janssen Research & Development, LLC, and the study was supported by Actelion Pharmaceuticals, Part of Janssen Pharmaceutical Companies, Allschwil, Switzerland.

EPR1176

Neurofilament light chain level in paired CSF and serum samples of patients with multiple sclerosis: a prospective study

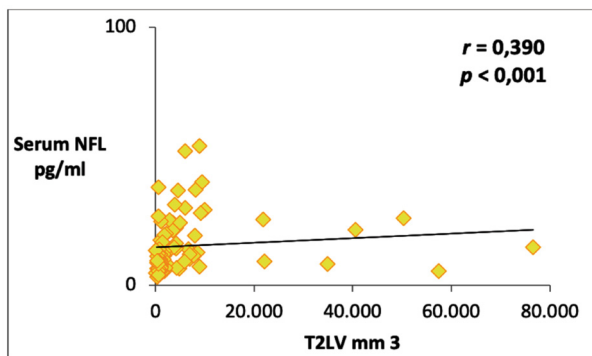
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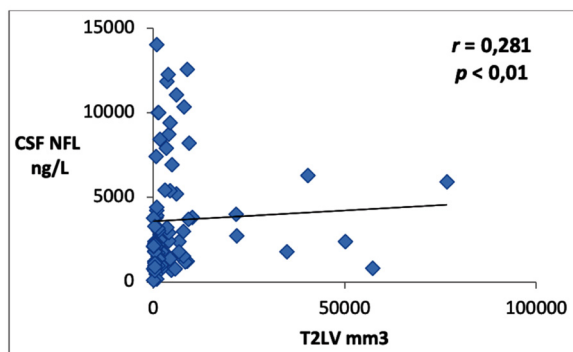
Background and aims: To assess whether neurofilament light chain (NFL) level in CSF and serum of multiple sclerosis (MS) patients could represent a clinically feasible biomarker of disease activity and progression.

Methods: Between 2014 and 2017, we consecutively recruited patients with clinically/radiologically isolated syndromes (CIS/RIS) or MS according to 2010 McDonald criteria, and availability of paired CSF/serum samples stored at -80°C at Verona University Hospital. NFL concentration was assessed in CSF by ELISA (UmanDiagnostics) and in serum by Single Molecular Array (Simoa[®], Quanterix). Possible associations of NFL levels with clinical and MRI measures of interest were analyzed, including relapses, disability worsening, and MRI measures (i.e. enhancing lesions, T2-lesion volume, cortical lesions, and brain volume).

Results: We enrolled 90 patients (55 females) with mean age at sampling 37±12 years. 75 patients had a relapsing form of disease, 14 progressive, and 1 RIS. Median follow-up duration was 32 months (0-133). CSF and serum NFL were correlated ($r=0.752$, $p<0.001$). We observed a correlation between serum NFL and EDSS score at sample collection ($r=0.22$, $p=0.045$). In addition, both CSF and serum NFL were higher in patients with enhancing lesions on brain MRI. There was a modest albeit highly significant correlation of both CSF and serum NFL with T2-lesion volume on brain MRI. We did not observe a fully significant association of NFL with both relapse occurrence and disability progression after sampling.



correlation between serum NFL and T2 lesion volume on brain MRI



correlation between CSF NFL and T2 lesion volume on brain MRI

Conclusion: NFL concentration mainly reflect acute disease activity in MS. Clinical implementation as predictive biomarker at the individual patient level requires additional evidence.

Disclosure: This work was supported by research grants of Merck and Cariverona Foundation

EPR1177

Cognitive change in people with multiple sclerosis – 5 year follow-up of the original Irish BICAMS validation cohort.

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Background and aims: Cognitive impairment affects 20-40% of people with recently diagnosed multiple sclerosis and greater than 50% of people with progressive MS. Cognitive impairment predicts future vocational status, income, adherence to treatment and behaviour. Limited data exists on evolution of cognition over time.

Methods: 67 pwMS who were part of the original BICAMS validation cohort in 2014 were invited for 5-year follow up assessment. Single Digit Modality Test (SDMT), California Verbal Learning Test (CVLT-2) and Brief Visual MTR (BVMTR) as well as comprehensive assessments of mood, fatigue and quality of life were performed. BVMTR (2014) was re-scored to ensure inter-rater reliability.

Results: 50 pwMS returned for follow up assessment. 33% of this cohort had cognitive impairment on at least one domain of BICAMS at baseline. The mean age at follow up was 49 years (SD12). There was no difference in SDMT at five years ($p=0.95$). There was a significant improvement in BVMTR ($p=0.002$) and CVLT ($p=0.002$) over 5 years. Anxiety scores were stable over time, but there was a significant improvement in depression scores ($p=0.0001$). There was no correlation between anxiety, depression or fatigue and cognitive measures. There was however a strong correlation between depression and fatigue scores ($r=.71$, $p<0.001$).

Conclusion: There is a trend towards cognitive stability over 5 years in a cohort of pwMS. Practice effects are unlikely to impact the results given the long interval between testing. Treatment with DMTs may have had an impact on preservation of cognition. Predictors of cognitive stability remain elusive.

Disclosure: This research is supported by Newman fellowship, University College Dublin.

Muscle and neuromuscular junction disease 1

EPR1178

The neglected IgG1-3 antibodies in MuSK myasthenia gravis: novel evidence for their pathogenicity

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Background and aims: Muscle Specific Kinase (MuSK)-myasthenia gravis (MG) is an autoimmune disease that impairs neuromuscular transmission leading to generalised muscle weakness. Under physiological conditions, MuSK is activated by agrin and initiates a phosphorylation cascade leading to the clustering of acetylcholine receptors (AChRs) at the neuromuscular junction. In MuSK-MG, MuSK autoantibodies - mainly monovalent IgG4 - inhibit MuSK phosphorylation and disperse AChR clusters. Divalent MuSK-IgG1-3s co-exist at lower levels and also inhibit agrin-induced AChR clustering in vitro. However, the mechanism of action of divalent IgG1-3 MuSK antibodies are unknown.

Methods: C2C12 myotubes were incubated with IgG1-3 or IgG4 antibodies purified from MuSK-MG patients. Phosphorylation and expression of MuSK, DOK7, and the β subunit of AChR were measured by western blotting. AChR clusters were labelled with α -bungatotoxin-594 and counted.

Results: After 45 min incubation, IgG1-3 increased MuSK and DOK7 phosphorylation compared with inhibition of phosphorylation by IgG4. After overnight exposure, IgG1-3 increased AChR microclusters (<3 μ m) but failed to induce fully-mature clusters (>3 μ m). Incubations for 1, 2, 4 and 8 hours showed that IgG1-3 and agrin increased MuSK, DOK7 and β AChR phosphorylation with a similar time-course but, whereas agrin progressively increased AChR cluster numbers, IgG1-3 did not.

Conclusion: MuSK-IgG1-3 antibodies are pathogenic but act through different mechanisms to MuSK-IgG4 antibodies. They stimulate MuSK-DOK7 phosphorylation cascade but fail to induce fully-formed AChR clusters. These effects are likely due the result of divalent binding to MuSK compared with binding of monovalent IgG4. The possible down-stream mechanisms are being explored further and will be discussed.

Disclosure: Nothing to disclose

EPR1179

Efficacy and safety of Rituximab in myasthenia gravis: a multicentric real life study

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Background and aims: 15% of patients suffering of myasthenia gravis (MG) are refractory and needed a 2nd line immunosuppressive treatment; some case reports and studies show the probable benefit of Rituximab in these cases. Our objective was to demonstrate the efficacy and safety of Rituximab in refractory and steroid-dependent MG.

Methods: In this French retrospective and multicentric study, inclusions criteria were age >18 years old, MG with Acetylcholine receptor (AChR) antibodies, Musk antibodies positive or significative decrement on electromyogram), MG Foundation America (MGFA) score >II, refractory or steroid-dependent MG, treatment by Rituximab.

The protocol of infusion was determined by the neurologist. Efficacy was evaluated by MGFA Post interventional (PIS) score at 6 months, the Garches' score and decrease of steroids under 10mg at 6 months. Adverse events were collected.

Results: 27 patients are included in 6 French departments of Neurology: 19 AChR MG, 4 Musk MG and 2 seronegative MG. 81.4% of patients had a MGFA PIS improved or better after 6 months of treatment (p<0.0001). The mean Garches' score increased from 65.29 to 84.23 at 6 months (p<0.0001). The decrease of steroids (<10mg), was effective in 66.6% of treated patients at 6 months. 40% of patients presented adverse events: 18% infections, 7% infusion reaction, 3.7% bradycardia, 7% cytopenia.

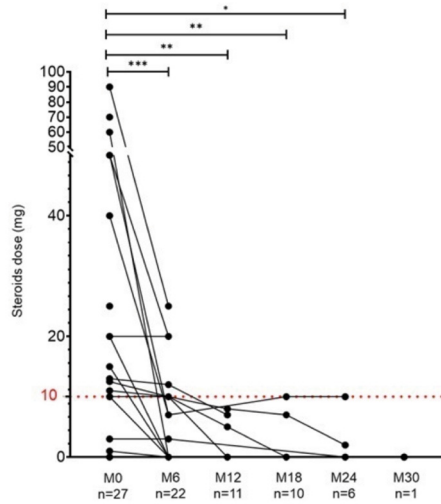


Figure 2: Dose of steroids at each cure of Rituximab. Dose of steroid by patients at cure of RITUXIMAB, M: Month, mg: milligrams Test de Wilcoxon; ***:p<0,001 **:p<0,01, *:p<0,05

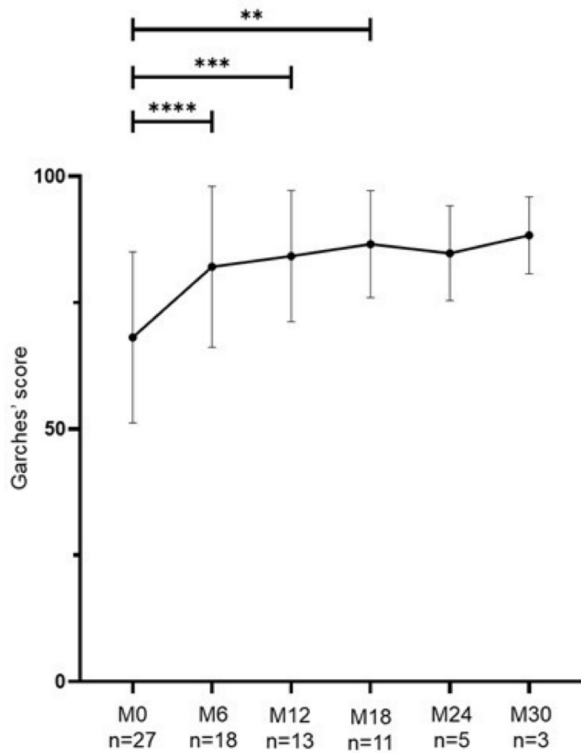


Figure 1: Garches' Score at each infusion of Rituximab. Mean± Standard deviation, M: months, n: number of patients at each infusion of Rituximab, mg: milligrams Wilcoxon test; ****: p<0.0001 ***: p<0.001, **: p< 0.01

	All MG n=27	AchR n=19	Musk n=4	SN n=2
MGFA PIS at six months				
MGFA PIS I or better (n, %)	22/27 (81,4%)	17/19 (89,4%)	2/4 (50%)	0/2 (0%)
MGFA PIS PR (n, %)	5/27 (18,5%)	3/19 (15,7%)	2/4 (50%)	0/2 (0%)
MGFA PIS at twelve months				
MGFA PIS I or better (n, %)	18/20 (90%)	14/15 (93%)	2/3 (66,6%)	NR
MGFA PIS CSR or PR (n, %)	7/20 (35%)	5/15 (33,3%)	2/3 (66,6%)	NR

Table 1: MGFA PIS score at sixth and twelve months after Rituximab introduction. AchR: Acetylcholine receptor, SN: Seronegative; CSR: Complete stable remission, PR: pharmacologic remission, I: Improved

Conclusion: Our study corroborated the efficacy and safety of Rituximab. Some complementary studies are necessary to confirm the place of Rituximab in pharmacopeia of MG treatment and to establish the recommendations of infusion protocol.

Disclosure: Nothing to disclose

EPR1180

Botulism: description of a potential life-threatening micro epidemic in 5 families

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Background and aims: Botulism is a presynaptic disorder of the neuromuscular transmission produced by the neurotoxin elaborated by the bacterium *Clostridium botulinum*, which can be acquired by contaminated food, infected wounds or iatrogenic. Despite being a potentially life-threatening disease, its presentation can consist on mild complaints.

Methods: Description of a case series.

Results: We describe the clinical course of 14 persons, members of 5 different families, that were exposed to home-canned tuna. 9 of these persons suffered from dry mouth during the next days. Patient ages ranged from 16 to 87 years. Onset of symptoms ranged from 1 to 4 days after the exposure. 7 patients also referred other symptoms such as blurred vision, diplopia, ptosis, dysphagia, facial weakness and/or gastrointestinal symptoms and were admitted to the Neurology department.

The 3 more symptomatic patients were transferred to the Intensive Care Unit in order to administrate heptavalent botulinum antitoxin. Electromyogram was performed to one patient showing a slight presynaptic dysfunction of the neuromuscular junction. Serum and/or stool samples were sent to the National Centre of Microbiology, without detection of neurotoxin. 2 samples of the suspected food source were also analysed, and neurotoxin was detected by mouse bioassay. All the patients remained stable and are completely recovered.

Conclusion: Botulism is a rare but life-threatening disease and a high level of suspicion is needed for making the presumptive diagnosis, specially when only prodromal or unspecific symptoms are present. Treatment with antitoxin may not be necessary in very mild cases with low toxin intake.

Disclosure: Nothing to disclose

EPR1181

Impact of spasticity and waning of effect of Botulinum Toxin A treatment on patients' employment and quality of life: results of a multinational online survey

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Background and aims: The aim of this survey was to present the self-reported impacts of spasticity and of waning of effect of BoNT-A treatment on patients.

Methods: An Internet-based survey was conducted through Carenity, an online patient community, in France, Italy, UK, Germany and the USA, from May to September 2019. Adult patients and/or caregivers of patients experiencing spasticity due to a stroke, traumatic brain injury (TBI) or spinal cord injury (SCI), having received ≥ 2 previous BoNT-A injections, currently treated with BoNT-A or having stopped BoNT-A treatment in the last 12 months were eligible.

Results: 210 respondents (mean age 47.2 years, 52.9% male) included. Overall, 42.9% of patients had spasticity due to stroke, 30.0% due to TBI, and 27.1% due to SCI.

Symptoms and areas of life impacted by the condition in the past 12 months are listed in Table 1. 82.9% of patients experienced the reappearance of spasticity-related symptoms between 2 BoNT-A injections. Stiffness/rigidity (74.1%) was the most reported recurring symptom. 46.6% of them had to take time off from work due to recurring symptoms. To avoid recurring symptoms, 72.2% reported wishing injections with longer-lasting effect.

The intensity of spasticity-related symptoms on patients' QoL varied between 2 BoNT-A injections: it was strongest on the day before the next session. (Table 2). The impact of spasticity on patients' Quality of Life (QoL) evolved similarly (Table 3).

Symptoms most experienced*	Overall (N=210)
Symptoms experienced by patients; n (%)	
Muscle stiffness/rigidity (including painful cramps)	148 (70.5)
Muscle spasms	132 (62.9)
Muscle pain	108 (51.4)
Difficulties moving my leg, falling, tripping, loss of balance	104 (49.5)
Unwanted movement of the affected limb	86 (40.9)
Areas of life impacted by the condition; n (%)	
Loss of self-confidence	110 (52.4)
Depression	96 (45.7)
Lack of sleep	86 (40.9)

*symptoms and conditions with frequencies >40%.

Table 1: Symptoms and areas of life impacted by the condition in the past 12 months*

	Intensity of the symptoms reappearing between two sessions of BoNT-A injections (N=174)		
	At peak treatment effect	When pre-existing symptoms start reappearing	1 day before next BoNT-A injection
Muscle stiffness/rigidity (including painful cramps) (n=129)	1.7	4.2	6.8
Muscle spasms (n=112)	1.5	4.3	6.6
Muscle pain (n=92)	1.6	4.2	6.7
Difficulties moving my leg, falling, tripping, loss of balance (n=85)	1.5	4.2	7.0
Unwanted movement of the affected limb (n=68)	1.6	4.1	6.6
Difficulties moving my arm/hand (n=56)	2.4	4.6	6.5

*mean scores out of 10: 0=no symptom, 10=very strong symptom.

Table 2: Patients' perception of the intensity of the symptoms reappearing between 2 sessions of BoNT-A injections*

	Impact of the symptoms reappearing between two sessions of BoNT-A injections (N=174)		
	At peak treatment effect	When pre-existing symptoms start reappearing	1 day before next BoNT-A injection
Ability to move around	1.9	4.2	6.5
Ability to perform daily tasks	1.8	4.2	6.4
Self-confidence	1.9	4.1	6.4
Lack of sleep/fatigue	1.7	4.0	6.3
Relationship with family and friends	1.6	3.8	6.0

*mean scores out of 10: 0=no impact, 10=very strong impact.

Table 3: Patients' perception of the impact of the symptoms reappearing between 2 sessions of BoNT-A injections on QoL*

Conclusion: Spasticity and the waning effect of BoNT-A injections impacts multiple aspects of patients' life, particularly self-confidence and ability to move around and to work.

Disclosure: This study was funded by Ipsen Pharma

EPR1182

Long-term outcomes in 50 patients with idiopathic inflammatory myopathies (IIM) and role of myositis-specific antibodies

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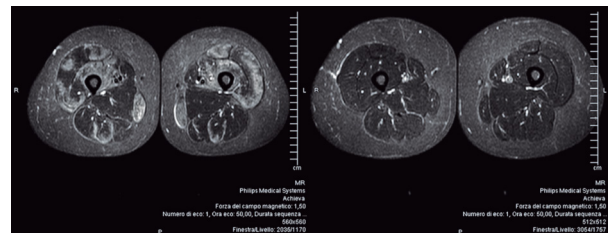
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Background and aims: IIM are the largest group of acquired and potentially treatable myopathies. 4 major distinct subsets are recognized: dermatomyositis (DM), polymyositis (PM), immune mediated necrotizing myopathy (NM) and inclusion-body myositis (IBM). Myositis-specific autoantibodies (MSAs) have an increasing role to identify subgroups with different treatment response and prognosis. Aim of the study was to correlate clinical characteristics and long term outcomes in 50 patients with IIM followed at Neuromuscular Center in Torino in the last 10 years

Methods: Diagnosis was established according the EMNC criteria, and included PM, DM and NM patients. MSAs were tested in all patients by commercial immunoassay. Therapy protocols included prednisone, Ig ev, azathioprine and/or rituximab. Mean follow up was 5 years.

Results: MSAs were positive in 27 patients (54%); anti-Jo1 Ab were positive in 9 patients (33%), followed by anti-HMGCR (18%), anti-SRP (15%) and anti-Mi2 (15%). The remaining patients were equally distributed with anti-Ku, anti-PM Scl-75, anti-TIF1-gamma, anti-NXP2 Ab.

Patients anti-Jo1 positive tended to a worse long-term prognosis; 1 severely affected patient responded positively only to rituximab. All anti-HMGCR positive cases had a NM, promptly responding to Ig ev therapy. Anti-SRP positive patients had a rapid, severe generalized course of NM, with complete remission with rituximab. All patients with anti-Mi2 positivity had a DM, responding completely to prednisone therapy. Seronegative patients responded more variably to prednisone and azathioprine and/or IgeV.



Skeletal Muscle NMR of patient with ab anti-jo-1 pre e post Rituximab

Conclusion: MSAs have an important role in defining subgroups of patients with IIM, indicating different specific therapeutic approaches as a first choice, resulting in complete remission in most cases.

Disclosure: Nothing to disclose

EPR1183

Bioimpedance analysis (BIA), dual energy X-ray absorptiometry (DEXA) and nutritional characteristics in myotonic dystrophy type 2 (DM2) patients

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Background and aims: Metabolic alterations are an important feature of DM2; therefore, recognition of changes in body composition by BIA and its correlation with other disease features might be useful as disease severity index.

Methods: We obtained anthropometric measures, nutritional data, BIA, DEXA, and blood tests in 18 DM2 patients and correlated with motor function tests including: 30-SCT, FI-2 and QMFT. BIA parameters were matched for age, sex, and BMI with healthy control volunteers. Descriptive statistics, Pearson's correlation coefficient and linear regression were performed.

Results: Waist circumference was above normal values in 100% of women and 78% of men. Based on body mass index (BMI), 66% of women and 89% of men were overweight or obese. Mineralization of bone by DEXA showed normal values in most of patients. PA was reduced in 61% of patients and showed direct correlation with 30SCT, FI-2 flexion and abduction test, and QMFT. Bia-derived fat mass (FM) was increased in 22% of women and 56% of men, fat-free mass (FFM) was reduced respectively in 33.3% and 78%. A direct correlation of BCMI with FI-2 flexion and abduction and of BMI with HOMA index ($p < 0.001$) was also found. PA was lower in DM2 compared to controls ($p < 0.05$).

Conclusion: This pilot study shows that an alteration in the relative prevalence of FFM versus FM, as suggested by reduction of PA is a common feature of DM2 and parallels motor function tests impairment. Therefore, further studies on larger cohorts and with a prospective approach could validate BIA as an outcome measure for DM2.

Disclosure: Nothing to disclose

EPR1184

Comparison of the diagnostic accuracy of the ice-pack test and single fiber EMG in patients with ocular myasthenia

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Background and aims: Single-fiber EMG (SF-EMG) is considered highly sensitive for the diagnosis of ocular myasthenia (OM), but it is not widely available. On the contrary, the ice-pack test (IPT) can be easily performed in an ambulatorial setting. However, no studies compared the diagnostic yield of ice-pack test and SF-EMG in a large population. Therefore, we aimed at comparing the diagnostic accuracy of these tests in patients with suspected OM presenting with ptosis.

Methods: We studied consecutive patients referred for the clinical suspicion of OM. Patients underwent stimulation SF-EMG on the orbicularis oculi muscle and the ice-pack test. ROC curve analysis was performed to determine the accuracy of IPT, SF-EMG and their combination.

Results: We included 155 patients, 102 OM and 53 with other diagnosis (OD). The IPT had a sensitivity of 86% and a specificity of 79%. SF-EMG showed a sensitivity of 94% and a specificity of 79%. Overall, IPT and SF-EMG showed discordant results in 30 cases, 16OM and 14OD. The combination of ice-pack test and SF-EMG, using the positivity of at least 1 test for OM diagnosis, increased the sensitivity to 98% reducing the specificity to 66% whereas using the positivity of both tests we obtained a sensitivity of 82% and a specificity of 92%. Comparison of the AUCs showed no differences in the diagnostic accuracy of IPT, SF-EMG and their combinations.

Conclusion: IPT and SF-EMG have a similar diagnostic accuracy in patients with OM presenting with ptosis. The negativity of both tests strongly suggests another diagnosis.

Disclosure: Nothing to disclose

EPR1185

Longer-term Nusinersen Treatment According to Age at First Dose: Results From the SHINE Study in Later-onset Spinal Muscular Atrophy

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Background and aims: SHINE is an open-label extension study (NCT02594124) for participants who completed previous nusinersen trials.

Methods: These analyses focus on participants with later-onset SMA who received nusinersen or sham procedure in the Phase 3 CHERISH study and transitioned to SHINE. Following a protocol amendment, all participants receive nusinersen 12mg every 4 months in SHINE. Motor function data (15 October 2018 interim analysis) were analyzed in three groups by age at first nusinersen dose (≥ 2.0 to < 3.5 years [n=35]; ≥ 3.5 to < 5.0 years [n=41]; ≥ 5.0 to < 9.5 years [n=34]) in participants reassessed for CHERISH inclusion criteria with a value windowed to Day 690 regardless of treatment group.

Results: At SHINE Day 690, the mean [SD] change in HFMSE total score from baseline improved in those youngest at first dose (+8.9 [5.7]), improved then stabilized in those of intermediate age (+3.1 [4.3]) and stabilized in children who were older at first dose (-2.1 [4.2]). The mean (SD) change from baseline to Day 690 in RULM total score also improved over time in those who were youngest (+8.0 [5.1]) or of intermediate age (+3.6 [3.3]) at 1st dose, and was stable in those older at 1st dose (+0.5 [2.9]). The youngest participants at 1st dose achieved the most gains in WHO motor milestones. Data from the 2019 SHINE interim analysis for these participants and those who transitioned from CS2/12 and EMBRACE will be presented.

Conclusion: Among individuals with later-onset SMA, the youngest participants at first dose of nusinersen showed the greatest improvement in motor function.

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Neuroimaging 1

EPR1186

Transcranial ultrasound in HIV infection: does it reflect infectious and neurological symptoms?

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Background and aims: HIV associates an increased frequency of neurological symptoms due to the infection itself and immunosuppression. Transcranial ultrasound (TUS) depicts abnormalities in substantia nigra (SN), 3rd ventricle (3V) and basal ganglia (BG), useful for parkinson's disease diagnosis. A former study found an association among SN hyperechogenicity and motor performance in 40 HIV patients.

Methods: Transversal study of consecutive outpatient HIV subjects with neurological (UPDRSIII and International HIV dementia scale) and TUS assessment, with a sample of 132 historic control subjects for comparison of ultrasound variables (Figure1).

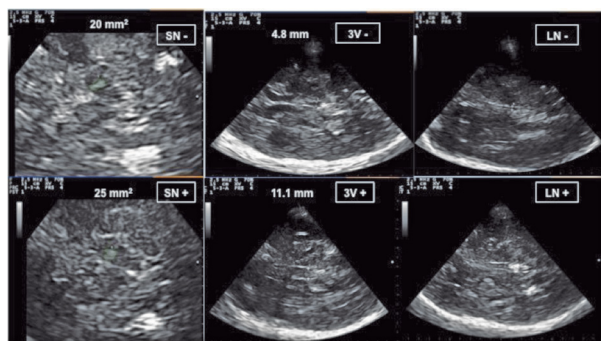


Figure 1

Results: 123 subjects (80% male, 43±13 years old, 15±12 years of HIV infection, 32% with CD4 nadir <200, 25% fulfilling AIDS criteria, 26% HCV co-infection) were included in a 6-days period. 7 had history of neurological complications (3 stroke, 2 HIV encephalitis, 2 toxoplasmosis, 1 multifocal progressive leukoencephalopathy, 1 varicella-zoster encephalitis). 19 subjects scored <11 in I-HIV-DS and 10 (4%) over 5 in UPDRSIII: the latter was associated with AIDS diagnosis and lowest CD4 nadir (Figure2). Among 115 (93%) with sufficient transtemporal bone window, 19 had SN hyperechogenicity (17% vs. 11%

controls, NS), 7 3V enlargement (6% vs. 5%, NS) and 31 BG hyperechogenicity (30% vs. 9%, p=0.00043), without association with any infectious or neurological clinical variable (Figure 3). MRI was available in 4 cases with BG hyperechogenicity and was abnormal in all them.

	UPDRS III			p	HIVDS			p
	Normal	Mild	Mod/Sev		Normal	Borderline	Abnormal	
AIDS +/-	18%/82%	29%/71%	70%/30%	0.0018	23%/77%	22%/78%	42%/58%	NS
CD4 Nadir								
>500	23%	15%	0%	0.0101	25%	17%	5%	NS
200-500	49%	48%	10%		41%	50%	47%	
<200	28%	36%	90%		33%	33%	47%	

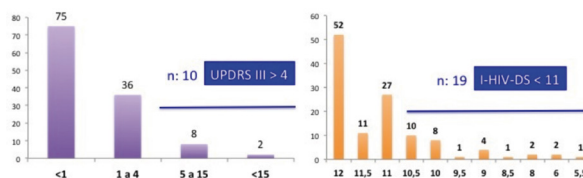


Figure 2

	SN hyperechogenicity (n:19)		Basal Ganglia hyperechogenicity (n:25)	
Male/Female	18%/9%	NS	27%/12%	NS
AIDS yes/no	22%/15%	NS	20%/25%	NS
Hepatitis C yes/no	17%/17%	NS	24%/23%	NS
CD4 Nadir				
• >500	18%	NS	32%	NS
• 200-500	18%		22%	
• <200	16%		19%	
Drug abuse yes/no	17%/17%	NS	23%/24%	NS
HIVDS				
• NORMAL	12%	NS	20%	NS
• BORDERLINE	24%		33%	
• ABNORMAL	12%		12%	
UPDRS III				
• NORMAL	20%	NS	30%	NS
• MILD	13%		10%	
• MODERATE-SEVERE	11%		22%	

Figure 3

Conclusion: SN hyperechogenicity was not more frequent in HIV+ than in control subjects, unlike previous evidence suggested. Conversely, an increased prevalence of BG hyperechogenicities of unknown significance, previously not described, was found.

Disclosure: Nothing to disclose

EPR1187

Microstructural tissue changes in Alzheimer's disease: insights from Magnetization Transfer Imaging

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Background and aims: Reductions of the magnetization transfer ratio (MTR), a magnetic resonance imaging-derived measure, has been associated with microstructural damage of the brain. Recent studies have demonstrated global MTR reductions in Alzheimer's disease (AD), but regional changes and their associations with cognition are less explored. In this study, we therefore assessed MTR in the grey matter (GM) and in normal appearing white matter (NAWM) in patients with AD and in normal elderly. Additionally, we analyzed the relationship between MTR and cognitive functioning.

Methods: 77 patients with moderate AD (mean±SD age=72.03±7.71) and 77 age-matched (±1 year) controls underwent clinical and MRI examination at 3 Tesla. Cognitive performance was assessed in the patients only and included MMSE and CERAD. The MTR was assessed regionally in the cortex, NAWM, hippocampus, and deep gray matter structures.

Results: MTR reductions in AD patients were global and were found in the hippocampus, deep gray matter, cortex, white matter hyperintensities (WMH) and in the NAWM. After correction for atrophy AD patients had lower MTR values in the occipital lobe and in NAWM than controls. Reduced MTR values in the cortex, NAWM, Globus pallidus and hippocampus were associated with a worse performance on MMSE and on CERAD subtests for constructional praxis, object naming, verbal memory and cognitive flexibility, independent of atrophy, age, sex and WMH volume.

Conclusion: The MTR allows to assess AD related tissue changes of the brain. A decrease of MTR in cortical structures and NAWM contributes to cognitive impairment beyond atrophy.

Disclosure: Nothing to disclose

EPR1188

Longitudinal analysis of brain iron in Alzheimer's disease

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Background and aims: Recent studies have demonstrated higher iron concentrations in patients with Alzheimer's disease (AD) compared to healthy controls. However, to our knowledge, to date, no published study has examined the relationship between the longitudinal iron change in the neocortex and cognitive decline in AD. We aimed to investigate using R2* relaxation rate mapping the association between longitudinal changes in R2* and cognition in patients with AD.

Methods: Our study included 57 participants with AD from the Prospective Dementia Registry Austria study (mean age 71.4±9.4 years, men/women=26/31). All study participants underwent longitudinally subsequent neuropsychological and neuroimaging assessment with an MRI protocol at 3 Tesla identical between baseline and follow-up, including R2* relaxation rates mapping, corrected for macroscopic field variations, with a mean follow-up time of 17 months. Anatomical structures were segmented and median R2* rates were calculated in the neocortex and cortical lobes, the basal ganglia, hippocampi and thalami.

Results: R2* in parietal lobe decreased whereas R2* relaxation rates of global basal ganglia, putamen, caudate nucleus and thalamus increased over time (Table 1). R2* change in the temporal and occipital lobes, after adjustment for change in brain volume over the observational period, correlated significantly with change in cognition over 17 months ($\beta=-0.31$, $p=0.02$, $\beta=-0.34$, $p=0.01$, respectively) (Table 2).

Table 1. Annualized percentage rates of R2* levels in study participants with Alzheimer's disease after 17 months follow-up

Region	R2* annualized rate	
	median (%)	p value*
Total cortex	-0.13	0.28
Global basal ganglia	1.48	<0.01
Frontal lobe	-0.02	0.61
Temporal lobe	0.31	0.63
Parietal lobe	-0.68	0.04
Occipital lobe	0.66	0.32
Caudate nucleus	1.94	0.01
Globus pallidus	1.07	0.03
Putamen	1.07	<0.01
Hippocampus	-1.18	0.27
Thalamus	0.83	0.05

*computed using Wilcoxon Signed Ranks Test

Table 2. The association between annualized R2* and MMSE changes in study participants with Alzheimer's Disease

Annualized R2* change	Annualized MMSE change		
	Multivariable regression, corrected for age and annualized change of regional volumes		
	β	p value	95% CI
Total cortex	-0.19	0.16	-2.97; 0.50
Global basal ganglia	0.02	0.89	-0.39; 0.45
Frontal lobe	-0.10	0.43	-2.24; 0.96
Temporal lobe	-0.31	0.02	-2.44; -0.27
Parietal lobe	-0.04	0.79	-1.14; 0.88
Occipital lobe	-0.34	<0.01	-2.25; -0.37
Caudate nucleus	-0.07	0.57	-0.50; 0.28
Globus pallidus	<0.01	0.99	-0.28; 0.29
Putamen	0.07	0.64	-0.28; 0.44
Hippocampus	-0.25	0.07	-0.93; 0.03
Thalamus	0.10	0.47	-0.69; 1.47

β = regression coefficient; CI = confidence interval, MMSE = Mini-Mental State Examination.

Conclusion: Our results demonstrate that an iron increase in the temporal and occipital lobes correlated with cognitive decline. These findings support the view that impaired iron homeostasis may be involved in the pathophysiology of AD.

Disclosure: Nothing to disclose

EPR1189

Functional brain connectome in drug-naïve Parkinson's disease patients

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Background and aims: Graph analysis may be applied to characterize functional architecture changes related to Parkinson's disease (PD) development and progression.

Methods: 147 drug-naïve PD patients underwent motor, non-motor and neuropsychological assessments as well as resting-state functional MRI at baseline. 38 age- and sex-matched controls were also enrolled. Non-hierarchical cluster analysis using clinical data were applied to stratify PD patients in 2 subtypes: 77 patients were grouped as "early/mild" and 70 as "early/severe". Graph analysis and connectomics assessed global and local topological network properties and regional functional connectivity (FC) at baseline in both PD patients and controls. Multivariate regressions were used to investigate whether functional imaging data at baseline were predictors of clinical impairment over a 2-year period.

Results: At baseline, widespread FC abnormalities were detected in several networks encompassing basal ganglia, sensorimotor and occipital areas in PD patients compared to controls. Moreover, decreased FC involving mainly striato-frontal, striato-temporal and limbic connections differentiated "early-mild" from "early-severe" PD patients. "Early/mild" PD patients showed a preserved global functional brain architecture compared to controls. FC abnormalities at baseline were found to be an independent predictor of cognitive outcome and levodopa requirement over 2 years.

Conclusion: Our findings revealed that a specific subtype of PD patients, characterized by severe motor and non-motor burden as well as widespread FC abnormalities, may be identified at the time of diagnosis. We hypothesize that this pattern may reflect the presence of more diffuse neuropathological changes. Combined clinical and neuroimaging tools are promising to stratify risk of PD progression overtime.

Disclosure: Nothing to disclose

EPR1190

Resting state functional MRI improves outcome prediction in middle cerebral artery stroke

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Background and aims: Resting-state functional MRI (rfMRI) has been suggested to improve prediction of post-stroke recovery. We assessed whether rfMRI improves outcome prediction in addition to conventional predictors after acute stroke.

Methods: We assessed 56 patients (mean age 64 years, 38% female, median admission NIHSS 9.5) with MRI-confirmed middle cerebral artery infarction who have received intravenous thrombolysis and/or mechanical thrombectomy at the acute stage (24-72 hours after symptom onset) and at 3 months follow-up. Outcome was assessed by the modified Rankin Scale (mRS) score at follow-up. MRI data of 6 patients had to be excluded due to severe motion artefacts or lesion-related registration errors. We used an ordinal regression model including demographics, clinical scores, lesion size, whole brain white matter integrity assessed by DTI and functional connectivity of the ipsilesional primary motor area (FC iM1) to identify outcome predictors.

Results: At follow-up, 20 patients had mRS 0 (35.7%), 21 patients (37.5%) had mRS 1, 8 patients (9.6%) mRS 2 and 7 patients (8.4%) mRS 3 or 4. Spearman correlations showed that NIHSS at baseline ($r=0.65$), lesion volume ($r=0.47$), whole brain white matter integrity ($r=-0.40$), and FC of iM1 ($r=0.42$) were associated with mRS scores at follow-up. Although NIHSS at baseline was the strongest independent predictor of mRS scores at follow-up (Nagelkerke=44.2%), baseline FC of iM1 improved prediction to 62.4%.

Conclusion: RfMRI improves prediction of outcome in a homogeneous group of acute stroke patients. Early changes in FC might be a promising biomarker for post-stroke outcome.

Disclosure: Nothing to disclose

EPR1191

The interpretation of brain CT scans throw direct analysis and via WhatsApp: Moroccan experience

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Background and aims: The use of smartphones in medical practice (telemedicine) is becoming more and more widespread. Ischemic strokes, eligible for thrombolysis, are one of many disorders having benefited from this technology for a proper and quicker management. The aim of this study is to evaluate intra and inter-individual interpretation of brain CT scans, analysed directly and those shared via WhatsApp, in order to assess the reliability of this tool.

Methods: A double-blind cross-sectional study was conducted, including neurology residents, of the Ibn Rochd university hospital, having completed at least 2 years of residency. These doctors were asked to estimate the ASPECT (Alberta Stroke Program Early CT) Score using 2 different methods: throw a direct analysis or via WhatsApp shared images.

The scans of 30 patients treated using intravenous thrombolysis, between 2018 and 2019, were randomly selected and both, a sender and receiver, high image-resolution smartphones were implemented for this task.

Results were analysed using an SPSS software.

Results: 7 doctors, with a mean residency length of 42 months, completed the study. Intra-individual results (WA versus direct analysis scores) were consistent in 71% of cases ($n=5$, $p<0.05$) with a maximum correlation of $R=0.44$. Results were identical between residents and professors in 85% of cases ($n=6$, $p<0.05$).

Conclusion: The use of WA in brain CT scan analysis seems highly reliable. Larger studies would probably be of great interest.

Disclosure: Nothing to disclose

EPR1192

Prognostic value of 18F-FDG PET in unresponsive wakefulness syndrome patients.

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Background and aims: The diagnostic and prognostic usefulness of neuroimaging-based approaches has not been established in a clinical setting. We did a validation study of FDG PET imaging in prognosis VS/UWS

Methods: 18F-FDG PET was performed in 172 patients DOC patients between 2006-2018. Outcomes were assessed 12 months after TBI and 6 months after hypoxia. 109 patients after TBI and 63 with hypoxia: UWS 77 patients, MCS + 62 patients, MCS – 34 patients, mean age 28 y.o. Duration of DOC was 1-6 months in TBI and 4 months in hypoxic brain damage.

Results: Prognostically favorable for further recovery of consciousness were following findings: preservation of glucose metabolism in the cortical regions above 45% of the cerebellar metabolism level, in particular, preservation of the 18F-FDG metabolism at the level above 50% of the cerebellar metabolism level in the frontal and parietal lobes indicated the possibility of transition from UWS to MCS in patients with both traumatic and non-traumatic brain damage. Correlation was found between the outcome of UWS (CRS-R score) and the level of metabolism in the brain stem. All studies were conducted at the level of significance. Correlation analysis showed that the greatest importance in predicting of the UWS outcome (CRS_R score) was the preservation of the 18F-FDG metabolism in the cortex of the frontal, parietal, temporal and occipital lobes of the right hemisphere, brain stem.

Conclusion: Cerebral (18)F-FDG PET could be used to complement bedside examinations and predict long-term recovery of patients with unresponsive wakefulness syndrome.

Disclosure: The study was funded by RFBR (Russian Foundation for Basic Research) project number 19-29-01066/2019

EPR1193

Brain Microstructural Changes in CADASIL

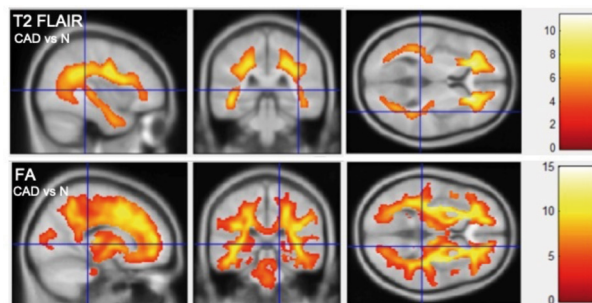
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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is the most common hereditary monogenous form of cerebral small vessel disease (SVD). The aim of this study was to evaluate the spatial distribution and features of brain microstructural changes, associated with CADASIL.

Methods: We enrolled 105 patients with genetically confirmed CADASIL (40), hypertensive microangiopathy, multiple sclerosis and 34 healthy control. Patients were evaluated with different clinical scales. The conventional MRI and DTI with calculation of fractional anisotropy (FA), mean (MD), axial (AD) and radial (RD) diffusivity maps were performed. Brain tissue lesions were assessed using Standards for Reporting Vascular changes on neuroimaging (STRIVE). Voxel-wise group analysis was carried out using SPM12 software and also ROI analysis was carried out to study the white matter microstructure.

Results: In CADASIL group MRI shows all the types of SVD signs: recent small subcortical infarcts, lacunes, white matter hyperintensities (WMH), perivascular spaces and microbleeds. Whole-brain and ROI analysis of diffusivity maps in CADASIL patients revealed dramatic changes in white matter (WM) both in regions of WMH and normal appearing WM (Fig. 1). The FA was decreased and MD, AD and RD were increased in all ROI.



Between-group analysis showing areas of WMH (top) and significantly decreased FA (bottom) in patients with CADASIL as compared to healthy controls.

Conclusion: Neuroimaging signs of brain lesions are common for all types of cerebral small vessel disease, including CADASIL. However, the distribution of WMH and patterns of microstructural changes specify the differences observed in CADASIL. These changes correspond more to demyelination but differ between the anatomical regions and need the further studies.

Disclosure: Nothing to disclose

EPR1194

Lesion distribution and substrate in Type 1 Myotonic Dystrophy: comparison with Multiple Sclerosis

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Background and aims: A typical feature of type 1 Myotonic Dystrophy (DM1) is the presence of widespread white matter lesions. This study compares the lesion distribution and substrate between patients with DM1 and patients with Multiple Sclerosis (MS).

Methods: 28 patients with DM1, 29 patients with relapsing remitting MS, and 15 healthy controls had an MRI scan, including FLAIR quantitative magnetization transfer (qMT) imaging. Lesions were outlined on FLAIR; qMT data were processed to compute the pool size ratio (F), known to correlate with myelin content. The average F was computed within lesions and normal appearing white matter (NAWM) for every participant. The lesion masks were warped into MNI space and lesion probability maps were obtained for each patient group. The total lesion load, and the tissue-specific mean F were compared between groups.

Results: The mean lesion volume was higher in MS than DM1. DM1 presented higher prevalence of anterior temporal lobe lesions, but none in the cerebellum and brainstem. In both patient groups the mean F of lesions was lower than the NAWM ($p < 0.01$, CI 0.06-0.07), but it was lower in MS than DM1 ($p < 0.01$, CI 0.01-0.04). NAWM F did not differ between DM1 and controls.

Conclusion: DM1 show a greater lesion distribution in the temporal lobe regions compared to MS. Using qMT, we demonstrated significantly reduced F values within DM1 lesions, suggesting a loss of myelin density. Nevertheless, the mean F is lower in MS lesions than DM1 lesions, indicating a lesser degree of demyelination in the former.

Disclosure: Nothing to disclose

EPR1195

Possible role of the ONSD in predicting malignant media stroke

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Background and aims: The prevalence of hemispheric malignant media infarction (mMCA) has been reported to be 2% to 8% of all ischemic stroke. The optic nerve sheath diameter (ONSD) has been demonstrated to be a non invasive assessment for detecting raised intracranial pressure (ICP). We tested whether ONSD measurements could support clinical evaluation to predict occurrence and promptly diagnose of malignant infarction.

Methods: In a single-center prospective observational study we recruited patients with MCA infarction and age- and sex-matched controls. Demographics, clinical characteristics including National Institutes of Health Stroke Scale and ONSD measurement were assessed prospectively upon admission and during the 1st 5 days after symptom onset.

Results: We included 29 patients with MCA infarction, among them 10 developed an mMCA infarction, and 14 controls. ONSD already on admission was larger in patients who had developed an mMCA (mean 5.99mm, (SD) 0.318) compared to patients with MCA infarction (4.98mm, SD 0.532; $P = 0.003$), and to control patients (4.57mm, SD 0.285; $P < 0.001$). Correlation was observed between the largest ONSD and volumetric evaluation of cerebral infarction in the CT scan ($r = 0.757$; $P < 0.001$). An ONSD value of 5.595mm predicted an mMCA with a sensitivity of 100% and specificity of 90% yielding a PPV of 83% and NPV of 100%.

Conclusion: ONSD measurement might be accurate for the noninvasive detection of increased ICP. The serial ONSD measurements could help to detect the deterioration of patients.

Disclosure: Nothing to disclose

EPR1196

Automated brain volumetry at different field strengths - a feasibility study

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Background and aims: Comparability study of quantitative brain volumetry at 1.5T, 3T and 7T

Methods: In this study, brain scans of 7 volunteers (25±5y) were acquired on three Siemens MR Scanners (1.5T-AERA, 3T-PRISMA and 7T-MAGNETOM) using 3D-T1w images (0.5x0.5x0.59mm³, no interpolation). Volumetric measurements were performed with the AI-powered commercial software mbrain from mediaire as it showed high stability for repeated measurements in previous studies and its short calculation time. The evaluation pipeline includes a bias correction accounting for intensity non-uniformities. For statistical evaluation, repeated measures ANOVA was calculated followed by a post-hoc paired t-tests focusing on a selection of seven brain regions (grey-and white-matter (GM, WM), hippocampus, putamen, amygdala, caudate and thalamus)

Results: As rated by a radiologist, images were of good quality for all 3 scanners (Figure1). Except for the hippocampus, the repeated measures ANOVA revealed significant differences between the conditions 1.5T, 3T and 7T (p<0.05). The post-hoc paired t-tests showed significant differences for the 1.5T/3T data versus the 7T data: Volumes of WM and amygdala were decreased by 10% and 5% while caudate was increased by ~4%. Except for the thalamus (~6% decrease), no significant differences between 1.5T and 3T were present (Table1).

Figure 1. Representative axial slices of the same volunteer for different field strengths (1.5T, 3T and 7T). Respective brain volumes are superimposed with the original image, showing grey matter (green), white matter (yellow), putamen (red), caudate (orange) and thalamus (blue).

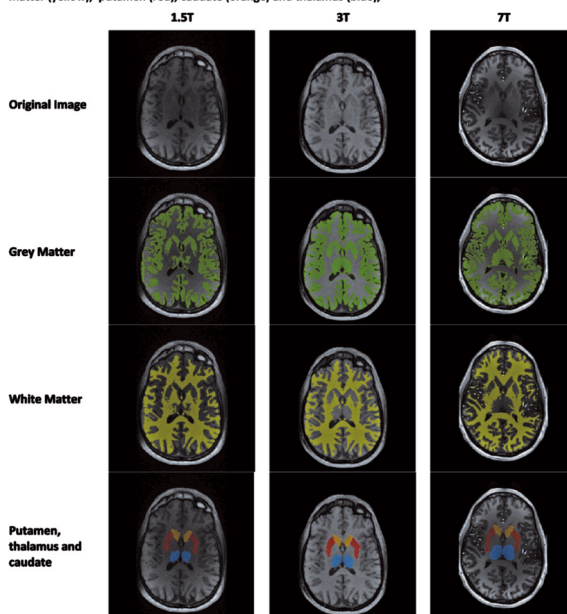


Table 1

Paired t-tests	Region						
	GM	WM	Hippocampus	Amygdala	Caudate	Putamen	Thalamus
1.5T vs. 3T	0.05	0.55	0.41	1.00	0.87	1.00	0.01
1.5T vs. 7T	0.01	0.06	1.00	0.06	0.08	0.25	0.01
3T vs. 7T	0.20	0.01	0.44	0.02	0.02	0.02	0.27

Paired t-test including seven volunteers calculated for 7 brain regions that were acquired on 3 MR scanners of various field strengths and were segmented using mbrain. High correlation was found for 1.5T and 3T for all regions except Gm and the Thalamus. 7T data, however, showed significant differences for most brain regions as compared to 1.5T and 3T.

Conclusion: To our knowledge, this is the 1st study where quantitative brain volumetry at 3 different field strengths was performed. Results showed that quantitative brain volumetry at different field strengths is possible. However, comparability cannot be guaranteed which has to be taken into account when longitudinal volumetry measurements shall be performed. This is especially true for measurements at 7T.

Disclosure: Nothing to disclose

Neuroimmunology 1

EPR1197

Use of disease-modifying therapies in paediatric relapsing remitting multiple sclerosis in the UK: A multi-centre retrospective study

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Background and aims: The approach to treatment of relapsing remitting multiple sclerosis (RRMS) in children is rapidly evolving, with 14 disease-modifying therapies (DMTs) currently licensed for adults. In this study, we aimed to describe the frequency of relapses and side effects in children on DMTs in a real-life cohort.

Methods: Children (<18yrs) with a diagnosis of RRMS, treated with DMTs, were identified from four tertiary paediatric neurology centres between 2012-2018. Annualised relapse rates (ARR) prior and on treatment were calculated.

Results: Of 82 children included, 43 (52.4%) were treated with one DMT; 34 (41.5%) with 2 DMTs, and 5 (6.1%) with three or more DMTs. The median time from initial presentation to 1st-line DMTs was 1.0 years (IQR: 0.6-2.0) and 1.8 years (IQR 1.4, 2.5) for 2nd-line DMTs. Side effects were reported in 44 (53.7%) children on 1st-line treatment and 15 (42.9%) children on 2nd-line DMTs. ARR was reduced from 2.0 to 1.2 with interferon- β / glatiramer acetate (n=66, p=0.002); 0.81 to 0.78 with dimethyl fumarate (n=8, p=0.5); 1.9 to 0.3 with fingolimod (n=11, p=0.01) and 1.8 to 0.3 with natalizumab (n=10, p<0.001).

Conclusion: There have been limited randomised trials to date for 1st-line DMTs in the paediatric population; nevertheless, newer DMTs are increasingly being used in paediatric MS. In this cohort, a reduction in ARR was observed with all DMTs. Escalating treatment to second-line DMTs resulted in a large ARR reduction.

Disclosure: Nothing to disclose

EPR1198

Differential diagnosis spectrum in paraneoplastic neurological syndromes: a population-based study.

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Background and aims: To characterize the differential diagnosis spectrum and potential clinical pitfalls in the evaluation of patients with suspected paraneoplastic neurological syndromes (PNS).

Methods: A 9-year (2009-2017) population-based epidemiological study of PNS was performed in the Friuli-Venezia Giulia region (Italy). All patients undergoing search for antibodies indicative of PNS were screened. PNS diagnosis was defined by the 2004 criteria. Data on alternative diagnoses were collected and categorized according to disease etiology.

Results: Among 878 patients extensively studied for suspected PNS, 89 were diagnosed with definite PNS and 128 with possible PNS. An alternative neurological diagnosis was made in the remaining 661, as follows: neurodegenerative (93; 14.07%), autoimmune (85; 12.86%), toxic-metabolic (40; 6.05%), epilepsy/seizures (32; 4.84%), neoplastic (30; 4.54%), infectious (24; 3.63%), vasculitis (21; 3.18%), vascular diseases (23; 3.48%), psychiatric/functional (13; 1.97%), myelopathies (11; 1.67%), dizziness and vertigo (10; 1.51%), cephalalgia (5; 0.75%), peripheral nervous system diseases not better specified (129; 19.52%), cognitive dysfunction (15; 2.27%), miscellaneous neurological conditions (67; 10.29%), other non-neurological conditions (32; 4.84%) and undetermined diagnosis (13; 1.97%). Based on this differential diagnosis spectrum, a diagnostic algorithm for suspected PNS was proposed and adopted by our Center.

Conclusion: This observational, real-life study, based on clinical practice, showed that there are many different diseases that can mimic PNS, including treatable disorders that require prompt identification. This data allowed us to set up a specific diagnostic algorithm that can be used in patients with suspected PNS.

Disclosure: Nothing to disclose

EPR1199

Immune-mediated neurotoxic syndromes related to immune checkpoint inhibitors: experience in a tertiary care center.

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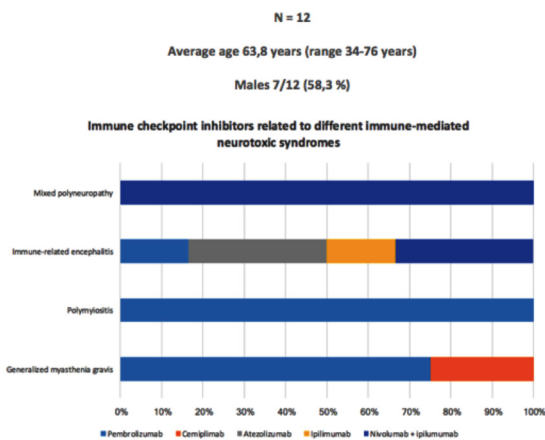
Background and aims: Immunotherapy with immune checkpoint inhibitors (ICI) is revolutionizing the systemic treatment of cancer. Immune-related adverse events affecting the nervous system could be fatal and remain to be properly characterized. We aim to share our experience in the management of these patients.

Methods: Retrospective study including patients on ICI manifesting immune-related neurotoxicity along a 3-year period (2016-2019) in a tertiary care center.

Results: 12 patients were included. 8 were on anti-programmed death-1 receptor (anti-PD-1) or its ligand (anti-PD-L1), only 1 on anti-cytotoxic T lymphocyte antigen-4 (anti-CTLA4) and 3 on combined therapy. Generalized myasthenia gravis (GMG) was developed in 4 patients, immune-related encephalitis (IRE) in 6, mixed polyneuropathy in 1 and polymyositis in 1. Regarding GMG patients, 3 were seropositive, 3 debuted within the 1st 21 days of immunotherapy and all were on anti-PD-1/PD-L1. Concerning IRE patients, 3 showed pleocytosis in CSF, no patient showed changes in cranial MRI and 4 were on single anti-PD-1/PD-L1 therapy. Referring to treatment, 11 patients suspended immunotherapy and received intravenous steroids. Intravenous immunoglobulins were administered in half of patients. 10 patients presented total or partial improvement and 4 eventually died (2 with GMG).

Conclusion: Our results were consistent with literature: most of neurotoxicity (IRE, GMG) involved anti-PD1/PD-L1 and appeared within the 1st 21 days of immunotherapy. Of relevance, most of patients were early diagnosed and showed good outcomes after early treatment. Lethality was particularly notable among GMG patients.

Disclosure: Nothing to disclose



Immune checkpoint inhibitors related to different immune-mediated neurotoxic syndromes.

EPR1200

Clinical, pathological and prognostic heterogeneity in immune checkpoint inhibitors-induced myositis

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Background and aims: Treatment with immune checkpoint inhibitors (ICIs), including monoclonal antibodies against programmed death-1 (PD-1) and its ligand (PDL-1), is approved in many tumor types. By unbalancing immune system, ICIs may generate several multi-organ immune-related Adverse Events (irAEs), including neuromuscular manifestations.

Methods: Among 406 patients with solid tumors treated with ICIs in Siena's Center for Immuno-Oncology between 2013 and 2019, we identified 4 (<1%) metastatic melanoma patients presenting clinical, electromyographic and laboratory findings suggestive of myopathy, alone or associated to other neurological irAEs. All patients underwent muscular biopsy.

Results: Patient 1 presented ptosis, fluid dysphagia, myalgias and lower limbs weakness after first anti-PD1 administration. Muscular biopsy showed granulomatous myositis. Specific antibodies and repetitive nerve stimulation showed concomitant Myasthenia Gravis (MG). Patient recovered in 7 weeks with oral steroids. Patient 2 presented dropped head, bilateral ptosis, hypophonia, fatigue and dyspnea after 2nd anti-PD1 administration. Muscular biopsy showed necrotizing myositis with minimum inflammation. Specific antibodies showed concomitant MG. Patient required non-invasive ventilation and intravenous and oral steroids, slowly recovering within 6 months. Patients 3 and 4 showed polymyositis-like pathological pattern after anti-PD1 therapy, with markedly different courses: the 1st had mild disease, fully recovered in 3 months with oral steroid, whereas the 2nd had severe and prolonged course, requiring hospitalization, invasive ventilation and multiple immunoactive therapies.

Conclusion: ICIs-induced myositis can present with different clinical and pathological features, isolated or associated to MG. Ocular muscles are frequently involved (4/4 in our series) regardless MG co-morbidity. Severity, course and prognosis are heterogeneous and apparently unrelated to different pathological patterns.

Disclosure: Nothing to disclose

EPR1201

Epileptic seizures of suspected autoimmune etiology: a multicenter retrospective characterization.

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Background and aims: Specific scores were recently proposed to identify antibody-positive patients (APE2) and predict immunotherapy response (RITE2) in subjects with otherwise unexplained epilepsy. Aim of our study was to compare clinical/paraclinical data with autoantibodies status in a European multicenter cohort and validate the predictive value of the proposed scores.

Methods: We retrospectively analyzed clinical/paraclinical data of 92 patients referred to the Neurology Unit of Verona and Salzburg between January-2014 and July-2019 with new onset epilepsy, status epilepticus, or chronic epilepsy of unknown etiology and with available paired serum/CSF samples. Fixed and live cell-based-assays, tissue-based assays, immunoblot, and live rat hippocampal cell culture were performed at the reference laboratories to detect anti-neuronal and anti-glia antibodies. The APE2/RITE2 scores were then calculated and compared with clinical and laboratory data.

Results: Autoantibodies were detected in 29 patients, with multiple positivity observed in 6 cases. The APE2 score correlated significantly with antibody positivity ($p=0.014$). In particular, the presence of neuropsychiatric symptoms ($p<0.01$), movement disorders ($p<0.01$), dysautonomic symptoms ($p=0.03$), faciobrachial dyskinesias ($p=0.03$), and cancer history ($p<0.01$) significantly correlated with the presence of autoantibodies. Status epilepticus was significantly more frequent in seronegative patients ($p<0.01$). Among the items of the RITE2 score, only early initiation of immunotherapy correlated with a good treatment response ($p=0.001$), whereas an oncologic anamnesis was significantly more common in the non-responders ($p<0.01$). Persistence of neuropsychiatric symptoms and seizures significantly influenced prolonged treatment choices.

Conclusion: The extensive clinical and laboratory analyses here reported provide novel cues on the possible autoimmune origin and management of epilepsy of otherwise unknown etiology.

Disclosure: Nothing to disclose

EPR1202

Hippocampal Regional Vulnerability to Damage Differs Between MS and Neuromyelitis Optica

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Background and aims: In multiple sclerosis (MS), hippocampal subfields have different susceptibility to damage and there is in-vivo evidence of dentate gyrus (DG) hypertrophy as a possible response to the inflammatory environment. Less is known about other inflammatory diseases like neuromyelitis optica spectrum disorders (NMOSD).

Methods: 28 seropositive NMOSD patients, 24 age- and disease duration-matched relapsing-remitting MS and 20 healthy controls (HC) underwent a 3.0T MRI. From 3D-T1-weighted sequence, manual hippocampal segmentation was performed. Brain T2 and T1 lesion volumes (LV) were also assessed. From diffusion weighted sequences, a probabilistic tractography was run to assess microstructural damage of hippocampal connections (fornix, uncinate fasciculus [UF] and cingulum).

Results: Compared to HC, NMOSD patients had similar global hippocampal volumes and mild atrophy in the Cornu Ammonis (CA) 1 subfield, whereas MS patients had significant global and regional hippocampal atrophy (especially in the CA1 and Subiculum, $p < 0.001$). DG hypertrophy was found in MS (right $p < 0.05$, left $p < 0.001$), but not in NMOSD. Hippocampal anatomical connections were damaged in MS ($p < 0.001$) and preserved in NMOSD. No correlation between regional hippocampal atrophy, brain T2 and T1 LVs and measures of hippocampal disconnection emerged in NMOSD patients. In MS, hippocampal volume abnormalities were significantly related to brain T2 and T1 LVs and to damage of the cingulum and UF ($r = -0.8$, $p = 0.01$).

Conclusion: The preferential susceptibility to damage of the CA1 is a common feature in neuroinflammatory diseases. However, DG hypertrophy is peculiar to MS, suggesting that other factors, in addition to inflammation, contribute to this process.

Disclosure: Nothing to disclose

EPR1203

MRI characterization of brain and hippocampal atrophy in Limbic Encephalitis and correlation with cognitive outcome.

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Background and aims: Limbic Encephalitis (LE) is an Autoimmune Encephalitis frequently leading to severe disability, including cognitive deterioration. During the 1st stage of the disease T2-weighted Magnetic Resonance imaging (MRI) usually shows increased signal of 1 or both medial temporal lobes whereas whole-hippocampal atrophy is frequently observed in advanced stages. To date, in LE, association between brain atrophy and cognitive outcome is poorly characterized and no data exist regarding hippocampal subfields involvement.

Methods: Consecutive patients, age >18, fulfilling the 2016 LE diagnostic criteria, admitted in the Careggi University Hospital between 2013 and 2017 and followed for a median of 52 months, were retrospectively included. In these patients, whole brain and hippocampal atrophy were evaluated by MRI using dedicated softwares (FSL SIENA/SIENAX and FreeSurfer), comparing in each of them the latest follow-up scan with the 1 closest to disease onset. Neuropsychological evaluation of cognitive functions was also performed during follow up.

Results: In all the patients included ($n=6$) pathological rates of both global cerebral and hippocampal atrophy were observed. Most patients did not show relevant deterioration of memory domains whereas residual impairment of frontal functions was frequently observed. Cognitive impairment was strongly associated with global atrophy. Memory impairment was associated with residual hippocampal volume more than with hippocampal atrophy rate. In all patients, specific hippocampal subfields, as the amygdala transition area were more involved than others, regardless of auto-antibody status.

Conclusion: In LE residual cognitive deficit is the result of an extended/global structural damage more than confined in the hippocampus.

Disclosure: Nothing to disclose

EPR1204

Clinical and serological characteristics of patients with double seronegative Myasthenia Gravis

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Background and aims: Myasthenia gravis (MG) patients without AChR or MuSK antibodies by radioimmuno-precipitation assay (RIPA) are classified as seronegative (SNMG). Live cell-based assays (CBAs) can detect AChR or MuSK antibodies in RIPA negative samples. We compared the CBA-screening of MG antibodies using single antigen transfection with a combinatorial assay, incorporating AChR and MuSK in a single test, and describe the features of a well-characterized cohort of SNMG patients.

Methods: Sera from 70 SNMG patients with electromyography signs of post-synaptic neuromuscular transmission failure were retrospectively tested by CBAs using HEK-cells transfected to express clustered-AChR (adult or foetal form), full-length MuSK or LRP4. 55/70 patients with SNMG had generalized disease, 22/70 (31%) were sampled at disease onset and 33/70 (47%) were untreated at sampling-time. 65 SNMG sera, 50 healthy-controls and 70 disease-controls were then tested on HEK-cells transfected to co-express both clustered-AChR (both adult and foetal forms) and full-length MuSK.

Results: AChR-antibodies were detected in 11/70 (16%) and MuSK-antibodies in 6/70 (8.5%). None had LRP4-antibodies or were double positive. These results were reproduced using a CBA co-expressing clustered-AChR and MuSK. For all assays, all disease and healthy-controls were negative. Both patients with clustered-AChR and MuSK antibodies had a less severe disease course than RIPA-positive MG patients. In particular, 2/6 MuSK patients presented with purely oculomotor signs.

Conclusion: Around 25% of SNMG patients had AChR or MuSK antibodies which were reliably detected with a combinatorial CBA, co-expressing AChR and MuSK. These data support the use of a combinatorial CBA for screening SNMG patient sera.

Disclosure: Nothing to disclose

EPR1205

Clinical significance of seronegative, but CSF antibody positive, anti-NMDA receptor encephalitis

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Background and aims: To determine the frequency of anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis without detectable NMDAR antibodies in serum (only positive in CSF), and to compare the clinical features of these patients with those with antibodies in serum and CSF.

Methods: Retrospective assessment of antibody serostatus and clinical features of 489 patients with anti-NMDAR encephalitis studied at Hospital Clínic, Barcelona, between January 2007 and December 2017. Serum and CSF NMDAR antibodies were determined with rat brain immunostaining, in-house cell-based assay (CBA), and a commercial CBA. Patients were considered seronegative if all 3 techniques were negative for serum antibodies.

Results: All patients had NMDAR antibodies in CSF. Serum NMDAR antibodies were not detected in 75/489 (15%) patients. Compared with the 414 seropositive patients, the seronegative were older (23.5 years [IQR: 17-43] vs. 20.5 [IQR: 14-31]; $p < 0.0001$), less frequently female (39 [52%] vs. 313 [76%]; $p < 0.001$), and had less tumors (6 [9%] vs. 128 [32%]; $p < 0.001$). In multivariate analysis, older age at diagnosis (O.R.: 1.35 [per decade]; 95% C.I.: 1.10-1.67), absence of tumor (O.R.: 0.14; 95% C.I.: 0.05-0.43), and less need for ICU admission (O.R.: 0.35; 95% C.I.: 0.18-0.69) were independent variables associated with the absence of NMDAR antibodies in serum. Time to diagnosis, treatments, relapses, and outcome were similar in seronegative and seropositive patients.

Conclusion: 15% of patients with anti-NMDAR encephalitis did not have detectable NMDAR antibodies in serum. These patients were older and had milder neurological symptoms with less frequency of tumors compared with seropositive patients.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EPR1206

Autoantibodies to Annexin A2 and Cerebral Thrombosis: Insights from a Mouse Model

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Background and aims: Antiphospholipid syndrome (APS) is an autoimmune disorder, manifested by thromboembolic events, recurrent spontaneous abortions and elevated titers of circulating antiphospholipid antibodies. In addition, the presence of antiphospholipid antibodies seems to confer a 5fold higher risk for stroke or transient ischemic attack. Although the major antigen of APS is β 2 glycoprotein I, it is now well established that antiphospholipid antibodies are heterogeneous and bind to various targets. Recently, antibodies to Annexin A2 (ANXA2) have been reported in APS. This is of special interest since data indicated ANXA2 as a key player in fibrinolysis. Therefore, in the present study we assessed whether anti-ANXA2 antibodies play a pathological role in thrombosis associated disease.

Methods: Mice were induced to produce anti-ANXA2 antibodies by immunization with ANXA2 (iANXA2) and control mice were immunized with adjuvant only. A middle cerebral artery occlusion stroke model was applied to the mice. The outcome of stroke severity was assessed and compared between the 2 groups.

Results: Our results indicate that antibodies to ANXA2 lead to a more severe stroke as demonstrated by a significant larger stroke infarct volume (iANXA2 $133.9 \pm 3.3 \text{mm}^3$ and control $113.7 \pm 7.4 \text{mm}^3$; $p=0.017$) and a more severe neurological outcome (iANXA2 2.2 ± 0.2 , and control 1.5 ± 0.18 ; $p=0.03$).

Conclusion: This study supports the hypothesis that autoantibodies to ANXA2 are an independent risk factor for cerebral thrombosis. Consequently, we propose screening for anti-ANXA2 antibodies should be more widely used in patients with young onset stroke.

Disclosure: Nothing to disclose

EPR1207

Neurological involvement in Eosinophilic Granulomatosis with Polyangiitis (EGPA) – is there a difference in biological biomarkers?

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Background and aims: Although nervous system involvement may occur in Eosinophilic Granulomatosis with Polyangiitis (EGPA), its clinical manifestations and pathophysiology are still poorly understood. Our goals are: 1-characterize CNS/PNS involvement; 2-analyze if there is a difference in biological markers in patients with and without neurological manifestations.

Methods: Retrospective observational study, including EGPA patients with and without neurological manifestations. Demographics, clinical data and biological markers were collected. Descriptive and inferential statistics were applied.

Results: A total of 14 cases were analyzed, 9 with (group-1) and 5 without (group-2) neurological involvement. Patients from group-1 were older at EGPA diagnosis. Neurological involvement preceded EGPA diagnosis in 5 patients, and occurred during follow-up in 4 patients after a median of 4,5 years. Main CNS manifestations were stroke (n=2), bilateral central retinal artery occlusion (n=1), labyrinthine haemorrhage (n=1) and compressive dorsal myelopathy due to extradural granulation tissue (n=1). Main PNS manifestation were axonal polyneuropathy (n=3), sensorineural hearing loss (n=3) and multiplex mononeuropathy (n=1). 2 patients had both PNS and CNS affected. There were no statistical differences concerning biological markers (eosinophil count, MPO titers) between the 2 groups. All patients were treated with immunosuppressive drugs, with 2 patients unresponsive to treatment belonging to group-1.

Conclusion: EGPA related nervous system manifestations can be very pleomorphic, highlighting 4 distinct neurological scenarios in our sample - peripheral neuropathy, VIII cranial nerve neuropathy, ischemic and hemorrhagic lesions and compressive myelopathy. In our cohort, patients with neurological manifestations did not have different eosinophilic count and MPO titer comparing with patients without neurological involvement.

Disclosure: Nothing to disclose

EPR1208

Patients With Hereditary Transthyretin Amyloidosis: Insights From A Genetic Testing Program

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Background and aims: Hereditary transthyretin (hATTR) amyloidosis is a progressive and fatal disease that results from the deposition of misfolded transthyretin (TTR) protein and leads to multisystem dysfunction, including peripheral neuropathy, cardiomyopathy, and autonomic dysfunction. The hATTR Compass Program offers genetic testing to patients suspected of having, or with a family history of, hATTR amyloidosis in the United States, Canada, and Puerto Rico. We report real-world data from this program.

Methods: Data were analyzed from 165 patients with TTR mutations identified by the hATTR Compass Program using a single gene test or gene panel.

Results: Common mutations were p.V142I/V122I (n=130), p.V50M/V30M (n=10), and p.T80A/T60A (n=12). Average patient age was 64.8 years, and 53.9% (n=89) were male. In patients testing positive for a TTR mutation, 37.6% (n=62) had a known family history, while 53.3% (n=88) and 9.1% (n=15) of patients had no family history or did not know, respectively. The TTR mutation-positive patients were 66.7% (n=110) African American, 16.4% (n=27) white, 6.1% (n=10) other ethnicities, and 10.9% (n=18) unknown. Most patients in this cohort were referred by a cardiologist (n=110; 66.7%), while neurologists referred 8 (4.8%) patients. Patients had clinical histories of sensory, motor, and autonomic dysfunction, gastrointestinal dysfunction, heart disease, and bilateral carpal tunnel syndrome. Most patients (n=97; 58.8%) were 1st referred for genetic testing and diagnosed with hATTR amyloidosis after age 60. Notably, 10.3% (n=17) of patients were diagnosed at or before age 35.

Conclusion: Recognition of hATTR amyloidosis symptoms and subsequent genetic testing facilitates diagnosis of this debilitating, fatal disease.

Disclosure: Commercial/institutional support of research statement: This study was sponsored by Akcea Therapeutics and medical writing support was provided by Apotecom.

EPR1209

Disease Burden and Healthcare Utilization Among Patients with Acute Intermittent Porphyria Experiencing Chronic Neuropathy: Analyses from a National Healthcare Database

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Background and aims: Acute hepatic porphyria (AHP) refers to a family of rare, metabolic diseases that includes four types, acute intermittent porphyria (AIP) being the most common. AHP is characterized by potentially life-threatening acute attacks and, for some patients, chronic debilitating symptoms.

This study aimed to identify AIP patients diagnosed in a nationally representative health care database to estimate healthcare resource utilization among various segments of the AIP patients defined by porphyria attack rates, chronic symptoms, and comorbidities.

Methods: This retrospective analysis utilized the IBM® MarketScan® Commercial Claims and Medicare Supplemental Databases. Patients with at least 1 claim for AIP (ICD-10 diagnosis code E80.21) between October 1, 2015–June 30, 2018 were selected for analyses. AIP patients were segmented by frequency of attacks, presence of chronic symptoms and the presence of comorbidities. This analysis focused on the patient segment specific to chronic neuropathy. Means were reported as per patient per year (PPPY).

Results: 56 (24.9%) patients with chronic neuropathy were identified; 80.4% female, mean (SD) age 49.9 years (14.8). Mean observation time of identified diagnosed patients was 2.0 years. Patients had a mean (SD) of 2.7 (3.4) attacks PPPY; 30.4% had ≥3 attacks/year. The majority had ≥1 hospitalization (57.1%) and emergency department (ED) visit (75.0%), with a mean (SD) of 1.0 (1.4) admissions and 7.5 (23.2) ED visits PPPY.

Conclusion: Results from this national representative healthcare claims database demonstrated AIP patients experiencing chronic neuropathy have high disease burden and healthcare utilization.

Disclosure: This research was funded by Alnylam Pharmaceuticals.

EPR1210

Sjogren's Syndrome and nervous system impairment: A multi-faceted connectivity

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Background and aims: Other than the occurrence of exocrine glands, Sjogren's Syndrome (SS) can be complicated by extraglandular events such as neurological disorders that can inaugurate this autoimmune disease. We aim to study the clinical, biological, radiological characteristics of neurological manifestations of SS.

Methods: This is a retrospective study involving 28 patients hospitalized at our neurology department over a period of 9 years [2010-2019] for neurological events resulted in SS not previously diagnosed. The SS diagnosis was selected according to the criteria developed by the European Consensus Group revised in 2016.

Results: 28 patients were included. The average age at diagnosis was 46.4 years. The average time between the 1st neurological event and the diagnostic confirmation was 2.4 years [20 days, 9 years]. In 15 cases, the clinical manifestations were purely neurological. 18 patients had central signs (ischemic stroke (n=6), acute/subacute myelitis (n=6), cerebellar ataxia (n=2), and focal epileptic seizure (n=4). The hyper signals of the deep white substance (n=9), subcortical (n=11), medullary (n=7), and under cortical atrophy (n=8) were diagnosed by neuroimaging. Anti-SSA and/or anti-SSB antibodies were positive in 18 patients. Primary SS diagnosis was selected in the majority of patients (n=18) with positive SSA antibodies (p=0.002). The best prognosis factors were a young age, the mono-phasic evolution, peripheral nervous system impairment (p<0.05) and a primitive SS.

Conclusion: The clinical diversity of neurological manifestations of SS can often be like ischemic or inflammatory disease, so it needs an identification of biomarkers and therapeutic protocols for better management of that disease.

Disclosure: Nothing to disclose

EPR1211

Analysis of prevalence, prognosis and related factors for neurologic complications in infective endocarditis.

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Background and aims: Neurologic complications (NC) have been associated with poor prognosis in infective endocarditis (IE). We aimed to determine the prevalence of NC in patients with IE, identify related factors and define their prognostic impact.

Methods: An observational/retrospective study in patients diagnosed with IE between 2008 and 2017. Demographic and clinical characteristics were obtained. A descriptive/comparative analysis was performed.

Results: 496 patients diagnosed with IE were included. 318 (64.1%) were male, with a mean age of 64.76 years (SD±2.02). Staphylococcus aureus (28.6%) was the most frequent microorganism. Mitral valve (48.6%) was the most frequently affected valve. 66 subjects developed NC (13.3%). 46 (69.7%) cases of ischemic stroke, 13 (19.7%) of intracranial hemorrhage, 5 (7.6%) of brain abscesses and 3 (4.5%) of encephalopathy were identified. In 42 (63.6%) patients, the NC preceded the diagnosis of IE; in the rest, the median to the appearance of NC was 14 days (RIC:19). NC implied changes in the treatment of IE in 28 patients (42.4%), mainly cessation of anticoagulation (16.7%). NC delayed the surgical treatment in 15 (22.7%) subjects. Patients with NC had higher mortality than those without NC (42.4% vs 27.9%; p=0.016). In univariate analysis, subjects with NC showed a higher frequency of previous stroke (27.3% vs 15.6%; p=0.018), hypertension (75.8% vs 54.4%; p=0.004), valvulopathy (69.7% vs 53.7%; p=0.040) and systemic embolisms (28.8% vs 16.5%; p=0.030). In multivariate analysis, hypertension (OR=2.45; 95%-CI=1.30-4.62) and systemic embolisms (OR=2.82; 95%-CI=1.49-5.34) remained as associated factors.

Conclusion: NC are associated with higher mortality in patients with IE. Hypertension and systemic embolisms are factors related to the development of NC.

Disclosure: Nothing to disclose

EPR1212

A clinical and instrument-based investigation of large and small nerve fibre impairment impacts on patients' management in ATTR-amyloidosis and provides new insights in wild-type ATTR-amyloidosis

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Background and aims: Polyneuropathy in ATTR amyloidosis is frequently underdiagnosed delaying effective treatment. In these patients, applying a comprehensive diagnostic algorithm could improve the detection of large and small nerve fibre impairment.

Methods: Clinical and instrument-based algorithm, including nerve conduction studies-NCS, quantitative sensory testing-QST, sympathetic skin response-SSR, quantitative sudomotor axon reflex testing-QSART and skin punch biopsies in ATTR-amyloidosis patients of the Interdisciplinary Amyloidosis Center of Northern Bavaria.

Results: 24 patients (20 wild-type-ATTRwt, 4 hereditary-ATTRv) with a median age of 76 years for ATTRwt and 70 years for ATTRv were examined. Clinical and electrophysiological findings of large fibre polyneuropathy were found in 75% of ATTRv (sensory and motor, axonal) and in 60% of ATTRwt patients (sensory and motor, predominantly axonal). In 45% of ATTRwt patients no other cause for polyneuropathy was identified after reviewing for relevant co-morbidities. Small-fibre impairment was shown in both groups. QST was abnormal in all ATTRv patients and in 80% of ATTRwt patients, SSR at the foot was absent in 5/24 patients (2 with ATTRv). QSART-response in ATTRwt group was disturbed in a length-dependent pattern. Skin biopsies (from 14 patients) showed reduced intraepidermal nerve fibre density-IENFD in all ATTRv and 7 ATTRwt patients (in 5 generalized and in 2 distal IENFD reduction). Disease progression was determined according to our test results in 3 ATTRv patients leading to change of therapy.

Conclusion: Interestingly, there is a high percentage (45%) of polyneuropathy with small fibre and autonomic impairment in ATTRwt amyloidosis patients. Using a comprehensive neurological work-up program in ATTR amyloidosis influenced treatment in our cohort.

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EPR1213

Erdheim-Chester disease (ECD) case-series: expanding the clinical and neuroradiological spectrum

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Background and aims: Erdheim-Chester disease (ECD) is a subtype of adult-onset and multi-systemic histiocytosis (non-Langerhans histiocytosis), often associated with central nervous system (CNS) involvement. In this report we describe a 4 patients case-series, affected by ECD, through a full-comprehensive clinical and instrumental characterization, to expand the clinical and neuroradiological spectrum of this rare disease.

Methods: 4 patients (mean age at 1st evaluation 62.7-years old), evaluated in our neurological center from December 2015 to November 2019, underwent multisystemic clinical and radiologic examination, plus neuropsychological, neurophysiological and histopathologic studies (tibia, femur, cerebellar biopsies). 1 patient, with the rare CNS histiocytic sarcoma variant, underwent haematopoietic stem-cell transplantation (HSCT).

Results: 4/4 patients presented with cerebellar symptoms (gait ataxia and dysarthria), 2/4 manifested pseudobulbar crying and laughing at disease onset. All brain MRI showed cerebellar and brainstem alterations (in 2/4 punctiform white matter contrast-enhancement, basal ganglia iron accumulation in 2/4, cerebellar atrophy in 1/4).

Conclusion: This report expands the clinical and radiological spectrum of ECD, describing possible atypical clinical onset of this rare disease, such as pathological crying and laughing, probably explained by the alteration in pontine-cerebellar-cortical network; besides, the case-series highlights atypical MRI patterns such as contrast-enhanced punctiform cerebral white matter alteration and outline different disease progression. Moreover, in 1 fatal case, we hypothesized the coexistence of the typical ECD inflammatory/infiltrative pattern and a pseudo-degenerative progression with cerebellar atrophy and brain iron accumulation in basal ganglia areas.

Disclosure: Nothing to disclose

EPR1214

Arterial wall stiffness measured by the cardio-ankle vascular index (CAVI) is associated with neurocognitive impairment in people living with well-controlled HIV in Thailand

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Background and aims: HIV-associated neurocognitive disorders (HAND) remain prevalent in people living with HIV (PLWH) despite widespread use of antiretroviral therapy (ART). Endothelial dysfunction potentially contributes to HAND pathogenesis. In this cross-sectional pilot study we tested whether cardio-ankle vascular index (CAVI), a novel blood method to assess arterial stiffness, is associated with HAND.

Methods: We recruited 75 non-diabetic adult PLWH from an HIV clinic in Thailand. All subjects took ART and had viral loads <50copies/mm³. We collected information regarding demographics, HIV history, medications, and comorbidities. We calculated Thai CVD scores (RAMA-EGAT; estimating 10-year risk of cardiovascular disease/stroke) and measured CAVI using the VaSera SystemTM. Subjects completed a comprehensive neurocognitive battery. Neurocognitive impairment, accounting for age and education, was defined according to the Frascati criteria (Antinori et al.2007). We constructed logistic regression models to test if high CAVI (≥8) was independently associated with neurocognitive impairment.

Results: 52.0% of the sample (age 45.6±8.3 years, 30.1% male) met criteria for neurocognitive impairment. None had dementia. The population had few cardiovascular risks - see Table 1. 12 patients had high CAVI (≥8), signifying stiffer arteries. High CAVI was independently associated with HAND (odds ratio=7.6; p=0.04), accounting for gender, income, CD4 nadir, recent CD4, and CVD score (see table 2).

Table 1. Characteristics of the sample, n=75

Variable	mean ± S.D. / n(%)	Variable	mean ± S.D. / n(%)
Age	45.6 (8.3)	Income (Thai Baht per month) ⁶	
Male gender	23 (30.7)	less than 3,000	5 (6.7)
Cardio-ankle vascular index	7.1 ± 0.93	3,000-7,999	13 (17.3)
Dyslipidemia history	34 (45.3)	8,000-14,999	30 (40.0)
Body mass index ≥ 25.0	9 (12.0)	greater than 15,000	27 (36.0)
Body mass index < 18.5	12 (16.0)	Educational attainment	
Body mass index	21.6 (3.7)	some primary school	23 (30.7)
CVD score ^a	2.2 ± 1.6	some secondary school	24 (32.0)
Total cholesterol ^a	174.4 (35.4)	some college	9 (12.0)
Triglycerides ^a	125.4 ± 71.2	bachelor degree or higher	19 (25.3)
High density lipoprotein (mg/dL) ^a	57.2 ± 15.6	CD4 nadir < 50 cells/mm ³ ^d	25 (33.3)
Low density lipoprotein (mg/dL) ^a	11.4 ± 34.9	CD4 nadir (cells/mm ³) ^e	149.5 ± 176.2
Fasting blood sugar (mg/dL) ^b	94.3 ± 9.1	Years since CD4 nadir	10.6 ± 4.8
Systolic blood pressure (mmHg)	124.0 ± 11.9	Most recent CD4 (cells/mm ³)	659.3 ± 277.7
Diastolic blood pressure (mmHg)	79.2 ± 9.9	Years since initial HIV diagnosis	14.7 ± 7.2
Statin use		Years on antiretroviral therapy	11.6 ± 5.2
yes	10 (13.3)	History of abacavir use	5 (6.7)
no	46 (61.3)	History of efavirenz use	51 (68.0)
maybe (in placebo-controlled trial)	19 (25.3)	History of protease inhibitor (PI) use	23 (30.7)
Active smoker	13 (17.3)	Didanosine or stavudine (d-drug) history	47 (62.7)
Hypertension history	7 (9.3)	Cumulative PI exposure (years)	1.7 ± 3.4
History of AIDS defining infection	26 (34.7)	Cumulative d-drug exposure (years)	3.1 ± 3.5

S.D.=standard deviation; CVD score = Thai 10-year risk of cardiovascular disease or stroke; ^an=71; ^bn=72; ^c1 US dollar = 30 THB; ^dn=74

Table 1

Table 2. Results from logistic regression analysis demonstrating the adjusted relationship between high cardio-ankle vascular index (CAVI) and neurocognitive impairment^a

Variable	p-value	Exp(B)/odds ratio	95% CI of Exp(B)
High CAVI (≥ 8)	0.04	7.6	1.1-50.2
Gender	0.06	3.4	1.0-12.4
CD4 nadir < 50 cells/mm ³	0.30	0.5	0.2-1.8
Recent CD4	0.33	1.0	1.0-1.0
10-year CVD score ≥ 3%	0.68	0.7	0.2-3.3
Income < 8,000 baht (~ \$270) per month	0.05	4.0	1.0-16.0

^aResults from logistic regression analysis ("enter" method, criteria for entry p < 0.05, removal p > 0.10); model Nagelkerke R² = 0.2, p = 0.04, 71 subjects with complete data

Table 2

Conclusion: CAVI is a promising measure of endothelial dysfunction that may be independently associated with neurocognitive impairment in relatively healthy PLWH. Larger studies are necessary to confirm these findings; extend them to other HIV-infected populations; and test whether CAVI predicts neurocognitive decline in PLWH.

Disclosure: Nothing to disclose

EPR1215

Hypertrophic pachymeningitis: new horizons in diagnosis.

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Background and aims: Hypertrophic pachymeningitis (HP) is a rare entity characterized by an inflammatory thickening of the dura mater. The etiologies of HP include infections, malignancy, inflammatory or autoimmune diseases. Recently an association between different antibodies such as p-ANCA and HP has been described. Our goal is to analyze the main etiologies of HP and its clinical, analytical and radiological characteristics.

Methods: We reviewed the medical records of 9 patients with HP in the Neurology Department of the Hospital Central de Asturias.

Results: We found 9 patients with a diagnosis of HP, 5 men with a mean age of 64.8 years. The most frequent symptom was headache and 3 patients developed intracranial hypertension. The most frequent radiological pattern was diffuse cerebral pachymeningitis in 6 patients, 2 presented spinal involvement and 1 associated bilateral temporal parenchymatous edema. Regarding the etiology, 3 were granulomatous polyangeitis, 2 of them with positive MPO-type p-ANCA, 2 tuberculous infections, one associated with systemic lupus erythematosus and another 1 with rheumatoid arthritis, a post-traumatic 1 and another 1 of unknown etiology although presumably inflammatory due to its good response to corticosteroids. The HP with positive MPO-type p-ANCA were the best response to immunosuppressive treatment.

Conclusion: HP is an entity whose etiopathogenesis was unknown until recently. With the recent appearance of new antibodies involved such as p-ANCA (MPO) it is possible that many of the HP previously classified as idiopathic have an autoimmune substrate and therefore an effective treatment by immunosuppressants, especially those that have associated meningeal and parenchymal inflammation.

Disclosure: Nothing to disclose

Neuro-ophthalmology/neuro-otology

EPR1216

Visual function disorders and brain morphometric changes in development visual hallucinations in Parkinson's disease

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Background and aims: Pre-geniculate visual disturbances are part of non-motor symptoms in Parkinson's disease (PD). Visual processing deficiency due to brain regulating structures dysfunctions causes visual hallucinations (VH). The question arises about relationship between visual perception condition and structural changes in the brain.

Aim: to identify the correlation between visual functions and morphometric MRI parameters in PD patients with VH.

Methods: 38 non-demented PD patients were divided into 2 groups according to the presence or absence VH. 20 age-matched controls were also examined.

All participants underwent electroretinography (ERG) and computer perimetry with using 24-2-SITA and 60-4-SITA algorithms for determination of sensitivity thresholds in the central and peripheral retina. MRI study was performed with using voxel-based morphometry.

Results: PD patients with VH had longer disease duration, without differences between groups in age and PD severity. For PDpatients characteristic was a significant decrease in rod-response (scotopic ERG) and sensitivity thresholds in the peripheral retina as compared with the control group, but more pronounced in PD patients with VH (table).

MRI morphometry determined some features in patients with VH: they have significantly reduced brain volumes in the posterior parietal cortex, optic chiasm and increase in the amygdale in comparison with PDpatients without VH.

Conclusion: Predominance the blurred VH at the peripheral border of the VF in PDpatients has a direct relationship with rod system involvement and decreased visual input from retinal peripheral regions. These changes are combined with more pronounced hypotrophy in the ventral visual pathways structures (responsible for localization external objects in the space), probably amid amygdale over-activation.

Disclosure: Nothing to disclose

Table. Comparative assessment of the parameters of the studied groups

Parameters	Control group	1st group	2nd group
	n = 20	(patients with VH) n = 18	(patients without VH) n = 20
	Me (Q1, Q3)		
Age (years)	55 (50; 62)	58 (53; 64)	56 (51; 64)
UPDRS total	--	49 (40; 63)	47 (41; 60)
Part I	--	8 (6; 9)	7 (5; 9)
PD duration	--	8 (5; 12)	6 (3; 9)*
Maximal ERG	N1 Latency, ms	23.1 (19.0; 24.3)	22.5 (18.0; 23.5)
	N1 Amplitude, µB	160.0 (134.0; 173.0)	84.6 (65.6; 114.5)
	P1 Latency, ms	44.0 (40.5; 45.8)	43.2 (40; 44.5)
	P1 Amplitude, µB	282.0 (260.0; 290.0)	168.5 (139.3; 225.8)
Rod ERG	P1 Latency, ms	63.5 (60.0; 65.0)	64.5 (61.0; 67.5)
	P1 Amplitude, µB	63.1 (57.7; 69.2)	32.0 (23.5; 44.0)*Δ
24-2-SITA threshold tests			
Total photosensitivity of the central retina, dB	1351 (1243; 1457)	1330 (1221; 1423)	1328 (1216; 1448)
60-4-SITA threshold tests			
Total photosensitivity of the peripheral retina, dB	1225 (1189; 1274)	737 (709; 887)	909 (875; 942)*Δ

* - Statistically significant difference (p < 0.05) between 1st and 2nd groups (Mann-Whitney test);

Δ - Statistically significant difference (p < 0.05) between control, 1st groups and 2nd groups (Kruskal-Wallis test)

Table. Comparative assessment of the parameters of the studied groups

EPR1217

Vergence deficits in focal cerebrovascular lesions: a prospective study in 305 inpatients

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Background and aims: A widely distributed network of midbrain, pontine, cerebellar and cortical areas subserves the neural control of vergence. I might therefore anticipate various vergence deficits in stroke patients. Here, we investigated the localizing value of bedside vergence testing with respect to different supra- and infratentorial infarction locations.

Methods: 305 patients stroke patients and 50 age-matched controls were assessed prospectively by means of bedside tests in order to evaluate slow and fast binocular (i.e. symmetrical) as well as slow and fast monocular (i.e. asymmetrical) vergence. Stroke locations, as identified on MRI, were correlated to vergence function using multinomial logistic regression.

Results: Vergence performance declined with age in both stroke patients and healthy controls. Most infarction locations were not systematically associated with vergence parameters, apart from cases with parietal lobe lesions, which showed insufficient monocular, slow and fast, vergence. Finally, patients with severe ischemic small vessel disease (Fazekas 2 or 3) showed a slight but significant decrease in their fast binocular vergence function.

Conclusion: There is only a limited localising value of vergence insufficiency in stroke. Parietal lobe lesions are more frequently associated with deficient binocular and monocular convergence. Older subjects show poor slow binocular, as well as slow and fast monocular vergence, since age was the most robust factor to emerge from our data. Extended small vessel disease also correlated with deficient vergence function suggesting a role for subcortical wide range connections in maintaining an intact vergence circuitry.

Disclosure: Nothing to disclose

EPR1218

Acute Unilateral Vestibulopathy Does Not Impair Cognition

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Background and aims: To evaluate cognition in patients with acute unilateral vestibulopathy (AUV).

Methods: 21 patients with (AUV) diagnosed both clinically and with caloric testing and cervical VEMP testing were evaluated for the cognitive functions by using Mini Mental State Examination, Oktem Verbal Memory Process, Forward and Backward Digit Span, Benton's Judgment of Line Orientation, Verbal and non-verbal Cancellation and Rey-Osterrieth Complex Figure tests. Beck depression and Anxiety inventories were also given. The results were compared with the results of 20 age and sex matched healthy controls. IBM SPSS Statistics 25.0 package program was used for the statistical analysis.

Results: Demographic and clinical features of the patients are given in Figure 1. Mean percentage of canal paresis was 62% (SD: 22.4%). In 4 patients p13/n23 potential was absent and in the remaining 17 delayed on the affected side (p<0.005).

Comparison of the results of the Verbal and non-verbal Cancellation (p=0.005), Benton's Judgment of Line Orientation (p=0.042) and Backward Digit Span (p=0.029) test of the patients with the healthy controls revealed abnormalities. A very prominent difference was present regarding Beck depression (p=0.012) and anxiety inventories (p<0.001) (Figure 2). Unlike the results of the univariate multiple regression analysis revealed that Cancellation, Benton's Judgment of Line Orientation and Backward Digit Span test results were not significantly different from the healthy controls (p>0.05) when depression and anxiety scores were taken into consideration.

	Patients	Controls
Number	21 (12M, 9 F)	20 (13M, 7F)
Age (years)	Mean: 54.3, SD: 10.3 Median: 56 (min: 35, max:)	Mean: 49.3, SD: 8.5 Median: 48 (min:, max:)
Education (years)	Mean: 12.3, SD: 4 Median: 12 (min:5, max: 16)	Mean: 13.7, SD: 3.4 Median: 16 (min 5, max: 16)
Date of the test (days)		Mean:13.4, SD: 10.2 Median: 12 (min:, max:)
Affected ear		R: 10 L: 11
p13 latency (ms)		Affected ear: Mean: 14.2, SD: 3.5 Non-affected ear: Mean: 12.3, SD: 1
n23 latency (ms)		Affected ear: Mean: 25.4, SD: 5.1 Non-affected ear: Mean: 23.4, SD: 3.1

Figure 1

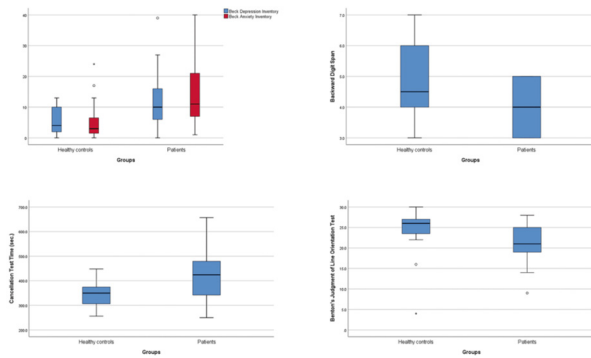


Figure 2

Conclusion: Cognitive tests mainly assessing concentration, immediate recall and spatial attention seem to be affected due to accompanying anxiety in patients with AUV.

Disclosure: Nothing to disclose

EPR1219

Modulation of slow-phase velocity and graviceptive perception in the roll plane in patients with idiopathic downbeat nystagmus

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Background and aims: Downbeat-nystagmus (DBN) exhibits a well-known gravity dependent modulation in the pitch-plane. We examined DBN modulation in the roll-plane in patients with idiopathic DBN. Furthermore we assessed dynamic graviceptive perception using the Subjective Visual Vertical (SVV).

Methods: DBN was assessed in 26 patients with idiopathic DBN using videooculography at head upright position and tilted $\pm 30^\circ$ in the roll plane. SVV was assessed at the same head positions using an illuminated bar. SVV-estimates from 13 healthy subjects served as normal controls.

Results: Slow-phase velocity (SPV) of DBN in patients at 0° head position ranged from 1 to 9deg/sec, Median 2deg/sec (IQR 1, 3). SPV at 30° head tilt to the left ranged from 1 to 8deg/sec, Median 2deg/sec (1, 4) and at 30° head tilt to the right from 1 to 8deg/sec, Median 2deg/sec (1, 3), thus yielding no statistically significant differences between 0° head position and 30° head-tilts (30° left: $p=0.22$; 30° right: $p=0.14$). SVV-responses at 0° head position showed no significant difference between groups ($p=0.35$, MD 1,08). Also no significant SVV-differences were found between groups at 30° head tilts (30° left: $p=0.86$, MD 0,17; 30° right: $p=0.06$, MD 4,08).

Conclusion: We showed that DBN does not exhibit a gravity-dependent modulation in the roll-plane. Furthermore, we could demonstrate that dynamic graviceptive perception in DBN patients, using SVV estimates, does not differ significantly from normal controls. However, patients showed a higher variability in their SVV-adjustments at all head positions.

Disclosure: Nothing to disclose

EPR1220

Optic Neuropathy: a 15-year retrospective observational studyJ.M. Alves¹, M. Seabra², L. Braz², J. Guimaraes²¹Faculty of Medicine of the University of Porto, Porto, Portugal, ²Porto, Portugal

Introduction: Optic neuropathies (ON) have several aetiologies and sometimes the diagnosis established ab initio is redefined after further investigations and/or new neurological events.

We aim to identify possible predictive factors that may dictate that diagnostic change during follow-up.

Methods: We retrospectively reviewed the medical records of 156 patients with ON admitted to the ward of our Neurology Department, between January 2004 and August 2019. Clinical, laboratory and imaging data, as well as treatment protocols and follow-up were analysed.

Results: At the time of discharge from the ward, our cohort comprised 83 idiopathic ON (53.2%), 38 multiple sclerosis-related ON (24.4%), 23 ischemic ON (14.7%), 5 neuromyelitis optica spectrum disorder-related ON (3.2%), and 7 with other diagnoses (4.5%). During follow-up, 129 patients retained the ward's discharge diagnosis (82.7%) while in 27 it was redefined (17.3%). The median time between admission and change in diagnosis was 12.3 (5.4-42.9) months. Multivariate Cox regression analysis demonstrated that the patients with atypical optic neuropathy (presence of one of these clinical findings: bilateral eye involvement, visual acuity ≤ 0.1 at admission, worsening or non-substantial recovery of visual acuity during hospitalization) had lower risk of having the initial diagnosis changed (HR=0.320, 95% CI=0.138-0.743, p=0.008).

Conclusion: Our study illustrates that some patients admitted with optic neuropathy may have their diagnosis redefined during follow-up. Furthermore, it demonstrates that patients with atypical ON are those in which the diagnosis is more likely to remain during follow-up.

Disclosure: Nothing to disclose

EPR1221

Ocular flutter as a treatment-responsive symptom in Lyme disease

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Background and aims: Ocular flutter has been reported only once before as 1st manifestation in Lyme disease (Gyllenborg and Milea, Neurology 2009). We observed gait ataxia and ocular flutter as major clinical symptoms in a 71 year old man with confirmed diagnosis of Lyme disease.

Methods: Vestibular- and ocular motor function tests were performed using video-oculography and a rotational chair system (System 2000, Micromedical Technologies, Illinois, USA). Testing was performed upon hospital admission as well as 4 weeks after symptomatic onset and after antibiotic treatment has been stopped.

Results: The diagnosis was made based on pleocytosis in CSF as well as a positive antibody index (CSF-to-serum) against *Borellia burgdorferi*. An additional MRI of the brain was negative. Ocular flutter was objectified by video-oculography. After 14 days of intravenous therapy with Ceftriaxone and subsequent oral therapy with Doxycycline, the patient's condition improved significantly. 4 weeks after the onset of the disease there was a complete remission with normalization of the pre-existing ataxic gait. In addition, a follow-up video-oculography showed normal eye movement parameters without evidence of ocular flutter.

Conclusion: We hereby report a 1st case of ocular flutter and gait ataxia as the main symptom of a confirmed Lyme disease with complete remission after antibiotic treatment.

Disclosure: Nothing to disclose

EPR1222

Effectiveness of intravenous zoledronic acid in the prevention of benign paroxysmal positional vertigo in the elderly with osteoporosisD.W. Kwack¹, D.W. Kim²¹Neurology, Konkuk University Medical Center, Seoul, Korea, Korea, Republic of, ²Neurology, Konkuk University Medical Center, Seoul, Korea, Republic of

Background and aims: Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo in the elderly. Recent studies suggest that osteoporosis may be related to the occurrence of BPPV. We examine the efficacy and safety of intravenous zoledronic acid (ZOL) in elderly patients with idiopathic BPPV.

Methods: A prospective study was conducted to examine the recurrence of BPPV and adverse effects of ZOL in elderly BPPV patients. The mean T-scores were assessed by dual energy x-ray absorptiometry (DXA). Patients who met the diagnostic criteria of osteoporosis were recommended to treat with ZOL. The developments of side effects were evaluated and recurrences of BPPV were followed up 1 year later.

Results: 104 BPPV patients were enrolled and 101 of them underwent DXA. The mean lowest T-score of all patients was 2.44 ± 1.11 (range $-4.90 \sim 1.00$) and 54 patients were diagnosed with osteoporosis. The prevalence of osteoporosis was higher in women and the advanced age. 51 patients were treated with ZOL and 8 of them complained of flu-like symptoms. 1 year later, only 2 patients had recurrence of BPPV among 49 patients (4.08%). 23 patients underwent follow-up DXA at one year later, and the mean T-score was improved from -3.23 ± 0.51 to -3.05 ± 0.58 ($p=0.001$, by paired t test).

Conclusion: This result shows that the high incidence of osteoporosis in elderly patients with idiopathic BPPV. It can be suggested treatment with ZOL in old age BPPV patients with osteoporosis might prevent the recurrence of BPPV for 1 year.

Disclosure: Nothing to disclose

EPR1223

A novel CACNA1A gene mutation causing Episodic Ataxia Type 2J. Penkava¹, P. Zu Eulenburg¹, D. Huppert¹, M. Strupp², S. Becker-Bense¹¹German Center for Vertigo and Balance Disorder, Ludwig Maximilians University, Munich, Germany, ²Department of Neurology, University Munich, Munich, Germany

Background and aims: Autosomal-dominant episodic ataxias (EA) represent rare neurological disorders with recurrent atactic attacks. EA 2 is caused by a wide range of mutations of the CACNA1A gene on chromosome 19p13 encoding the alpha subunit of the P/Q-type voltage-gated calcium channel with high expression in cerebellar Purkinje cells, thereby inducing channelopathy. Here we report a novel CACNA1A mutation in a 47-year-old female patient with an EA 2 phenotype: Since the age of 17 she suffers from recurrent attacks typically triggered by emotional stress, that last for several hours and are accompanied by postural imbalance, headache, and rarely nausea. Intermittently she feels permanently dizzy and postural unstable.

Methods: Detailed patient history, clinical and orthoptic examination, video-Head-Impuls-test (v-HIT), video-oculography (VOG) and bithermal caloric testing were assessed. For genetic testing Next Generation and Sanger sequencing methods were applied.

Results: The patient showed clinically and in the VOG permanent cerebellar ocular motor dysfunction (horizontal gaze evoked and rebound nystagmus, horizontal/vertical saccadic pursuit, hypermetric horizontal saccades, optokinetic deficit) and a bilateral central VOR-deficit. Finger following showed slightly hypermetric movements. Genetic testing uncovered a novel heterozygous variant in exon 16 of the CACNA1A gene leading to a frameshift during translation and an early stop of protein biosynthesis at codon position 698. Symptomatic standard treatment with acetazolamide and 4-aminopyridine was unfortunately not effective.

Conclusion: We report on a novel variant of a CACNA1A mutation in a female patient with a typical EA 2 phenotype. The non-responding to standard therapies raises the question of genotype-phenotype correlations.

Disclosure: Nothing to disclose

EPR1224

Benign paroxysmal positional vertigo: The “Sémont PLUS maneuver” is more effective than the Sémont maneuver – a prospective multinational randomized single-blinded trial

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Background and aims: To compare the efficacy of the Sémont (“SM”) with the new “Sémont PLUS maneuver” (“SM+”) in a prospective multinational randomized single-blinded trial in patients with posterior canal benign paroxysmal positional vertigo (pc-BPPV).

Methods: In a prospective multinational (Germany, Italy, Belgium) randomized single-blinded treatment trial patients with proven posterior canal BPPV – according to the diagnostic criteria of the International Classification of Vestibular Disorders – were randomly assigned (1:1) to the “SM” or “SM+”. The latter is characterized by an overextension of the head/body by 45° below earth horizontal line during step 2 of the maneuver. The 1st 3 maneuvers were performed by the physician. The patients were then instructed on how to do the maneuvers which they should perform 3times in the morning, 3times at noon and 3times at night. Each morning after the 1st maneuver of each day the patient documents in a standardized evaluation sheet, whether vertigo occurred or not. The primary endpoint was: “How long (in days) does it take until no attacks can be induced “in the morning” by the maneuvers?”

Results: In the 167 patients analysed it took 3.9 days (mean; range 1-33 days) for the “SM” and only 2.3 days (range 1-32 days) for the “SM+” for recovery ($p=0.015$, Mann-Whitney-u-test).

Conclusion: This prospective multinational randomized trial showed that the “SémontPLUS maneuver” is significantly more effective than the Sémont maneuver. It also confirms the hypothesis based on a biophysical model of BPPV.

Disclosure: M. Strupp is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. He has received speaker’s honoraria from Abbott, Actelion, Auris Medical, Biogen, Eisai, Grünenthal, GSK, Henning Pharma, Interacoustics, MSD, Otometrics, Pierre-Fabre, TEVA, UCB. He is a share holder of IntraBio. He acts as a consultant for Abbott, Actelion, AurisMedical, Heel, IntraBio and Sensorion.

EPR1225

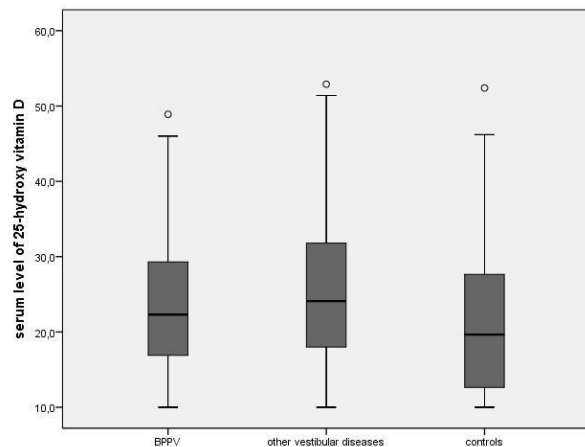
Vitamin D level in vestibular disorders: no evidence for a specific deficit in benign paroxysmal positional vertigo

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Background and aims: To investigate whether there is a difference in vitamin D levels in patients with benign paroxysmal positional vertigo (BPPV) vs. patients with other vestibular diseases or controls with other neurological diseases but no history of dizziness or vertigo presenting in the neurological outpatient clinic of the LMU in Munich.

Methods: In a prospective study, we measured the serum levels of 25-hydroxy vitamin D in 559 patients (302 male, age 18-91 years, mean age±SD 59±16) without intake of vitamin D supplementation. 146 patients had BPPV, 193 patients other vestibular diseases (including 103 patients with peripheral vestibular disorders, such as acute unilateral vestibulopathy or Menière’s disease; 39 patients with central vestibular disorders, such as vestibular migraine or cerebellar dizziness; 51 patients with functional dizziness), and 220 controls had other neurological diseases but no history of vertigo (including 105 patients with cognitive deficits, 18 with headache, 17 with depression, 80 with other diseases).

Results: There was no statistical difference in the 25-hydroxy vitamin D levels between patients with BPPV (min. <10, max. 49ng/ml, mean±SD 24±9ng/ml) and other vestibular disorders (min. <10, max. 53ng/ml, mean±SD 25±10ng/ml). Controls in our clinic had significantly lower blood levels (min. <10, max. 52ng/ml, mean±SD 21±10ng/ml) than both vertigo groups. There was also no difference between recurrent BPPV and one-off BPPV (26±10 vs. 23±9ng/ml).



Conclusion: Our analysis does not support the idea of a specific relationship between the levels of 25-hydroxy vitamin D and BPPV or other vestibular or neurological disorders.

Disclosure: Nothing to disclose

EPR1226

Quality of life and functional impairment in acute vestibular disorders

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Background and aims: Acute vestibular symptoms have a profound impact on patients' well-being. In this study, quality of life (QoL) and perceived impairment were investigated prospectively in different peripheral and central vestibular disorders during the acute symptomatic stage to decipher the most relevant underlying factors.

Methods: 175 patients with acute vestibular symptoms were categorized in the subgroups central, peripheral and episodic disorders (CV: n=47; PV: n=68; EV: n=67). QoL and symptom intensity was quantified in all patients (EQ-5D-5L, DHI). Vestibular-ocular motor signs were assessed by video-oculography, vestibular-spinal control by posturography and verticality perception by assessment of subjective visual vertical (SVV).

Results: Patients with PV had a poorer QoL and higher symptom intensity (EQ-5D-5L/DHI: $0.53 \pm 0.31/56.1 \pm 19.7$) than patients with CV ($0.66 \pm 0.28/43.3 \pm 24.0$) and EV ($0.75 \pm 0.25/46.7 \pm 21.4$). After adaptation for age, gender, cardiovascular risk factors and non-vestibular brainstem/cerebellar dysfunction PV patients persisted to have significantly poorer QoL (EQ-5D-5L: -0.17) and higher symptom intensity (DHI: +11.2) compared to CV patients. Horizontal spontaneous nystagmus (SPN) was a highly relevant factor for subgroup differences, while vertical SPN, SVV and sway path were not. EQ-5D-5L decreased with more intense horizontal SPN in CV ($R^2 = -0.57$) and PV ($R^2 = -0.5$), but not EV ($R^2 = -0.13$).

Conclusion: Patients with PV have the highest perceived impairment of all patients with acute vestibular disorders. Vestibular-ocular motor disturbance in the yaw plane has more impact than vestibular-spinal or -perceptive asymmetry in the roll and pitch plane, suggesting that horizontal visual stability is most critical for QoL.

Disclosure: Nothing to disclose

Sleep disorders 1

EPR1227

Cancelled

EPR1228

Narcolepsy type 1 associated with paraneoplastic limbic encephalitis in mediastinal seminoma

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Background and aims: Narcolepsy type 1 (NT1) is a chronic hypersomnia of central origin linked to the selective damage of hypothalamic hypocretin producing neurons. 2ndary NT1 has been associated with several conditions such as paraneoplastic/autoimmune encephalitis, hypothalamic damage. Here we report a case with NT1 arising in the context of a limbic encephalitis associated with mediastinal seminoma.

Methods: Clinical, neuroradiological, anatomopathological, biological and polysomnographic single patient study.

Results: A 19-year-old man developed insomnia, hyperphagia and sexual dysfunction, rapidly followed by excessive daytime sleepiness with frequent sleep attacks. Brain MRI showed T2 hyperintense lesions involving hypothalamus and optic tracts, cerebrospinal fluid (CSF) revealed a mild pleocytosis consistent with limbic encephalitis. Test for anti-neuronal antibodies were negative, and Total-body CT showed a mediastinal mass, which was diagnosed with Mediastinal Multicystic Seminoma at biopsy. After surgery and chemotherapeutic treatment, despite neuroradiological findings progressively disappeared, the patient did not display any significant clinical improvement. Clinical and polysomnographic (night- and continuous polysomnography and multiple sleep latency test - MSLT) assessment at 21 year of age disclosed hypersomnia with multiple sleep onset REM periods, CSF-hypocretin-1 was 110pg/mL, leading to a NT1 diagnosis. The patient carried the HLA DQB1*0602 allele. Sodium Oxybate treatment improved nocturnal and daytime symptoms. During follow-up the patient developed a depressive syndrome and an obsessive compulsive disorder.

Conclusion: Paraneoplastic limbic encephalitis triggered NT1 in a genetically predisposed patient. Prompt disease recognition and treatment for narcolepsy could improve patients outcome.

Disclosure: Nothing to disclose

EPR1229

Association of probable REM sleep behaviour disorder with restless legs syndrome in Parkinson's disease population.

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Background and aims: Sleep disorders are prevalent in Parkinson's disease (PD). REM behaviour disorder (RBD) and restless legs syndrome (RLS) being among most frequent. RBD has stronger association with PD compared to RLS. Our aim was investigating prevalence of probable RBD (pRBD) in PD patients in relation to RLS.

Methods: PD was diagnosed by UK Parkinson's Disease Society Brain Bank criteria. pRBD diagnosis was based on history of witnessed dream enactment with speaking and moving in sleep. RLS was diagnosed using International RLS Study Group's four essential criteria. Our sample was divided into 2 groups: with RLS (PDRLS) and without RLS (PDNoRLS). PD disease duration (DD) and severity data were also included. Chi-Square test was used for statistical analysis.

Results: 85 patients (F-55.3%, age mean 63.3) were enrolled, with mean DD – 5.1 years and mean H&Y stage 2.1. RLS was diagnosed in 18.8% (16) of them and pRBD was diagnosed in 28.2% (24). Age, gender distribution and disease duration were equal between groups. H&Y score was higher in PDRLS: 2.5 vs 1.98 ($p<0.03$). The prevalence of pRBD in PDRLS group was 50% (8), while in PDNoRLS it was about half of that - 23.2% (16) ($p<0.05$).

Conclusion: Our data show that pRBD prevalence was significantly higher in PD patients with RLS compared to patients without RLS. This finding supports recent evidence of probable RBD being a risk factor for developing of RLS in PD. Also, our finding could contribute to the longlasting dispute on RLS-PD intrinsic relationship.

Disclosure: Nothing to disclose

EPR1230

Non-motor burden in Isolated REM Sleep Behaviour disorder: systematic evaluation in a prospective cohort

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Background and aims: Consistent evidence demonstrated how isolated REM sleep behaviour disorder (iRBD) can be the prodromal stage of an overt α -synucleinopathy. The presence of cognitive and autonomic impairment increases the risk of conversion, but a comprehensive and detailed evaluation is rarely available.

Methods: We consecutively enrolled a cohort of iRBD patients and a cohort of matched controls (CTRs). Each subject underwent a battery of standardized autonomic tests (cardiovascular reflexes tests), questionnaires evaluating symptoms of dysautonomia such as the Scale for Outcomes in Parkinson's Disease-Autonomic (SCOPA-AUT), a neuropsychological evaluation and an odour identification test.

Results: The study included 32 iRBD (mean age 67.94 ± 7.03 years, 7 females) and 29 CTRs (68.03 ± 9.25 years, 5 females). The difference in years of education was not significant between the 2 groups ($p=0.261$). At autonomic tests 18 iRBD and 1 CTR showed a pathologic Valsalva Manoeuvre ($p<0.001$), of them 9 iRBD patients and a different CTR ($p=0.009$) showed orthostatic hypotension (OH) at the 3rd minute of 65° tilting. Patients with OH had a longer iRBD duration: 11.74 ± 7.07 vs 6.36 ± 4.02 years; $p=0.039$. SCOPA-AUT score was significantly increased in iRBD (11.84 ± 8.70 vs 7.50 ± 7.81 ; $p=0.007$), especially within cardiovascular domain ($p=0.004$). iRBD in respect to 1 CTR fulfilled the criteria for mild cognitive impairment ($p=0.018$), with higher frequency of abnormal results in visuo-executive tasks ($p=0.026$ and 0.049). iRBD obtained a score of 6.11 ± 2.67 at odour identification test, lower than CTRs with 8.71 ± 2.72 ($p=0.001$).

Conclusion: iRBD shows a heavier non-motor burden, with dysautonomia usually developed over the years. The higher prevalence of dysautonomia and cognitive impairment an already present neurodegenerative process.

Disclosure: Nothing to disclose

EPR1231

Nocturnal Sleep Stability And Cerebrospinal Fluid Orexin-A Levels: Sleep And Wake Bouts

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Background and aims: To evaluate the relationships between cerebrospinal fluid (CSF) ORX levels and markers of nocturnal sleep stability assessed by polysomnography (PSG).

Methods: Nocturnal PSG data and CSF ORX levels of 300 drug-free subjects (29.9±15.5 yo, ORX 155±154pg/mL) with a complaint of hypersomnolence were collected in the Narcolepsy Reference Center, France. Several markers of nocturnal sleep stability were analyzed: wake (WB), sleep bouts (SB), and sleep/wake transitions (SWT). Groups were categorized according to ORX levels: two categories (≤ 110 , > 110 pg/mL, the established threshold of ORX-deficiency), and tertiles (≤ 26 , $]26; 254]$, > 254 pg/mL); and were compared using logistic regression models. Results were adjusted for age, gender and BMI.

Results: ORX-deficient subjects had more WB, SB, and SWT than the others. The WB duration was longer and the SB duration shorter in ORX-deficient category. The proportion of the shortest WB (30sec) was lower in the ORX-deficient category whereas the proportion of WB above 1min 30sec was higher. The proportion of SB ≤ 14 min was higher among ORX-deficient patients, with opposite results for longer SB. Subsequent analyses performed in the population categorized according to tertiles of CSF ORX-A confirmed all these findings, with a strong dose-response effect of ORX levels in post-hoc comparisons. All results remained highly significant in adjusted statistical models.

Conclusion: This study provides a strong evidence of the direct effect of ORX on nocturnal sleep stabilization in humans. WB and SB are reliable markers of nighttime sleep stability, strongly correlated to CSF ORX-A levels in a dose-dependent way. These PSG biomarkers are promising to be applied in clinical and research settings.

Disclosure: Nothing to disclose

EPR1232

Type 1 narcolepsy secondary to an anti-Ma2 encephalitis

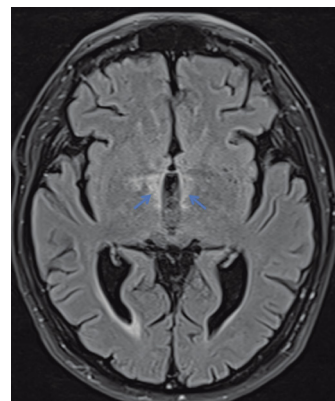
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Background and aims: Autoimmune encephalitis are rare causes of subacute cerebral dysfunction.

Methods: We report a case of narcolepsy secondary to an anti-Ma2 encephalitis.

Results: A 68-years-old man with elevated blood pressure, obesity and diabetes mellitus presented with a 1-year history of excessive daytime sleepiness with sleep attacks. Nocturnal continuous positive pressure in treatment of a proven obstructive sleep apnoea syndrome was ineffective. On the contrary, progressive cognitive decline appeared over 6 months along with walk impairment and a 4kg weight gain. Clinical examination revealed a nystagmus and static cerebellar syndrome and psychomotor slowing. EEG was normal. Protein levels in cerebrospinal fluid were of 0.86g/L. Brain MRI demonstrated hypersignals on the fluid attenuated inversion recovery sequence around the third ventricle and the cerebral aqueduct. Anti-Ma2 antibodies were found in both serum and cerebrospinal fluid. Multiple sleep latency tests were abnormal (mean sleep latency 6.2min, normal over 8min) but without sleep onset rapid eye movement periods. Hypocretin (orexin) in cerebrospinal fluid was under 50ng/mL, which allowed for type 1 narcolepsy diagnosis. Walk normalized after 3 monthly immunoglobulin perfusions, and excessive daytime sleepiness was treated effectively with pitolisant. Extensive search for cancer remains negative.



Patient's brain MRI. Fluid attenuated inversion recovery sequence with hyperintensities around the third ventricle (arrows).

Conclusion: Anti-Ma2 antibodies are present in 7% of auto-immune encephalitis or 22% of paraneoplastic encephalitis, in association with a lung or testicular cancer in up to 90% of cases. Its association with central hypersomnia, and with type I narcolepsy in rarer cases, has been described and is a consequence of auto-immune hypothalamic destruction, mirrored by a decreased in hypocretin levels in CSF.

Disclosure: Nothing to disclose

EPR1233

Slow Wave Sleep and response to Cognitive-Behavioral Therapy for Insomnia.

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Background and aims: The 1st-choice treatment for insomnia disorder (ID) is Cognitive-Behavioral Therapy for insomnia (CBT-I). Considering that subjective evaluation of sleep is fundamental for the diagnosis and treatment of ID, CBT-I efficacy has been mostly investigated through subjective measures. Moreover, objective indices do not seem to change significantly after CBT-I. However, specific sleep features from polysomnography (PSG) could be informative and could predict treatment response. The aim of the current study is to evaluate which PSG variables could forecast CBT-I effectiveness.

Methods: 130 chronic insomnia patients (72 females, mean age 53.3±13.5) underwent 1-night of PSG pre-treatment (7-sessions group CBT-I). Insomnia Severity Index (ISI) and sleep diaries were considered the main outcomes. We used General Lineal Model (GLM) to evaluate PSG indices that may predict CBT-I response.

Results: Patients showed a significant improvement after CBT-I both at ISI (16.75±4.54 vs 9.16±4.43; p<0.001) and at sleep diaries variables (Sleep Latency: 34.7±30.8min vs 20.9±21.9, p<0.001; Wake After Sleep Onset: 69.9±66.2min vs 31.5±38.4, p<0.001; Sleep Efficiency: 75.4±17.1% vs 85.1±12.3, p<0.001). GLM revealed a significant interaction between Wake After Sleep Onset (WASO) improvement after CBT-I and the percentage of Slow Wave Sleep (SWS%) before treatment (sig. treatment*SWS% p<0.05). Moreover, we found a positive and significant correlation between Delta WASO (WASO at the baseline – WASO at the end of treatment) and SWS% (p<0.05, r=0.175).

Conclusion: These results suggest the role of SWS in predicting patients' response to CBT-I, acting as a natural mediator of "process S".

Disclosure: Nothing to disclose

EPR1234

Objective total sleep duration is not reliable in predicting effectiveness of Cognitive-Behavioral Therapy for Insomnia (CBT-I)

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Background and aims: There is a growing literature investigating objective Total Sleep Time (TST) as indicative of two phenotypes of Insomnia Disorder (ID): normal sleepers (with TST \geq 6hours) and short sleepers (with TST $<$ 6hours). The aim of this study is to evaluate the possibility that these 2 groups differ in terms of Cognitive-Behavioral Therapy for Insomnia (CBT-I) response, the first-choice treatment for ID.

Methods: We divided 53 ID patients (females=50.9%; mean age=56.5 \pm 11.4) into “Short Sleeper” and “Normal Sleeper” according to polysomnographic and actigraphic evaluation performed before starting 7-session group CBT-I. Insomnia Severity Index (ISI) was considered the primary outcome, whereas Sleep Efficacy (SE), Sleep Latency (SL), Wake After Sleep Onset (WASO), Number of Awakenings (N^oawk) from sleep diaries, were considered secondary outcomes.

Results: All ID patients showed significant improvements after treatment for all clinical outcomes. Both using polysomnography and actigraphy, no significant differences between “Short Sleeper” and “Normal Sleeper” were found in terms of ISI, SE, SL, WASO and N^oawk. Moreover, the accordance between actigraphy and polysomnography was poor for the identification of the 2 subgroups.

Conclusion: These findings suggest the poor reliability of objective TST in predicting CBT-I effectiveness. Moreover, only a small percentage of patients were classified as short or normal sleepers according to both polysomnography and actigraphy, pointing out the instability of the index. We conclude that these results underline the instability and poor reliability of objective TST for subtyping ID and in predicting CBT-I effectiveness.

Disclosure: Nothing to disclose

EPR1235

REM-related complex behavior and REM sleep without atonia (RSWA) after subthalamic deep brain stimulation in Parkinson's disease with REM sleep behavior disorder

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Background and aims: Rapid eye movement (REM) sleep behavior disorder (RBD) is confirmed by polysomnographic (PSG) documentation of REM sleep without atonia (RSWA) and complex behaviors during REM sleep (CB-REM). The effect of DBS on RBD is controversial, since PSG data are usually missing.

This study aims to assess the effect of subthalamic-DBS on RSWA and CB-REM in patients with Parkinson's disease (PD) and RBD.

Methods: In this prospective case series, we analyzed polysomnographic studies and clinical data of 8 patients with PD and RBD before and 6 months after DBS. RSWA was evaluated by analysis of phasic, tonic or “any” REM-related EMG activity (EMG-REM). CB-REM was visually assessed.

Results: Post-DBS, the number of CB-REM increased significantly (12.98 \pm 15.90/h vs. 24.02 \pm 24.71/h, $p<0.05$). Conversely, no significant changes in phasic ($p=0.782$), tonic ($p=0.978$) or “any” ($p=0.293$) EMG-REM were found. The number of CB-REM correlated significantly with “any” EMG-REM (pre-DBS $r=0.542$, $p<0.001$, post-DBS $r=0.460$, $p<0.05$) and phasic EMG-REM (pre-DBS $r=0.663$, $p<0.001$, post-DBS $r=0.428$, $p<0.05$) but not with tonic EMG-REM (pre-DBS $r=-0.06$, $p=0.71$, post-DBS $r=-0.135$, $p=0.495$). Changes in RSWA and CB-REM were independent of changes in dopaminergic medication and PD motor scores.

Conclusion: Our results suggest that subthalamic-DBS has no direct effect on the severity and type of brainstem-related RSWA but impacts the behavioral component of RBD in PD patients. These results further highlight the notion that CB-REM and RSWA, especially tonic activity, are 2 distinct RBD elements and should be assessed separately, especially in studies that report on RBD outcome after treatment interventions.

Disclosure: Nothing to disclose

EPR1236

Exploring creative potential in narcoleptic patients

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Background and aims: The role of sleep on creative thinking has been supported by several studies, nevertheless only few studies investigated this relationship with respect to specific sleep stages (i.e. REM and NREM sleep). Narcolepsy type 1 (NT1) is a chronic neurological disorder characterized by hypersomnolence and untimely manifestations of REM sleep during wake and vice-versa. Cataplexy, sleep paralyzes, hypnagogic hallucinations, disrupted nocturnal sleep with overrepresentation of rapid eye movement sleep behaviour disorder and lucid dreaming complete the clinical picture. Recently, a study showed a positive correlation between REM sleep and creativity in narcoleptic patients. With this study we aimed at investigating if creativity in narcolepsy can be associated with certain symptoms and with mental dimensions (mind wandering and daydreaming) that could predict creative behaviour.

Methods: 94 NT1 patients took part in this study. Several measures of creativity have been performed: creativity achievement, explored in different life domains by a self-reported questionnaire; creative beliefs, assessed with a scale measuring the creative self; creative performance, evaluated through computerized tests assessing both convergent thinking skills (analytical and insight skills) and divergent thinking skills (generation of alternative original solutions to an open problem).

Results: Creative achievement and creative performance are both influenced by frequency of hypnagogic hallucinations and daydreaming, via a mediation effect of creative identity. Mind wandering influences creative achievement through a moderation effect of hypnagogic hallucinations.

Conclusion: Our results highlight the role of hypnagogic hallucinations in defining both the creative success and the creative performance of NT1 patients influencing their creative self-beliefs.

Disclosure: Nothing to disclose

EPR1237

Sleep duration increases after stroke: A prospective study of 438 patients

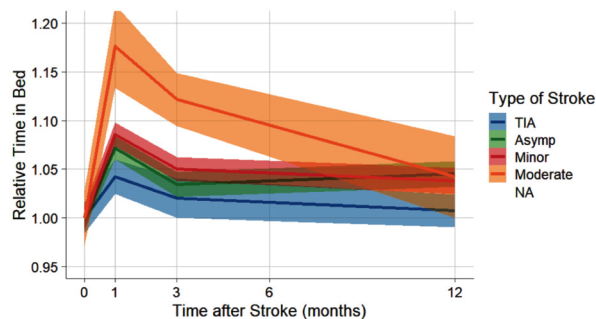
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Background and aims: Sleep/Wake Disturbances (SWD), including long and short sleep duration, are associated with increased stroke risk. In contrast, sleep may promote neuroplasticity and recovery after stroke. We assessed changes in sleep duration after acute stroke as a 1st step to examine its potential relationship with stroke severity and outcome.

Methods: We recruited 438 patients (mean age 65 [21-86]; 64% males). 85% suffered an ischemic stroke while 15% a TIA. We used validated questionnaires to assess sleepiness, fatigue, sleep duration and quality both retrospectively before and prospectively after stroke. Recurrent events and functional outcomes at hospitalization and again at month 1, 3 and 12 post-stroke were evaluated. A randomly selected subgroup of 114 patients underwent actigraphy.

Results: We recruited 438 patients (mean age 65 [21-86]; 64% males). 85% suffered an ischemic stroke while 15% a TIA. We used validated questionnaires to assess sleepiness, fatigue, sleep duration and quality both retrospectively before and prospectively after stroke. Recurrent events and functional outcomes at hospitalization and again at month 1, 3 and 12 post-stroke were evaluated. A randomly selected subgroup of 114 patients underwent actigraphy.



Subjective Time in Bed changes after stroke. Depicted is the change relative to prestroke Time in Bed. Asymptomatic stroke: NIHSS after treatment =0, Minor: NIHSS after treatment 1<=4, Moderate NIHSS after treatment >4.

Conclusion: These results show that transient increases in sleep duration after stroke are dependent on stroke severity. Future analyses will examine the determinants of these changes and the potential links of between increased sleep with stroke recovery and outcome.

Disclosure: This project was funded by the Swiss National Science Foundation

EPR1238

Auto-antibodies against brain antigens are not routinely detectable in serum and CSF of narcolepsy type I patients

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Background and aims: Narcolepsy with cataplexy (NT1) is a chronic hypothalamic disorder with a presumed autoimmune etiology leading to dysfunctional hypocretin transmission. Whereas hypocretin specific T-cells have recently been identified the role of auto-antibodies remains unclear. For NT1 no specific auto-antibodies have been consistently found so far.

Methods: From a total number of 86 patients with NT1 and a control group of 22 patients suffering from hypersomnolence of presumed psychiatric origin, insufficient sleep syndrome or excessive daytime sleepiness of unknown origin paired serum/CSF samples (n=59), only serum samples (n=41) and only cerebrospinal fluid (CSF) samples (n=8) were tested for the presence of the following anti-neuronal antibodies: Biochip mosaics containing non-fixed nitrogen-frozen tissue cryosections of rat hippocampus, monkey cerebellum and cerebrum; and recombinant T-cell substrates expressing different neural antigens (MOG, AQP4, NMDAR, AMPAR1/2, DPPX, GABA1/2, LgI1, and CASPR2) as well as Immunodot assays containing paranuclear antigens (Hu, Ri, Yo, Amphiphysin, CRMP, Ma1, Ma2, SOX-1, GAD, Zic4 and TR(DNER)).

Results: We identified one NT1 patient with positive and a 2nd 1 with borderline positive Anti-Yo in serum but not CSF samples. 1 NT1 patient had positive staining for serum anti-Flotillin on cerebrum and cerebellum brain slides. 1 control had positive staining for antinuclear antibody (ANA) on hippocampal brain slides.

Conclusion: Anti-neuronal antibodies are not routinely found in serum or CSF of NT1 patients. Therefore, the detection of antineuronal antibodies in suspected NT1 patients should raise doubts about the primary diagnosis of NT1 and suggest further diagnostic evaluations.

Disclosure: Nothing to disclose

EPR1239

Neurocognitive functions and REM sleep without atonia in isolated REM sleep Behavior Disorder

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Background and aims: Isolated REM sleep Behavior Disorder (iRBD) is characterized by the presence of REM Sleep Without Atonia (RSWA) leading to violent behaviors. Only few studies evaluated the association between RSWA and neuropsychological functioning. The aim of this study was to assess the relationship between cognitive impairment and RSWA in iRBD patients.

Methods: 35 iRBD patients and 18 healthy controls (HC) underwent a complete polysomnography (PSG) as well as a comprehensive neuropsychological evaluation. iRBD patients were divided into 2 groups based on the presence or absence of Mild Cognitive Impairment (MCI). The PSGs were analyzed by a scorer, blind to subjects' diagnosis, to quantify the RSWA of 6 different indices of muscle activity extracted by phasic and tonic events recorded in different time series (2,3 or 30 seconds) and muscle combinations (flexor digitorum superficialis, mentalis and tibialis muscles).

Results: iRBD had increased RSWA in comparison to HC. The combination of phasic and tonic events recorded in micro epochs of 3 seconds from the mentalis muscle and flexor digitorum superficialis best differentiate iRBD and HC. RSWA indices and neuropsychological measures in the iRBD group showed a negative correlation between the scores at the Mini Mental State Examination and the phasic events index recorded by the combination of mentalis and bilateral tibialis muscles in micro epochs of 2 seconds. Finally, MCI patients exhibited increased levels of RSWA in comparison to no-MCI in all indices considered.

Conclusion: These results suggest a relationship between the loss of atonia during REM sleep and neuropsychological impairment.

Disclosure: Nothing to disclose

EPR1240

Medical Cannabis in the Treatment of Patients with Autism Spectrum Disorder

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Background and aims: This study evaluates the safety and efficacy of medical cannabis (MC) treatment of pain and epilepsy in patients with autism spectrum disorder (ASD). Only 13 US states currently approve MC treatment for ASD. There are limited treatment options for patients with ASD and associated challenges including self-injurious behavior (SIB), elopement, pain, epilepsy, and behavior symptoms. This study reports a case series of patients with ASD treated with MC.

Methods: Chart review of 20 patients with ASD on MC included written evaluations by patient or caregiver. Autism/Caregiver Global Impression of Change (ACGIC) measured quality of life (QOL), activity limitations, symptoms, and mood. Changes in pain, seizures, and secondary effects were assessed by 10-point Likert Scales. MC product information: dosing, route, frequency, and cost were reported.

Results: Six patients with epilepsy improved seizure frequency ($p=0.0032$) and severity ($p=0.0332$). Fourteen patients with pain improved degree of overall pain ($p<0.0001$). ACGIC scale improved in all areas: QOL, activity limitations, symptoms, and mood ($p<0.0001$). Secondary effects: patients experienced improved sleep ($p<0.0001$), mood ($p<0.0001$), aggression towards self/others ($p<0.0001$), communication abilities ($p=0.0001$), and attention/concentration ($p=0.0002$). Patients tried an average of 6.4 other medications; 50% of patients discontinued or reduced other medications while on MC. Three patients reported mild SE from MC; none discontinued due to SE.

Variable	N	Mean	SD	P-Value ¹
Quality of Life	20	8.03	1.36	<0.0001
Activity Limitations	20	6.98	1.59	<0.0001
Symptoms	20	7.75	1.66	<0.0001
Emotions	20	7.43	1.66	<0.0001
Overall Change in Pain	14	8.36	1.82	<0.0001
Seizure Frequency	6	8.08	1.43	0.0032
Seizure Duration	6	7.08	2.06	0.0560
Seizure Severity	6	7.25	1.89	0.0332
				¹ H0: Mean = 5 (No Change)

Table 1. Mean rankings from ACGIC and Pain/Epilepsy Evaluations and results from t-tests performed against null value of 5, “no change” since beginning MC treatment.

Variable	N	Mean	SD	P-Value ¹
Attention/Concentration	20	6.93	1.89	0.0002
Sleep	20	7.35	1.69	<0.0001
Mood	20	7.38	1.53	<0.0001
Nausea/Vomiting	20	5.20	0.89	0.3299
Aggression	20	7.18	1.95	<0.0001
Communication	20	6.60	1.50	0.0001
				¹ H0: Mean = 5 (No Change)

Table 2. Mean rankings from Secondary Effects Evaluations and results from t-tests performed against null value of 5, “no change” since beginning MC treatment.

Conclusion: There is a paucity of research for MC treatment for patients with ASD. Findings support previous research for MC treatment of pain and epilepsy while exploring indications for behavioral issues and QOL improvement for ASD.

Disclosure: Research has been institutionally funded by the Harry Dent Family Foundation.

Sunday, May 24 2020

Ageing and dementia 2

EPR2001

Characteristics and progression of frontotemporal lobar degeneration syndromes in a regional memory clinic network

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Background and aims: The nosology of frontotemporal lobar degeneration (FTLD) syndromes has evolved outstandingly in the past decade. Using the updated clinical criteria, our aim was to identify characteristics and progression of the FTLD syndromes diagnosed in Meotis, our regional memory clinic network, between 2010 and 2016.

Methods: The FLTD population was divided in 3 groups: behavioral variants (bvFLTD), language variants FLTD (lvFLTD) and motor variants (mFLTD), i.e. cognitive presentations of progressive supranuclear palsy and FTLD with amyotrophic lateral sclerosis. All group were compared to the Alzheimer’s disease (AD) population as well to the other neurodegenerative diseases. Disease progression was measured in the subgroup of patients that had at least 2 MMSE scores with the 1st one being >10.

Results: During the time span of the study 690 FLTD syndromes (3% of the active case load) (Figure1) and 18 831 AD were diagnosed. Most FTLD syndromes were bvFLTD (64%). Compared to AD patients, FLTD patients were younger at 1st symptoms and displayed a higher MMSE score and a longer diagnosis wandering, especially in the bvFLTD subgroup (Figure 2). Disease progression did not show any statistical difference between bvFTLD and AD patients (Figure 3).

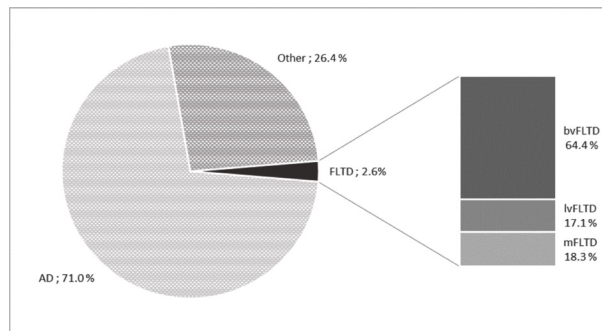


Figure 1 : Study population

Variable	bvFLTD			lvFLTD			mFLTD			AD	
	N	Mean (s)	p	N	Mean (s)	p*	N	Mean (s)	p**	N	Mean (s)
Female (%)	446	52.2	<0.0001	118	57.6	0.01	136	54	0.0003	18831	69.9
Age at first visit	446	69.4 (10.3)	<0.0001	118	72.7 (9.5)	<0.0001	136	72.0 (8.0)	<0.0001	18831	80.6 (7.5)
Age at diagnosis	446	70.2 (10.3)	<0.0001	118	73.6 (9.7)	<0.0001	136	72.8 (8.1)	<0.0001	18831	81.0 (7.3)
Delay referral (months)	359	40.0 (41.2)	<0.0001	99	30.8 (20.5)	0.63	102	35.8 (29.9)	0.03	13461	31.8 (32.0)
Diagnosis wandering (months)	446	9.9 (16.8)	<0.0001	118	10.5 (16.4)	<0.0001	136	9.1 (15.1)	<0.0001	18831	5.8 (14.2)
Follow up length (months)	446	25.2 (24.0)	<0.0001	118	24.2 (22.0)	<0.0001	136	20.2 (19.6)	0.05	18831	17.5 (21.4)
Family history (%)	446	39.9		118	23.7		136	26.2		18831	4.8
MMSE at first visit	329	22.1 (6.1)	0.02	91	20.6 (7.5)	<0.0001	88	21.9 (6.1)	<0.0001	16077	18.9 (6.6)
MMSE > 0 (%)	247	81	<0.0001	80	90	0.0054	72	75	<0.0001	12143	69.6

Figure 2 : Demography

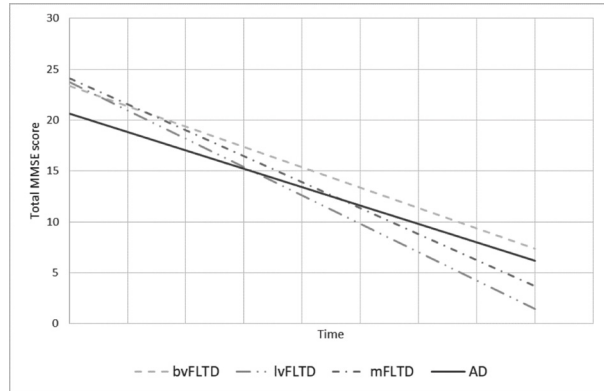


Figure 3 : Disease progression

Conclusion: To our knowledge, no other study compared patient characteristics and progression in FLTD subtypes using the new diagnostic criteria. Our results show that FTLD is still underdiagnosed, especially in the behavioural presentations. Unexpectedly, MMSE progression is not different in FLTD and AD patients.

Disclosure: Nothing to disclose

EPR2002

Investigating the clinical correlation between sCJD and presence of other neurodegenerative pathologies

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Background and aims: Sporadic Creutzfeldt Jakob Disease (sCJD) is a rapidly progressive and fatal neurodegenerative disorder. Age-specific mortality rates for sCJD have increased up to 65-79 years over the past 4 decades. Of interest is an apparent reduced incidence at 80 and over. It has been hypothesised that the apparent decline in incidence of sCJD in older adults could be due to the inhibitory effects of the Alzheimer's disease (AD) associated amyloid β -protein ($A\beta$) on prion propagation.

Methods: Retrospective case note review of cases of definite sCJD over a 3 year period from 2016-2018. Cases evaluated for the presence of additional neurodegenerative pathology on neuropathological examination of brain material. Specifically $A\beta$, tau, α -synuclein and cerebral amyloid angiopathy (CAA).

Results: 123 cases of definite sCJD were identified in the UK between 2016-2018. 56/112 (50%) of cases show evidence of co-existing pathology in addition to sCJD. Cases with co-pathology had a higher age at death by 6.3 years (95% CI (2.95, 9.59) $p < 0.001$). Cases with co-pathology had a shorter disease duration by 3.7 months (95% CI (-7.04, -0.44) $p = 0.027$). Co-pathology cases were more likely to present with cognitive decline or neuropsychiatric features ($p = 0.037$). Co-pathology cases were more likely to test negative for CSF RT-QuIC and MRI. Patients with co-pathology were less likely to be assessed by the National CJD Research and Surveillance Unit in life.

Conclusion: This data suggests a potential association between the presence of other neurotoxic proteins in the brain of sCJD patients with older age of onset, shorter disease duration, and negative investigations.

Disclosure: This is independent research commissioned and funded by the Department of Health and Social Care Policy Research Programme and the Government of Scotland ("The National CJD Research and Surveillance Unit (NCJDRSU)", PR-ST-0614-00008_18). The views expressed are those of the author(s) and not necessarily those of the Department of Health and Social Care or the Government of Scotland

EPR2003

Investigating the therapeutic value of transcranial Direct Current Stimulation on language disorders in the semantic variant of Primary Progressive Aphasia

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Background and aims: The semantic variant of primary progressive aphasia (sv-PPA) is the most frequent form of this neurodegenerative disease. Patients suffer great amount of language disabilities caused by atrophy of the Anterior Temporal Lobe (ATL) for which there is no effective treatment. Non-invasive brain stimulation by transcranial Direct Current (tDCS) is emerging as a therapeutic alternative in neurodegenerative conditions.

Methods: It is a double-blind sham-controlled study from 14sv-PPA patients who received daily tDCS sessions for 10 consecutive days (20 minutes, intensity: 1.57mA). Patients were randomized to 3 conditions: Left ATL-Anodal (excitatory), Right ATL-Cathodal (inhibitory) and Sham (Placebo). Participants carried out a battery of language, executive and face recognition tasks, a week prior to treatment onset, 3 days, 2 weeks and 4 months following the last session. Prior and 2 weeks following, patients underwent MRI and 18[F]-FDG-PET to assess baseline levels of ATL atrophy and hypometabolism and better understand tDCS mechanisms of action. Additionally, after each session, patients completed a questionnaire assessing comfort and tolerance. Age-matched controls were characterized for language abilities using the same tasks and underwent MRI and 18[F]-FDG-PET to obtain normative data.

Results: We did not find statistically significant improvements in semantic access. Nonetheless, the Left Anodal tDCS group showed medium effect sizes in visual semantic association visual task. Our tasks were significant in delineating patients from healthy controls. Excellent tolerance and a high level of subjective satisfaction were found for all tDCS modalities.

Conclusion: Further recruitment will be needed to conclude on the effectiveness of this modality for the treatment and its mechanism of action in sv-PPA patients

Disclosure: This project is funded by APHP (Assistance des hopitaux publics de Paris)

EPR2004

Neuregulin1 is a new CSF synaptic biomarker in Alzheimer's disease

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Background and aims: Neuregulin1 (Nrg1) is a presynaptic beta-secretase 1 (BACE1)-substrate that can activate post-synaptic ErbB4 receptors. Nrg1 gene has been associated with schizophrenia. The activation of Nrg1/ErbB4 pathway can induce synaptogenesis and plasticity, can enhance the expression of NMDA and GABA receptors and is also neuroprotective. This signaling pathway can trigger neuroinflammation and can impair memory formation. Neuritic plaques are associated with Nrg1 accumulations in Alzheimer's disease (AD). Whereas studies on BACE 1 have shown increased levels in AD brains and CSF, no study has evaluated CSF Nrg1 levels in AD and MCI-AD patients.

Methods: 172 patients suffering from AD dementias (56), MCI-AD (21), non-AD MCI (32) non-AD dementias (36) and neurological controls (27) were retrospectively included in the study. After informed consent neurological exams, MRI and neuropsychological evaluations were carried out. The CSFs of all patients were evaluated with ELISA for A β 1-42, A β 1-40, tau, ptau, BACE1, and Nrg1.

Results: CSF Nrg1 concentrations were significantly enhanced in AD and MCI-AD patients as compared to non-AD MCI, non-AD dementias and neurological controls. In addition, Nrg1 levels positively correlated with tau, ptau, A β 1-40, BACE1 levels and negatively with MMSE scores and frontal battery scores.

Conclusion: A β -induced neurotoxicity leads to synaptic demise with increased CSF BACE1 and Nrg1 levels. Lack of neuroprotection may be linked to decreased Nrg1 brain levels. Nrg1 is a new biomarker that could reflect BACE1 activity and cognitive alteration in AD patients.

Disclosure: This study was supported by Fondation Chatrier and Fondation Vaincre Alzheimer

EPR2005

Does apathy predict conversion from mild cognitive impairment (MCI) to Alzheimer's disease dementia (ADD)?

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Background and aims: Apathy has been associated with increased risk of conversion from MCI to ADD but the majority of data were obtained with the limited apathy subscale of the Neuropsychiatric Inventory and few data are available using the specific Apathy Evaluation Scale (AES) (Guercio et al., JAD 2015). We administered both the subject (AES-S) and the informant (AES-I) to MCI patients who were followed up for a mean time of 1.63 \pm 0.68 years.

Methods: 110 MCI patients (63 females, age:76.6 \pm 5.5; MMSE score:26.6 \pm 1.9) underwent neuroimaging, clinical-neuropsychological evaluation and the AES-S, while the informant was administered the AES-I. 40 patients converted (MCI-C) to ADD after 0.33-3.25 years (mean:1.76 \pm 0.76) while 53 were still MCI (MCI-NC) after 0.58-2.66 years (mean: 1.65 \pm 0.59) and 17 dropped out after 0.16-2 years (mean: 1.0 \pm 0.44). The AES scores were compared between MCI-C and MCI-NC and correlated with timing of conversion.

Results: AES-S global score did not differ between subgroups. AES-I global score was significantly (p<0.03) higher in MCI-C. At post-hoc analysis, both the AES-I 'cognitive' (p<0.016) and 'emotional' (p<0.046) sub-scores were significantly higher in MCI-C. No AES-I score was correlated with timing of conversion.

Conclusion: Informant's, but not patient's, perception of cognitive and emotional apathy is of value in predicting conversion to ADD in MCI patients. As these apathy scores did not correlate with timing of conversion, apathy might be an expression of a trait of the disease in a part of MCI patients rather than a symptom denoting a more severe impairment on the way of dementia.

Disclosure: Nothing to disclose

EPR2006

RT-QuIC detection of alpha-synuclein seeds in olfactory mucosa brushings of patients with Dementia with Lewy bodies

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Background and aims: According to the revised 2017 McKeith's et al. criteria, diagnosis of probable/possible Dementia with Lewy bodies (DLB) is based on core clinical features and indicative biomarkers. To date, there is active research to find out and validate an accurate, possibly non-invasive diagnostic procedure to reach an in vivo diagnosis by demonstrating disease-associated alpha-synuclein (a-syn) aggregates in peripheral tissues of patients with a clinical diagnosis of DLB. In this setting, real-time quaking induced conversion (RT-QuIC) has been proven to be a feasible and highly accurate technique, able to detect trace amount of a-syn aggregates in biological samples of patients with different a-synucleinopathies.

Methods: We consecutively enrolled 12 patients (mean age: 77.5±6.1) with probable DLB. Clinical diagnosis was based on clinical core and on at least one indicative biomarker (dopamine transporter SPECT, I-123 MIBG cardiac scintigraphy or polysomnography-proven REM sleep without atonia). Our database of healthy controls included 40 subjects (mean age: 65±10). Patients underwent olfactory mucosa (OM) brushing under video transnasal video-endoscopy.

Results: OM brushing was successfully performed without adverse events. 10 out of 12 patients tested positive for a-syn amplification on RT-QuIC analysis (sensitivity: 83%), whereas 3 out of 40 healthy controls tested resulted positive (specificity: 92%).

Conclusion: We demonstrated in a small group of DLB patients that OM is a-syn RT-QuIC positive with a promising diagnostic accuracy, providing evidence of the disease associated a-syn aggregates. If confirmed in larger and independent patient series a-syn RT-QuIC-could be the appropriate test for confirming DLB diagnosis in patients with possible/probable DLB.

Disclosure: Nothing to disclose

EPR2007

Cognitive, linguistic and neuroanatomical features of primary progressive aphasia due to frontotemporal dementia gene mutations

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Background and aims: Primary progressive aphasia (PPAs) caused by mutations in frontotemporal dementia (FTD) genes are rare. Few such patients have been reported thus far, but the specific linguistic features of genetic PPA have not been extensively characterized in large cohorts. Studying genetic PPA allows to characterize homogeneous groups of patients with predictable underlying pathology, and potentially link specific molecular dysfunctions with clinical phenotypes. We aimed at characterizing demographic, linguistic and neuroanatomical profiles specific to genetic forms of PPA.

Methods: We prospectively enrolled 1,696 FTD and PPA patients in a clinico-genetic study through a national network since 1996. 43 PPA patients carrying FTD mutations with complete clinical, neuropsychological and linguistic dataset were included. We analysed cortical thickness as a measure of brain atrophy with FreeSurfer 6.0.

Results: Amongst the 43 genetic PPA patients, 14 had logopenic (lvPPA), 11 non-fluent/agrammatic (nfvPPA), 10 mixed, and 8 semantic (svPPA) variants (Figure 1). GRN mutations were, by far, the most frequent cause of genetic PPA (32/43, 75%), before C9orf72 (16%) and other genes (9%). The commonest phenotype in GRN carriers (13/32) was lvPPA, which correlated with a peak of atrophy in left posterior temporal cortex and temporo-parietal junction (Figure 2). Conversely, the semantic variant was mainly caused by C9orf72 and other genes.

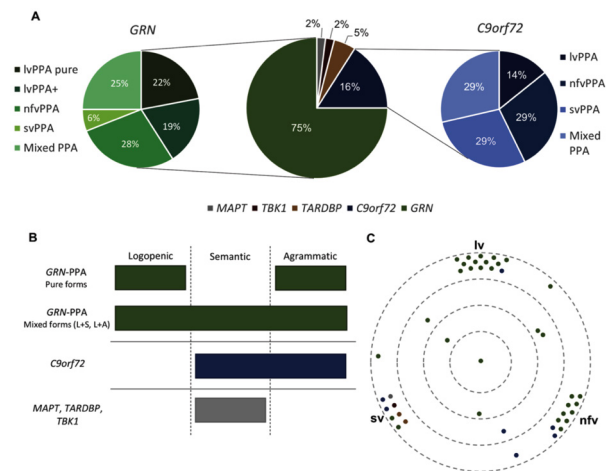


Figure 1. Overall description of the genetic PPA cohort. A: causative genes and proportion of clinical variants in the 2 main genetic forms. B: schematic representation of the contribution of each gene to the clinical phenotypes. C: distribution of the patients with respect to the linguistic deficits; the colour corresponds to the causative gene.

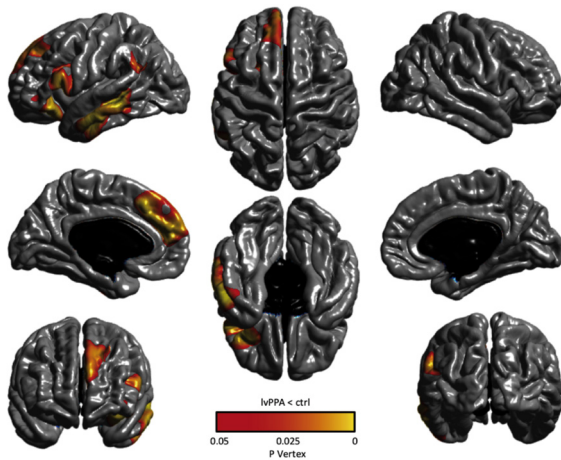


Figure 2. Cortical thickness analysis of 8 lvPPA-GRN patients compared to 20 controls. The voxelwise analysis was performed in FreeSurfer 6.0 and SurfStat, using vertex-wise correction with a threshold of $p < 0.05$. Patients displayed atrophy in left posterior middle temporal gyrus, temporo-parietal junction, prefrontal and orbitofrontal cortex.

Conclusion: This study, the first in-depth characterization of a large cohort of genetic PPA patients, highlights GRN mutations as a relevant cause of amyloid-negative lvPPA. Overall, different neurodegenerative trajectories distinguish PPAs due to GRN mutations from those associated with other less common causes.

Disclosure: Nothing to disclose

EPR2008

Normal pressure hydrocephalus as a neurodegenerative disorder – evidence from a monocentric study

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Background and aims: The hallmark of normal pressure hydrocephalus (NPH) is the reversal of cognitive decline, gait disturbance and urine incontinence upon drainage of 50ml cerebrospinal fluid (CSF). As NPH has recently been questioned to represent a neurological entity, we aimed at assessing if clinical and laboratory variables may differentiate an idiopathic NPH from a neurodegenerative NPH.

Methods: Data of 66 consecutive patients with NPH (2016-2018) were analyzed with regard to cognitive and walking functions before and after CSF drainage. In CSF S100, NSE, amyloid β -protein, tau-protein, phospho-tau were measured. Statistical analysis was carried out with ANOVA and a multiple linear regression. An artificial neural network trained with the main clinical predictors was applied to verify the results and to classify another 37 consecutive patients (2019).

Results: Only those patients with a CSF constellation typical for Alzheimer's disease (N=28) improved significantly in specific cognitive and walking functions after CSF drainage. These "Alzheimer positive" patients (78 ± 6 years) were older ($p < 0.01$) than the "Alzheimer negative" patients (74 ± 6 years). The "Alzheimer positive" constellation in CSF predicted the improvement in the timed up and go test ($p = 0.014$) and the clock drawing test ($p = 0.045$) after CSF drainage. The artificial neural network analysis proved to succeed in patient classification.

Conclusion: Our data suggest a high coincidence of Alzheimer's disease in NPH patients. By contrast, NPH occurs seldom in patients with Alzheimer's disease. Moreover, our results substantiate the recently suggested dichotomy of a neurodegenerative NPH which is common and an idiopathic NPH which is rare.

Disclosure: Nothing to disclose

EPR2009

Significant discrepancies in amyloid status A+/A- in CSF based on A β 1-42 measurement or A β 1-42 /A β 1-40 ratio.

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Background and aims: Amyloid is a biomarker of Alzheimer's disease which can be assessed by quantification of A β 1-42 rates in the CSF after lumbar puncture. Although, the A β 1-42/A β 1-40 ratio is suggested to be more specific than A β 1-42 alone to distinguish subjects with Alzheimer's disease (Hansson et al., 2019), the discrepancies between both amyloid measurements have not been investigated yet.

Methods: We analysed the adjustment of amyloid status (A- or A+) after A β 1-42/A β 1-40 ratio calculation. CSF of 738 subjects admitted in our neurological department between January 2017 and June 2019 were analysed. A β 1-42/A β 1-40 ratio was calculated only in case of intermediate or ambiguous profile (n=176) in 2017-2018 and it was systematically performed (n= 110) in 2019. The biomarkers concentrations were measured by ELISA (INNOTEST, Fujirebio). We assessed the modification of the amyloid status in whole population and during these two periods of investigation by McNemar test.

Results: Mean age of our population was 69. 67% of A+ subjects after A β 1-42 measurement became A- after A β 1-42/A β 1-40 ratio calculation (p<0.0001) and 18% of A- subjects became A+ (p<0.0001). These proportions were similar as in 2017-2018 group (68% and 29% respectively, p<0.0001), and in 2019 group (70% and 8% respectively, p<0.0001).

Conclusion: Amyloid status estimation is different between A β 1-42 and A β 1-42/A β 1-40 ratio. Our results strengthen the proposition to systematically use the A β 1-42/A β 1-40 ratio as an amyloid biomarker in the diagnostic of Alzheimer's disease. Nonetheless these conclusions must be replicated in an older cohort of patient.

Disclosure: Nothing to disclose

EPR2010

Neuroimaging characteristics of stable mild cognitive impairment, prodromal Alzheimer's disease and prodromal dementia with Lewy bodies

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Background and aims: Mild cognitive impairment is a heterogeneous condition that is a risk factor for developing dementia. Many studies have focused on prodromal Alzheimer's disease (Prod-AD). However, few have addressed prodromal dementia with Lewy bodies (Prod-DLB). The aim of this study was to compare MRI visual measures in stable mild cognitive impairment patients (Stable-MCI), Prod-AD and Prod-DLB.

Methods: Of 1814 patients assessed in the Essex memory clinic, 424 had MCI at baseline and had yearly follow-up data available. All patients underwent comprehensive clinical and cognitive assessment at each clinic visit. MRI scans were acquired at baseline, corresponding to the time of initial MCI diagnosis. At follow-up, patients were identified as stable MCI, AD or DLB; and retrospectively their baseline diagnoses were classified as Stable-MCI, Prod-AD and Prod-DLB. 2 raters blind to follow-up diagnosis rated all MRI scans for medial temporal atrophy (MTA), global cortical atrophy (GCA) and white matter lesions (WML, Fazekas score).

Results: MRI scans were available for 28 Prod-DLB patients and were matched against 27 Prod-AD and 28 Stable-MCI patients for age, sex and education. MTA scores were significantly greater in Prod-AD compared to Prod-DLB patients and Stable-MCI. There was no difference on GCA or WML between Prod-AD, Prod-DLB and Stable-MCI.

Conclusion: This study indicates that a simple visual rating of MTA already differs at a group level between Prod-AD and Prod-DLB. This could aid clinicians to differentiate between MCI patients who are likely to be developing AD, versus those who might progress to DLB or remain stable.

Disclosure: ZW received honoraria and grant support from GE Healthcare, HK received grant support from GE Healthcare neither related to present study

Autonomic nervous system disorders 2

EPR2011

Seropositive autoimmune autonomic ganglionopathy: clinical phenotype and autonomic biomarkers to monitor treatment response

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Background and aims: Autoimmune autonomic ganglionopathy (AAG) is a treatable disease characterised by subacute pandysautonomia. 50% have detectable antibodies towards the ganglionic acetylcholine receptor (gAChR-Ab).

Aim: to investigate seropositive AAG patients with a comprehensive autonomic testing protocol before and after treatment to characterise the full phenotype and identify objective autonomic biomarkers to monitor immunotherapy response.

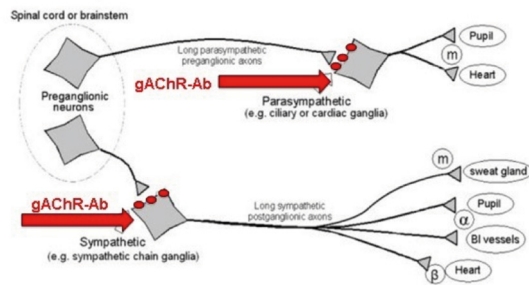


Figure 1: 50% of patients with autoimmune autonomic ganglionopathy (AAG) have a detectable antibody towards the ganglionic acetylcholine receptor (gAChR-Ab).

Methods: From 2005-2019, 15 patients were studied with autonomic failure and elevated gAChR-Ab > 100pM. 2 were excluded due to concomitant diseases. Patients underwent cardiovascular autonomic testing (head up tilt, deep breathing, Valsava manoeuvre), pupillometry, bladder, sudomotor, lacrimal and salivary testing, with autonomic symptom (COMPASS-31) and quality of life (SF-36) questionnaires, before and after immunotherapy.

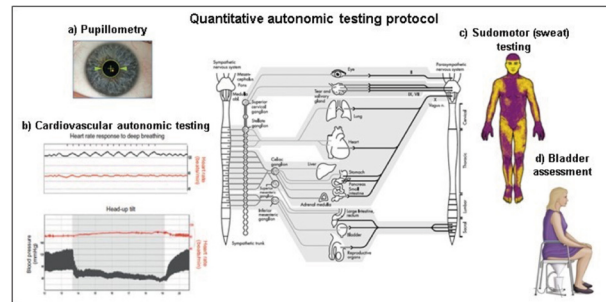


Figure 2: The comprehensive autonomic testing protocol included a) pupillometry b) cardiovascular autonomic testing c) sudomotor (sweat) testing, and d) bladder assessment.

Results: All 13/13 (100%) had sympathetic and parasympathetic cardiovascular and pupillary deficits, 9/11 (82%) had urinary retention, 7/8 (88%) had post-ganglionic sudomotor dysfunction and 6/8 (75%) had reduced saliva. 11/13 received immunotherapy. After treatment, there were significant improvements in orthostatic intolerance ratio (OIR, change in systolic blood pressure divided by time tolerated on head up tilt) (33.3[17.8-61.3] to 5.2[1.4-8.2], $P=0.007$), heart rate variability with deep breathing (1.5[0.0-3.3] to 4.5[3.0-6.3], $P=0.02$) pupillary light reaction (12.0%[5.5-18.0] to 19.0%[10.6-23.8], $P=0.02$), saliva production (0.01g/min[0.01-0.05] to 0.08g/min[0.02-0.20], $P=0.03$) and COMPASS-31 total score (52[34-64] to 17(8-31), $P=0.03$). OIR correlated with COMPASS-31 orthostatic intolerance ($P=0.03$, $\rho=0.792$) and SF-36 physical function subscores ($P=0.046$, $r=-0.716$).

Conclusion: Patients with seropositive AAG had objective evidence of widespread autonomic failure affecting multiple domains which improved significantly after immunotherapy. Quantitative testing using autonomic biomarkers should be used to define initial deficits, guide therapeutic decisions and document treatment response.

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EPR2012

Autonomic dysfunction in idiopathic Parkinson's Disease, GBA-PD and Multiple System Atrophy

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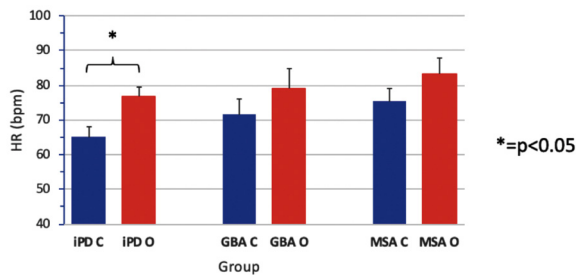
Background and aims: Autonomic dysfunction is a well-known feature of α -synucleinopathies. Pathogenic and clinical differences between Parkinson's Disease (PD) and Multiple System Atrophy (MSA) have been extensively described in the literature. Conversely, less is known about the impact of glucocerebrosidase (GBA) gene, associated with a more severe disease course in PD, on dysautonomic symptoms.

The aim of the study is to assess the differences of cardiovascular autonomic dysfunction in PD patients, with and without GBA mutations, compared to MSA patients.

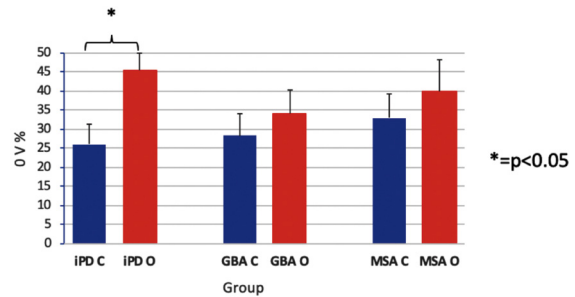
Methods: Autonomic cardiac control at rest and during orthostatic challenge in 9 idiopathic PD, 6 GBA-PD and 4 MSA patients was evaluated. ECG and respiration were recorded in supine position for 10 minutes and during active standing for another 10 minutes. Segments of 250±50 beats were selected for the analysis of Heart Rate Variability using two approaches, linear spectral analysis and non-linear symbolic analysis.

Results: Concerning demographic characteristics, the subgroups did not differ significantly in age nor disease duration.

At rest, autonomic parameters were similar in the 3 groups. iPD patients showed a significant increase of heart rate and sympathetic modulation, expressed by 0V%, in response to orthostatic stress. Differently, MSA and GBA-PD patients did not show any significant modification of autonomic parameters during standing. In details, orthostatic challenge caused an higher increase of 0V%, marker of sympathetic modulation, in iPD patients compared to MSA and GBA-PD cases (120% vs 53% and 33%).



Heart Rate response to orthostatic stress in the 3 subgroups



Sympathetic response (0V%) to orthostatic stress in the 3 subgroups

Conclusion: The study suggests that GBA-PD patients show a more severe cardiovascular autonomic dysfunction compared to IPD, similarly to MSA patients.

Disclosure: Nothing to disclose

EPR2013

A clinico-genetic study based on the Innsbruck MSA Registry (IMSA-R)

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Background and aims: Multiple system atrophy (MSA) is a rare, rapidly progressive atypical Parkinsonian disorder of the adulthood. Despite considered sporadic, few pedigrees of neuropathologically confirmed MSA with both autosomal dominant and recessive inheritance pattern have been described.

Methods: Here we retrospectively screened the Innsbruck MSA registry (IMSA-R) for patients with possible or probable MSA diagnosed according to the revised MSA consensus criteria (Gilman et al. 2008). In contrast to the consensus criteria we allowed a positive family history for neurodegenerative disorders documented in at least one additional family member of 1st, 2nd or 3rd degree. Clinical demographic characteristics were analysed in our cohort.

Results: 80% (183) out of 230 IMSA-R patients provided information on family history. At least one additional family member with neurodegenerative disorders was documented in 25% (46) of MSA patients. Family history was mostly positive for parkinsonism [56.5% (26)], followed by dementia [28.3% (13)], tremor [19.6% (9)], ataxia [6.5% (3)] and motor-neuron disease [2.2% (1)]. Familial clustering (>2 family members affected by neurodegenerative disease) was observed in 19.6% (9). Genetic screening for hereditary ataxia was performed in 21.7% (10) yielding mostly negative results. The median age at disease onset in MSA patients with positive family history was 53.4 (49.0; 60.8) years, with parkinsonism being the most common onset feature [47.8% (22)].

Conclusion: Although generally considered a sporadic disease, every 4th patient with MSA had a positive family history for neurodegenerative diseases in our cohort. Furthermore, we observed familial clustering in 20% of these patients.

Disclosure: Academic study, no external financial support allotted. The authors declare no conflict of interest. Dr. Leys is supported by the ParkinsonFond Österreich.

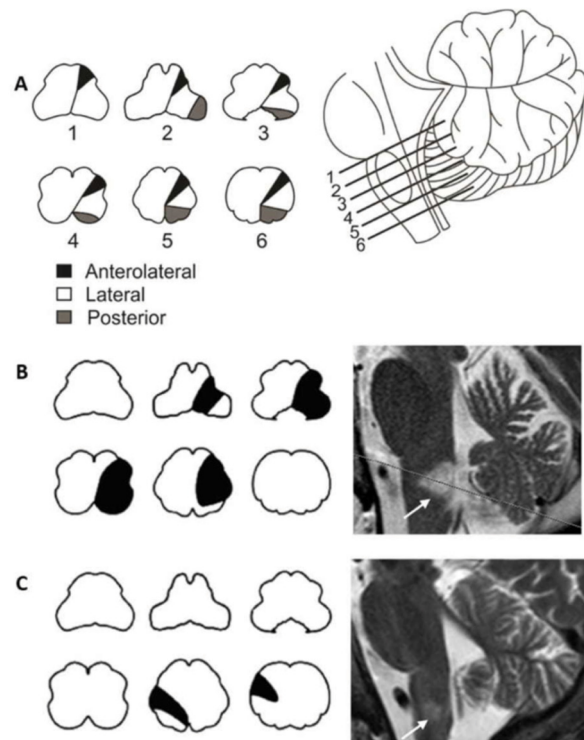
EPR2014

Abnormal breathing patterns and their relation to lesion extension and position in patients with acute unilateral lateral medullary infarction

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Background and aims: Different breathing abnormalities, from sleep-disordered breathing to overt respiratory failure, have been described in acute unilateral lateral medullary infarction (ULMI). Here we analyzed the relation of specific breathing pattern abnormalities to ULMI lesion location and extension.

Methods: We prospectively monitored breathing patterns using polysomnography (PSG) in 40 patients with MRI-confirmed acute ULMI (70% male, aged 57 (IQR 51-69) years) during the 1st 3 weeks after symptom onset. We compared the breathing patterns among MRI groups according to lesion location and extension. Lesions were categorized vertically into 4 groups according to their extension (localized/extensive: involving ≤ 2 / > 2 horizontal sections, respectively) and involvement of open/closed medulla, and horizontally into anterolateral, lateral or posterior (Figure 1).



Schematic presentation of lesion mapping. A) Sections 1-3: open medulla, sections 4-6: closed medulla. Shaded areas: horizontal territories. B) Vertically extensive open medulla lesion, involving posterior, lateral and anterolateral horizontal territories. C) Vertically localized closed medulla lesion, involving lateral horizontal territory.

Results: Abnormal breathing patterns of ≥ 10 minutes long episodes were observed in 26 (65%) patients; ataxic in 23 (58%), periodic in 16 (40%) and tachypnea in 8 (20%) (Figure 2). Abnormal breathing patterns occurred more frequently in vertically extensive and localized open medulla lesions than in localized closed medulla lesions ($p=0.027$, Table 1) and in horizontally large lesions involving \geq half of the lateral territory or multiple horizontal territories ($p=0.001$, Table 1). Ataxic breathing was significantly more frequent in patients with concomitant cerebellar lesions compared to pure ULMI (12/15 cases [80%] vs 11/25 cases [44%], respectively, $p=0.046$).

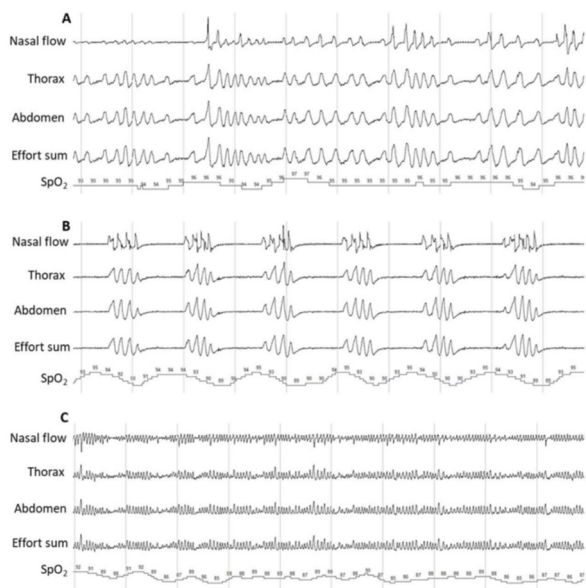


Figure 2. 5-min epochs of PSG recordings representing different abnormal breathing patterns. A) Ataxic breathing. B) Periodic breathing. C) Sustained tachypnea accompanied by low oxygen saturation.

Vertical lesion extension	Extensive inv. open (n=20)	Localized inv. open (n=9)	Extensive restr. to closed (n=5)	Localized restr. to closed (n=6)	p-value
Ataxic	14 (70%)	4 (44%)	4 (80%)	1 (17%)	0.078
Periodic	10 (50%)	3 (33%)	2 (40%)	1 (17%)	0.513
Tachypnea	5 (25%)	2 (22%)	1 (20%)	0 (0%)	0.714
Any abnormal breath. pattern	16 (80%)	5 (56%)	4 (80%)	1 (17%)	0.027

Horizontal lesion extension	P (n=6)	L small (n=10)	L large (n=10)	P+L (n=11)	P+L+AL (n=2)	L+AL (n=1)	p-value
Ataxic	1 (17%)	3 (30%)	8 (80%)	10 (91%)	0 (0%)	1 (100%)	0.001
Periodic	0 (0%)	2 (20%)	5 (50%)	7 (64%)	2 (100%)	0 (0%)	0.019
Tachypnea	1 (17%)	0 (0%)	2 (20%)	4 (36%)	0 (0%)	1 (100%)	0.127
Any abnormal breath. pattern	1 (17%)	4 (40%)	7 (70%)	11 (100%)	2 (100%)	1 (100%)	0.001

Table 1. Frequencies of abnormal breathing patterns in regards to vertical and horizontal lesion extension. P – posterior, L small – lateral lesion involving < half lateral territory, L large – lateral lesion involving \geq half lateral territory, AL – anterolateral.

Conclusion: Majority of our ULMI patients presented with abnormal breathing patterns, which were associated with vertically and/or horizontally extensive lesions as well as involvement of the open medulla. Concomitant cerebellar lesions seemed to contribute to ataxic breathing.

Disclosure: The study was funded by the Slovenian Research Agency (Grants Nos. P3-0171 and P3-0338).

EPR2015

Electrochemical skin conductance as a marker of autonomic failure in patients with Multiple System Atrophy

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Background and aims: Multiple System Atrophy (MSA) is a rare neurodegenerative disabling disease combining poorly levodopa-responsive parkinsonism, cerebellar ataxia and autonomic failure (AF). Severe cardiovascular AF is associated with poor prognosis. Since sweating dysfunction is less well known, we investigated the interest of a quick and non-invasive assessment of sweating (Sudoscans[®]) as a marker of AF in MSA.

Methods: 129 patients of the French Reference center for MSA with an annual follow-up including the Unified MSA Rating Scale (UMSARS) and measurements of electrochemical skin conductance (ESC) of feet and hands (Sudoscans[®]) participated to this study. 67 patients had annual follow-up data (mean \pm SD follow-up was 29.2 \pm 18.0 months). Statistical analysis included: (i) correlations between ESC and MSA type, age, disease duration, BP (supine and standing), autonomic symptoms (COMPASS), (ii) comparisons between groups with normal or abnormal ESC, and (iii) multivariate analysis by logistic regression. Relationship between MSA severity progression during follow-up with ESC and other variables were modeled by Generalized Estimating Equation (GEE).

Results: Feet or hand ESC were abnormal at the 1st visit in 72 (57%) and 103 (81%) patients. Abnormal ESC were related to greater systolic BP fall upon standing and UMSARS II scores. Significant and independent predictors of worsening were female gender, a probable diagnosis, longer disease duration and lower feet and hand ESC. Abnormal ESC baseline values were significant predictors of future worsening independently from other factors.

Conclusion: Feet and skin ESC were significantly related to MSA severity and orthostatic hypotension. Furthermore, baseline SUDOSCAN results could predict more severe disease progression.

Disclosure: Nothing to disclose

EPR2016

Temporal Relation of Ictal Asystole to Onset of Syncope in Focal Seizures

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Background and aims: Ictal asystole (IA) is the most common peri-ictal cardiac arrhythmia. IA may cause traumatic falls due to syncope with sudden loss of muscle tone. Pacemaker implantation may only help to prevent syncope in IA if cardioinhibition is the dominant pathomechanism. We investigated the temporal relation between IA and syncope to determine how often IA was the primary cause of syncope [Saal DP;2017].

Methods: Video-EEG databases of the participating centers were searched for subjects with recorded focal seizures and IA, defined as an RR interval of ≥ 3 2nds preceded by heart rate deceleration. We assessed time of onset and duration of asystole and syncope, if present. Presence of syncope was evaluated using video (loss of muscle tone) and EEG (generalized slowing or flattening). We determined that asystole < 3 seconds before syncope could not have been the primary cause of syncope [Saal DP;2017].

Results: We reviewed 39 seizures with IA from 30 subjects (17 male, median age 41 years [range 15-74 years]). Syncope occurred in 23 IA events; in all 21 IA events ≥ 10 seconds and in 2 out of 18 IA events < 10 seconds. IA always preceded syncope. According to the predefined criteria, in three cases IA could not have been the primary cause of syncope.

Conclusion: Our results show that IA is the likely cause of syncope in 20 out of 23 seizures and syncope is more likely to occur in IA events ≥ 10 seconds. Cardioinhibition is an important early but not exclusive mechanism causing syncope in IA.

Disclosure: Nothing to disclose

EPR2017

Abnormal circadian blood pressure and supine hypertension in patients with multiple system atrophy and pure autonomic failure - diagnostic and therapeutic implications.

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Background and aims: Supine hypertension and reversal of circadian blood pressure (BP) pattern occur in chronic autonomic failure due to multiple system atrophy (MSA) and pure autonomic failure (PAF). 24-hour ambulatory BP monitoring (24hr-ABPM) has been specifically modified to additionally assess both supine hypertension and orthostatic hypotension (OH) during daily activities in patients with MSA and PAF. This has not been compared in these disorders alongside with BP and heart rate (HR) responses during head-up tilting (HUT). The aim of this study is to characterise supine hypertension and circadian blood pressure rhythm in MSA and PAF patients.

Methods: 45 patients (26 MSA, 19 PAF) without anti-hypotensive medications underwent cardiovascular autonomic testing and 24hr-ABPM. Age, gender, clinical features and disease duration were recorded with BP and HR responses during HUT and 24-hr ABPM.

Results: Both groups had confirmed autonomic failure and OH during HUT, greater in PAF ($p < 0.01$) despite similar disease duration. With 24hr-ABPM, nocturnal hypertension was present in $> 25\%$ of both groups. Supine hypertension was present in 10/26 (38%) MSA and 10/19 (53%) PAF. A higher proportion of PAF had abnormally reversed circadian rhythms compared to MSA (68% vs 54%, respectively), without statistical significance. Nocturnal hypertension was significantly correlated with longer disease duration in MSA ($p = 0.03$).

Conclusion: Supine hypertension and reversed circadian BP rhythms are present in MSA and PAF. 24hr-ABPM does not differentiate between the groups. However, it provides information contributing to risk evaluation of supine hypertension, and should aid therapeutic intervention and efficacy of different (non-pharmacological and drug) measures in MSA and PAF.

Disclosure: Dr Shiwen Koay was funded by the Guarantors of Brain Entry Fellowship. Dr Valeria Iodice is grateful to the NIHR Biomedical Research Centre for their support.

EPR2018

Effects of Once-Daily Amprelosetine (TD-9855), a Norepinephrine Reuptake Inhibitor, on Blood Pressure in Subjects With Symptomatic Neurogenic Orthostatic Hypotension Associated With Synucleinopathies

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Background and aims: In neurogenic orthostatic hypotension (nOH), standing blood pressure (BP) falls due to inadequate norepinephrine (NE) release. Amprelosetine, a novel, long-acting, NE reuptake inhibitor, has shown durable symptom improvement in subjects with nOH associated with synucleinopathies. The objective of this study was to evaluate BP regulation in subjects with symptomatic nOH treated with open-label amprelosetine.

Methods: In a phase 2 study, subjects received amprelosetine once-daily (3–20mg) for up to 20 weeks, with 4-week follow-up after amprelosetine withdrawal. Assessments included Orthostatic Hypotension Symptom Assessment Item 1 score (OHSA#1; dizziness, lightheadedness, feeling faint); standing/sitting/supine systolic BP (SBP); standing duration; and plasma NE.

Results: 17 symptomatic subjects (baseline OHSA#1 score >4) were enrolled (mean age, 65 years). Mean increase in 3-minute standing SBP from baseline at Weeks 4 and 20 was 9.0mmHg and 10.8mmHg, respectively; >50% of subjects maintained SBP >80mmHg. Sitting SBP changes were less, with little change in supine SBP. At Week 4, 67% of subjects could stand for >5 mins, 31% improvement from baseline. NE plasma levels rose from pre-dose to Week 4 (1664.93–2231.67pmol/l). Baseline NE plasma levels correlated with standing BP increase. Amprelosetine was well tolerated.

Durable symptom improvement in nOH was accompanied by increase in standing and sitting SBP, standing duration, and NE plasma levels, with little effect on supine SBP.

Conclusion: These encouraging findings on BP regulation in nOH with amprelosetine treatment for up to 5 months are being evaluated in ongoing Phase 3, double-blind, confirmatory studies in subjects with nOH.

Disclosure: R Vickery is an employee of Theravance Biopharma Ireland Limited and stockholder of Theravance Biopharma US, Inc.

EPR2019

Automated calculation of baroreflex sensitivity (BRS) indices

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Background and aims: Baroreflex sensitivity (BRS) indices provide information about the sympathetic adrenergic function by defining the parameters of the blood pressure (BP) response to Valsalva manoeuvre (VM). Indices are usually calculated manually which is time consuming and dependent on the subjective assessment and subject to human error. The aim of this research was to objectify the method with automatization of calculation of BRS indices.

Methods: In 69 individuals with a history of vasovagal syncope and no other neurological or systemic illnesses (mean age 47.04±11.18, 55 females) autonomic nervous system testing that included BP response to VM was performed. For each participant BRS indices were calculated from the systolic BP curves during the VM: BRSa1, alpha BRSa (α -BRSa) and beta BRSa (β -BRSa). BRS indices were calculated manually and through an automated process with MATLAB R2019b. Automatization software was created according to previously known formulas for BRS indices, with additional calculation of average baseline BP values.

Results: Median values for manually calculated indices were 21.45 for BRSa1, 7.01 for α -BRSa, and 1.37 for β -BRSa, and for automatically calculated 23.91 for BRSa1, 6.99 for α -BRSa, and 1.19 for β -BRSa. There was statistically significant correlation between the manually and automatically calculated results for all three coefficients (BRSa1: $r_s=0.920$, $p<0.001$; α -BRSa: $r_s=0.879$, $p<0.001$; β -BRSa: $r_s=0.889$, $p<0.001$).

Conclusion: Automatization of BRS indices calculation shows results highly correlated with manually calculated indices, reduces time required for calculation and reduces the impact of subjective human component on the calculations.

Disclosure: Nothing to disclose

EPR2020

Cognitive impairment in multiple system atrophy versus Lewy body disorders

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Background and aims: Dementia is considered a non-supportive diagnostic feature for multiple system atrophy (MSA). Nevertheless, post-mortem verified dementia with Lewy bodies and Parkinson's disease masquerade as MSA. Cognitive impairment (CI), especially executive dysfunction, may occur in MSA patients. It is, however, unclear whether CI manifests in early disease stages.

Objective: To compare the prevalence of CI in MSA versus other Lewy Body disorders (LBD), including dementia with Lewy bodies and Parkinson's disease, in early (<3 years from symptom onset) versus more advanced disease stages (≥3 years from symptom onset).

Methods: A total of 364 patients (LBD: n=83; MSA: n=281) of the natural history study of synucleinopathies register have been analysed. Consensus diagnostic criteria for dementia with Lewy bodies, Parkinson's disease and MSA were applied. To assess CI, the Montreal Cognitive Assessment (MoCA) has been used.

Results: In early disease stages, median MoCA scores did not differ significantly between MSA and LBD. In advanced disease stages, MSA patients had a significantly higher median MoCA score compared to LBD patients (27 versus 25, p=0.006).

Table 1: Comparison of the median MoCA Scores of Lewy Body disorders versus MSA patients at early and advanced disease stages

Early disease stage (<3 years disease duration)			
	Lewy Body disorders	MSA	P*
No. of patients	15 (16.5%)	76 (83.5%)	
Female	6 (40%)	28 (36.8%)	0.817
Age	74.00 (66.00; 77.00)	61.00 (55.00; 66.75)	< 0.001
MoCA	27.00 (23.00; 30.00)	29.00 (26.25; 30.00)	0.784
Advanced disease stage (≥3 years disease duration)			
	Lewy Body disorders	MSA	P*
No. of patients	68 (24.9%)	205 (75.1%)	
Female	15 (22.1%)	92 (44.9%)	0.001
Age	69.50 (62.25; 75.00)	61.00 (56.00; 67.00)	< 0.001
MoCA	25.00 (20.25; 28.00)	27.00 (23.00; 29.00)	0.006

Dichotomous variables are reported by frequency (percentage), quantitative variables by median (1st quartile; 3rd quartile). * Gender was tested with the Pearson's Chi-Square-Test, Age with the T-Test and MoCA with the Mann-Whitney-Test; No.: Number; MSA: Multiple System Atrophy; MoCA: Montreal cognitive Assessment

Comparison of the median MoCA Scores of LBD versus MSA patients at early and advanced disease stages

Conclusion: In patients with longer disease duration severity of CI helps to differentiate LBD from MSA.

Disclosure: Nothing to disclose

Cerebrovascular diseases 3

EPR2021

The clinical benefit of mechanical thrombectomy after 6 to 24 hours of acute large vessel occlusion in very elderly stroke patients.

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Background and aims: Previous studies evaluating 90-day outcomes of acute large vessel occlusion patients with late window in elderly patients ≥ 80 years have been limited to small numbers undergoing endovascular reperfusion therapy.

Methods: Using a multicenter prospective stroke registry adult patients (aged ≥ 18 years) with acute large vessels occlusion in patients with ischemic stroke, who were hospitalized in one of the 15 participating centers between March 2010 and December 2018. And patients who underwent endovascular reperfusion therapy at 6 to 24 hours and had available measured 90-days modified Rankin scale was collected for this study. We compared neurological and functional outcomes between patients in patients ≥ 80 vs. < 80 years.

Results: We included 146 patients with ≥ 80 (mean age 83.4 ± 3.3 , 38.4% males) and compared them to 758 patients with < 80 years (mean age 65.4 ± 11.5 , 66.6 % males). Only eighteen percent of our elderly cohort achieved good 90-day mRS compared to 45.1% in younger patients ($p < 0.001$). 20.5% percent of elderly patients died compared to 11.7% ($p = 0.006$), respectively of younger patients. Old age (OR 3.99; 95% CI 1.11–17.57, $p < 0.046$) and higher baseline NIHSS (OR 1.10; 95% CI 1.01–1.20, $p < 0.03$) correlated with poor prognosis in study patients.

Conclusion: Mechanical thrombectomy performed late time window was significantly less effective in older patients. A more careful approach is needed before performing the EVT in these patients.

Disclosure: Nothing to disclose

EPR2022

Endovascular treatment in orally anticoagulated stroke patients: An analysis from the German Stroke Registry-Endovascular Treatment

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Background and aims: Endovascular treatment (ET) in orally anticoagulated (OAC) patients has not yet been evaluated in randomized clinical trials and data regarding this issue are sparse.

Methods: We retrospectively analyzed the German Stroke Registry-Endovascular Treatment (GSR-ET). Primary outcomes were successful recanalization defined as modified thrombolysis in cerebral infarction (TICI 2b-3), good outcome at 3 months according to modified Rankin scale (mRS 0-2 or back to baseline) and intracranial hemorrhage (ICH) until hospital discharge.

Results: Out of 2521 patients, 442 (17.6%) were treated with OAC, 201 (8.0%) with Vitamin-K-antagonists (VKA), and 241 (9.6%) with non-Vitamin-K-antagonist oral anticoagulants (NOAC). OAC-patients were older (VKA 77.6 years, NOAC 76.2 years vs no-OAC 71.6 years, $p < 0.005$), had more often known atrial fibrillation (88.1%, 85.3% vs 30.9%, $p < 0.005$) and a higher rate of arterial hypertension (85.0%, 83.6% vs 73.7%, $p < 0.005$). With regards to efficacy, the rate of mTICI 2b-3 were similar among the 3 groups (82.7%, 85.5% vs 82.7%, $p = 1.00$ and 0.57). On day 90, good outcome was less frequent in OAC patients (28.4%, 31.1% vs 40.9%, $p < 0.005$ and < 0.05). ICH rates were similar among the 3 groups (12.1%, 12.4% vs 10.4%, $p = 1.00$ and $p = 0.86$). (For patient details see table 1) Regression analysis revealed no influence of OAC status neither on good outcome (OR 1.03, 95% CI 0.99-1.08) nor on ICH (OR 1.03, 95% CI 0.94-1.05).

Parameter	No OAC	Thrombolysis	p-value	NOAC	p-value	Missing values
n (%)	2079 (82.5)	201 (8.0)	n. a.	241 (9.6)	n. a.	0 (0)
Age, mean \pm SD	71.6 \pm 13.4	77.6 \pm 10.7	< 0.005	76.2 \pm 10.5	< 0.005	0 (0)
Female, n (%)	1051 (49.6)	114 (56.7)	0.108	127 (52.7)	0.722	0 (0)
Anticoagulant therapy, n (%)	790 (38.0)	12 (6.0)	< 0.005	30 (12.4)	< 0.005	0 (0)
Arterial hypertension, n (%)	1527 (73.7)	170 (85.0)	< 0.005	199 (83.6)	< 0.005	12 (5.0)
atrial fibrillation, n (%)	414 (20.0)	44 (21.9)	1	69 (28.6)	< 0.005	8 (3.3)
Hypertension, n (%)	868 (41.4)	82 (40.7)	0.004	93 (38.4)	0.008	18 (7.5)
Atrial fibrillation, n (%)	638 (30.9)	177 (88.1)	< 0.005	203 (85.3)	< 0.005	18 (7.6)
History of smoking, n (%)	464 (22.4)	22 (10.9)	< 0.005	38 (15.8)	0.008	320 (12.7)
psfKI, median	0 (0, 1)	0 (0, 2)	< 0.005	0 (0, 1)	< 0.005	90 (3.7)
NIHSS, median	15 (10, 19)	15 (11, 19)	0.788	16 (12, 20)	< 0.005	30 (12.2)
ASPECTS, median	9 (8, 10)	9 (8, 10)	0.384	9 (8, 10)	0.384	584 (23.2)
Reperfusion rate (mTICI)	1688 (82.7)	162 (82.7)	1	206 (85.5)	0.37	44 (1.7)
2b-3, n (%)	125 (12.1)	25 (12.4)	1	25 (10.4)	0.858	0 (0)
ICH until discharge, n (%)	795 (40.9)	50 (28.4)	< 0.005	64 (28.1)	< 0.05	399 (15.6%)

Table 1: Baseline patient, stroke, imaging and treatment characteristics. Abb.: OAC=oral anticoagulation, NOAC=non-Vitamin K antagonist oral anticoagulant, SD=standard deviation, psfKI=perceived modified Rankin scale, NIHSS=National Institutes of Health Stroke Scale, ASPECTS=Alberta Stroke Program Early CT Score, mTICI=modified thrombolysis in cerebral infarction, ICH=intracranial hemorrhage

Table 1

Conclusion: Data from daily routine suggest that ET can be performed successfully and safely in LVO stroke patients treated with OAC.

Disclosure: Nothing to disclose

EPR2023

Atrial fibrillation as the hidden cause of cryptogenic stroke The Nordic Atrial Fibrillation and Stroke Study (NOR-FIB) – an interim analysis

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Background and aims: Studies with insertable cardiac monitors (ICMs) show that up to 30% of cryptogenic stroke patients have an underlying atrial fibrillation (AF) that would not be detected with standard clinical follow-up. There is, however, no consensus about the timing and duration of rhythm monitoring. Furthermore, there are no specific biomarkers widely used in clinical praxis for selecting patients for prolonged cardiac rhythm monitoring. **Methods:** NOR-FIB is an international multi-center prospective observational study of the occurrence of AF in cryptogenic stroke / TIA patients with ICMs for 12 months. Blood samples measuring biomarkers are taken in the acute phase and at 12 months' follow-up. Patient inclusion started in January 2017 and will continue until March 2020. Patients are included within 14 days from symptom onset. Threshold for the AF or atrial flutter diagnosis is set to 2 minutes.

Results: By January, a total of 235 patients have been included in 16 participating centres. 7 patients were excluded due to reclassification to another stroke subtype after acquiring additional data. 1 patient with neoplasm was incorrectly classified as having ischemic stroke at the 1st evaluation. 2 patients have experienced adverse events that required earlier removal of the device and there was registered 1 spontaneous explantation. From 227 studied patients, AF or atrial flutter was detected in 54 patients, resulting in detection rate of 23.8%.

Conclusion: ICMs are effective in detecting atrial fibrillation in patients with cryptogenic stroke and are associated with low complication rate. New interim analyses and update will be presented.

Disclosure: Nothing to disclose

EPR2024

Brain imaging as the predictor of atrial fibrillation The Nordic Atrial Fibrillation and Stroke Study (NOR-FIB)

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Background and aims: The presence of simultaneous acute infarctions in different arterial territories and affection of predominantly anterior circulation is suggestive of cardioembolism. In the ongoing Nordic Atrial Fibrillation and Stroke study (NOR-FIB) we evaluate the incidence of atrial fibrillation (AF) in patients with cryptogenic stroke using insertable cardiac monitors. The purpose of the single-center interim analysis was to evaluate whether there is a specific imaging pattern associated with post-stroke detected AF or atrial flutter lasting at least 2 minutes.

Methods: 86 patients were included by 8th January 2020 in Østfold Hospital Trust with 51 patients concluding the 1-year observation period. 1 patient was excluded. Brain MRIs or CTs were evaluated for the presence and localization of acute and chronic ischemic lesions. T-test for numerical and Chi-Square test for categorical variables were used.

Results: 16 patients had newly diagnosed AF or atrial flutter within 12 months (detection rate of 32%). Median (IQR) time to inclusion after the index event was 9 (7-13) days and to AF detection 23.5 (7.25-156.25) days. No sex differences between patients with and without AF were observed but patients with AF were significantly older ($p=0.005$). There was no specific imaging pattern of acute lesions associated with AF. Previous ischemic lesions in posterior circulation and particularly cerebellar lesions were significantly associated with AF [OR 5.8 95% CI (1.482, 22.694) and OR 6.2 95% CI (1.305,29.459) respectively].

Conclusion: Previous infarctions in posterior circulation and especially cerebellum were suggestive of underlying AF. New interim analyses with updated results including other markers will be presented.

Disclosure: Nothing to disclose

EPR2025

Cognitive Outcome after Carotid Endarterectomy in Patients with Carotid Artery Stenosis

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Background and aims: The effect of carotid revascularization on the neurocognitive functioning remains elusive. The study aimed to evaluate the change in cognitive performance and its predictors in patients with symptomatic internal carotid artery (ICA) stenosis undergoing carotid endarterectomy (CEA).

Methods: Patients with history of transient ischemic attack within the past 6 months and ipsilateral high-grade stenosis of ICA undergoing CEA were prospectively enrolled. Cerebral hemodynamics was assessed by cerebral vasomotor reactivity (CVR) measured through transcranial Doppler ultrasonography. Colored Progressive Matrices plus Complex Figure Copy Test, and phonemic plus categorical Verbal Fluency tests were performed to assess right and left hemisphere cognitive functions, respectively. Cerebral hemodynamics and cognitive functions were assessed before and 6 months after CEA.

Results: 183 patients were included. The mean age was 73.1 (6.9) years. At 6 months from CEA, cerebral hemodynamics and neurocognitive functioning were significantly improved. The performance change in cognitive tests exploring the revascularized hemisphere was inversely associated with pre-operative ipsilateral CVR and positively associated with the improvement in cerebral hemodynamics. At the multivariable analysis, the cognitive improvement was associated with exhausted CVR ($\beta=2.36$, 95% CI 0.37- 4.35; $p=0.020$) and mean velocity of middle cerebral artery below normal values ($\beta=4.47$, 95% CI 2.66- 6.28; $p<0.001$) on the side of ICA stenosis before CEA.

Conclusion: In patients with symptomatic high-grade ICA stenosis, cognitive performance was enhanced at 6 months since CEA. The cognitive improvement was related to the increase in CVR on the side of stenosis correction and predicted by baseline cerebral hemodynamic status.

Disclosure: Nothing to disclose

EPR2026

Stroke patients' adherence to direct oral anticoagulants – preliminary results from the MAAESTRO Study

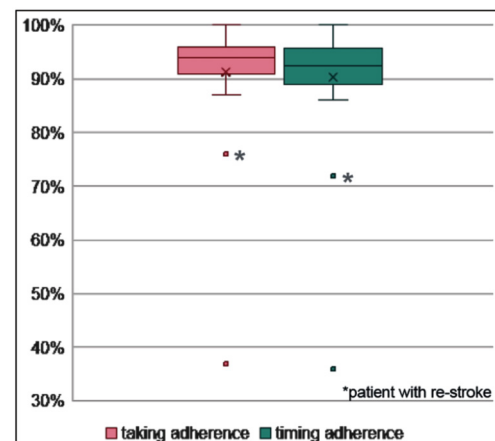
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Background and aims: Non-adherence to direct oral anticoagulants (DOACs) is a matter of concern, especially in secondary stroke prevention. Here, we present preliminary results on stroke patients' adherence to DOACs from the MAAESTRO study's observational phase.

Methods: MAAESTRO includes DOAC-treated AF patients with a recent ischemic stroke. Adherence is measured electronically with the Time4Med™ device, on which patients self-register their medication intakes by pressing a button. Taking adherence was calculated as (total number of recorded intakes)/(total number of prescribed doses). Timing adherence was defined as (total number of intakes recorded within 25% of the average dosing time)/(total number of prescribed doses). Drug holidays were defined as ≥ 3 consecutive days without recorded intake.

Results: We report on the 1st 28 patients who completed the 6-month observational phase (36% female, median age 77.5, median CHA2DS2-VASc score 5). 21 patients (75%) took a twice-daily DOAC and 17 patients (60.7%) used a pillbox. The median (IQR) taking and timing adherence were 94.1% (90.8-96.4) and 92.3% (88.8-95.5) respectively (Figure). Among patients with a twice-daily DOAC, taking adherence in the morning was significantly higher than in the evening (95.2% vs. 93.4%, $p=0.02$). 10 patients (36%) had at least one drug holiday. There was 1 recurrent stroke in a patient with 75.5% taking adherence and concomitant large artery atherosclerosis.



Taking and timing adherence of 28 MAAESTRO patients

Conclusion: Stroke patients showed high adherence rates to DOACs. However, the lower adherence to evening intakes among patients with twice-daily DOACs and the high number of patients with drug holidays are alarming.

Disclosure: Nothing to disclose

EPR2027

Clinical features and frequency of paediatric stroke code. An uncommon emergency.

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Background and aims: Our aim is to analyse the frequency, clinical features and diagnosis of extrahospitalary stroke code at pediatric age (from 1 month to 16 years-old) in a stroke centre with a multidisciplinary paediatric stroke management pathway attending a total population of about 500,000 in-habitants .

Methods: Retrospective analysis of all the consultations from the pediatric emergency department to the on-duty neurologist selecting those corresponding to extrahospitalary stroke code between January 2014 to March 2018. We analysed demographic data, final diagnosis and treatments.

Results: A total of 204 consultations were analysed, of which 22 (10.7%) were activated as stroke codes (6 cases per year on average). The diagnosis was confirmed in 7 children (31.8%), with 2 hemorrhagic (29 %) and 5 ischemic strokes (71 %). The mean door-to-neuroimaging time was 177 minutes (IQR 267) and the mean NIHSS was 11 (IQR 10). 2 ischemic stroke patients out of 5 (40%) were treated with recanalization therapies: 1 patient with intravenous thrombolysis and both of them with mechanical thrombectomy. The main diagnosis in the group of patients without confirmed stroke was migraine (7 out of 15 patients).

Conclusion: The paediatric stroke code is an uncommon emergency in a stroke centre, being the migraine the main stroke mimic. The paediatric stroke code facilitates an early evaluation and the proper indication of recanalization treatment for ischemic stroke.

Disclosure: Nothing to disclose

EPR2028

Extracellular vesicles as circulating biomarkers linked to intracerebral haemorrhage severity and outcome.

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Background and aims: After intracerebral haemorrhage (ICH), extracellular vesicles (EVs) can be released from any type of cell, that could reflect the severity of the process but also the underlying restorative processes. We explore the relationship between circulating EVs with the severity and functional outcome of ICH.

Methods: Observational prospective study including patients with ICH. Demographics, risk factors, comorbidities (Charlson index), etiology, ICH volume, clinical severity according to NIHSS score at baseline, 24 hours and 7 days [categorized as mild (<4), moderate (5-15) or severe (>15)] and functional outcome (mRS) at 7 blood samples at 24-48h and at 5-7 days (ExoQuick Kit) and quantified by ELISA.

Results: 28 patients were included. 18 (62%) men; age [median (IQR)]: 70 (22.75); NIHSS [median (IQR)] at baseline: 12 (12), at 24h: 8.5 (10.5), at 7d: 7.5 (8.75). The number of EVs at 24h was higher in the most severely affected patients ($p=0.035$, Kruskal Wallis test) and a significant correlation between the number of EVs and NIHSS scores at 24h was found ($p=0.039$, Spearman's Rho). At 7 days, there was a decrease in the number of EVs, that was significantly greater in patients with mRS 0-2 at 3 months at 3 months ($p=0.017$, Wilcoxon rank-sum test).

Conclusion: This study suggests a relationship between the release of EVs with the severity and outcome of ICH. These findings deserve further research on the role of EVs as a prognostic biomarker of ICH.

Disclosure: Nothing to disclose

EPR2029

After stroke, apraxia of eyelid opening is associated with high morbidity and right hemispheric infarctions

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Background and aims: Apraxia of eyelid opening (AEO) refers to impaired voluntary eyelid elevation of presumed supranuclear origin. It is well described in neurodegenerative disorders and traumatic frontal lobe injury, but the frequency of AEO in stroke is unknown.

Methods: To investigate the prevalence of AEO after stroke, we consecutively enrolled stroke patients with an anterior circulation occlusion admitted for acute endovascular thrombectomy (EVT) to the Department of Neurology, Rigshospitalet, Copenhagen University Hospital. Exclusion criteria were posterior circulation stroke, impairment of consciousness and a history of other eyelid disorder. Patients were systematically screened for AEO, conjugated gaze palsies and cortical ptosis within 48 hours after EVT. Integrity of the pupillary light reflex was verified by automated pupillometry. CT of the brain 24 hours after thrombectomy were analyzed for stroke location by an independent neuroradiologist.

Results: 98 patients with anterior circulation large vessel occlusions were included. AEO was present in 6 patients, conjugated gaze palsy in 37 and cortical ptosis in 16. 54 did not have eye symptoms. AEO was associated with high National Institute of Health Stroke Scale and Modified Ranking Scale scores ($p<0.01$). AEO and conjugated gaze palsy were associated with right hemispheric infarctions ($p<0.01$).

Conclusion: AEO is frequent and underreported in acute large vessel stroke. Recognition of AEO is important because it signals increased mortality and morbidity. AEO was associated with right hemispheric infarctions, suggesting that supranuclear eyelid control may have a right hemispheric dominance.

Disclosure: Nothing to disclose

EPR2030

Withdrawn

EPR2031

Analysis of 13 Cases of adult PCNSV

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Background and aims: Primary central nervous system vasculitis (PCNSV) is a rare but a well-recognized cause of neurological injury. We aim to explore characteristics and outcomes of PCNSV diagnosed patients.

Methods: Total of 13 cases diagnosed as PCNSV from 2011 to 2019 in our hospital were enrolled and followed up for more than 3 months. Clinical, laboratory, radiographic, histological and therapeutic data were collected and analyzed. We differentiated patients into 2 groups due to size of involved vessels: large/proximal (angiogram confirmed) and small/distal vessel group (biopsy confirmed).

Results: 7 presented with focal neurologic deficits due to stroke, 6 with cognitive dysfunction, 5 with headache, 1 seizure and 1 palinopisa. 6 were diagnosed by brain biopsy with no findings of angiogram (small/distal vessel group) and 6 by angiogram only (large/proximal vessel group). Patients in small/distal vessel group frequently had cognitive dysfunction at presentation, radiologically leptomeningeal gadolinium-enhanced lesions, microbleeds, and subarachnoid hemorrhage on MRI. Patients in large/proximal vessel group had higher incidence of focal neurologic deficits and headache. All patients received prednisone, 2 treated with additional cyclophosphamide and another 2 with azathioprine. Relapse were more common in large/proximal vessel group.

Conclusion: PCNSV is a multifarious disease containing subdivided groups. Larger vessel type presents more aggressive course. The identification of PCNSV subgroups could help selection of adequate treatment and prediction of clinical course.

Disclosure: Nothing to disclose

Cerebrovascular diseases 4

EPR2032

Malignant left atrial appendage morphology: current classification vs H-L system

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Background and aims: A subset of patients with atrial fibrillation suffer recurrent embolic strokes despite appropriate anticoagulant therapy. In previous studies the risk of stroke recurrence has been associated with the left atrial appendage (LAA) morphology (non-chicken wing according to the current classification), knowing those with a greater risk as malignant LAA. Recently, it has been suggested a simpler classification with 2 categories: Low-risk (LAA-L) and High-risk (LAA-H) morphologies; which could be easier to apply and could correlate better with the risk of embolic stroke.

Methods: Retrospective analysis from a registry of patients with recurrent embolic strokes despite appropriate anticoagulant therapy, in which LAA morphology had been studied with cardiac CT scan for LAA occlusion in our tertiary hospital. LAA morphology was classified according to the four current categories and H-L morphology by the same cardiologist.

Results: 26 cases were included in the analysis. We identified 22 (84.6%) chicken wing, 1 (3.8%) windsock and 3 (11.5%) cactus by the current classification system, while 15 (57.7%) were classified as LAA-H and 11 (42.3%) as LAA-L by the new system. Half of the 22 cases with chicken wing morphology were considered LAA-H by the new classification (11; 50%), whereas all non-chicken wing LAA were also classified as LAA-H morphology (4; 100%).

Conclusion: Most cases were classified as chicken wing morphology, as opposed to other previous studies. However, applying the new classification system more than half of the cases were classified as high-risk morphology, which constitutes a more expected result in our series of malignant LAA.

Disclosure: Nothing to disclose

EPR2033

Predictors of long-term mortality in spontaneous intracerebral haemorrhage survivors.

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Background and aims: Factors associated with long-term mortality after spontaneous intracerebral haemorrhage (ICH) have been poorly investigated. Our objective was to identify predictors of long-term mortality in a prospective cohort of 30-day survivors of spontaneous ICH.

Methods: We prospectively included consecutive adults admitted between 2004 and 2009 within the 1st 24 hours of a spontaneous ICH, who survived at least 30 days. We evaluated clinical and radiological predictors of long-term mortality using univariate and multivariable Cox' proportional hazard regression models.

Results: Of 560 patients with spontaneous ICH, 304 survived more than 30 days and consented for the follow-up. During a median follow-up of 10 years (interquartile range [IQR] 8.0-10.5), 176 patients died, leading to a median survival of 6.8 (IQR 6.0-7.8) years after ICH. Age (hazard ratio [HR] per 10-year increase: 1.63; 95% confidence interval (CI): 1.42-1.87), national institutes of health stroke scale score at admission (HR per 1-point increase: 1.03; CI: 1.01-1.04), baseline ICH volume higher than 30 ml (HR: 1.62; CI: 1.10-2.38), on-going antiplatelet therapy before ICH (HR: 1.45; CI: 1.06-1.99) and pre-stroke modified Rankin scale >2 (HR: 1.72; CI: 1.20 to 2.43) were independent predictors of long-term mortality. In the subgroup of 239 patients who underwent a magnetic resonance imaging (MRI)-scan, cerebral atrophy (HR per 1-point increase: 1.48; CI: 1.11-1.97) was also independently associated with long-term mortality.

Conclusion: Characteristics related to both the ICH and pre-existing status influence long-term mortality. Cerebral atrophy was the only MRI marker independently associated with long-term mortality.

Disclosure: Nothing to disclose

EPR2034

Frailty predicts short and long-term outcomes of reperfusion treatment in acute stroke

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Background and aims: Frailty is the most important short and long term predictor of disability in the elderly. The aim of the study was to evaluate whether diagnosis frailty predicts short and long-term mortality and neurological recovery in old patients who underwent reperfusion acute treatment in stroke unit

Methods: Consecutive patients were older than 65 years who underwent thrombectomy or thrombolysis in a single Stroke Unit from 2015 to 2018. Predictors of stroke outcomes were assessed including demographics, baseline NIHSS, time to needle, treatment and medical complications. Premorbid frailty was assessed with a comprehensive geriatric assessment (CGA) including functional, nutritional, cognitive, social and comorbidities status. At 3 and 12months, all-cause of death and clinical recovery (using mRS) were evaluated.

Results: 102 patients, of whom 31 underwent mechanical thrombectomy and 71 venous thrombolysis (mean age 77.5, 65- 94 years) entered the study. Frailty was diagnosed in 32 out of 70 patients and associated with older age ($p=0.001$) but no differences in baseline NIHSS score or treatment strategies. At follow-up, frail patients showed higher incidence of death at 3 (25% vs 3%, $p=0.008$) and 12 (38% vs 7%, $p=0.001$) months. Frailty was associated with worse neurological recovery at 3 month (mRS 3.4+1.8 vs 1.9+1.9, $p=0.005$) and 1 year follow-up (mRS 3.2+1.9 vs 1.9+1.9) for free survival patients.

Conclusion: Frailty is an important predictor of efficacy of acute treatment of stroke beyond classical predictors of stroke outcomes. Larger prospective studies are warranted in order to confirm our findings.

Disclosure: Nothing to disclose

EPR2035

Lymphocyte-to-monocyte ratio and C-reactive protein as potential biomarkers of cerebral venous thrombosis severity

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Background and aims: Recent studies have shown that inflammatory biomarkers as C-reactive protein (CRP) and lymphocyte-to-monocyte ratio (LMR) are involved in thromboembolic diseases, including stroke. However, their role in cerebral venous thrombosis (CVT) is yet to be established. Our aim is to evaluate the association of LMR and CRP with clinical and imaging severity in CVT patients.

Methods: We performed a retrospective analysis of CVT cases admitted to a tertiary hospital from 2006 to 2019. We excluded cases of infection at admission, autoimmune inflammatory and haematological diseases. We evaluated the occurrence of focal neurological deficit at admission and parenchymal lesion due to CVT. Functional outcome was assessed by modified Rankin Scale (mRS) at discharge. Bivariate analyses were done with Mann Whitney U or Spearman correlation. For multivariate analyses we used binary logistic regression or linear regression.

Results: Our cohort included 78 adult patients, 74,4% female, median age of diagnosis of 43 years old. The median National Institutes of Health Stroke Scale at admission and discharge was 0. The median mRS at discharge was 1. Lower LMR levels correlated with the presence of focal neurological deficit ($p=0.016$; OR 0.663; CI 0.475-0.927) and with parenchymal lesion due to CVT ($p=0.017$, OR 0.656, IC 0.465-0.926). CRP correlated positively ($p=0.046$, OR 1.017, CI 1.000-1.035) with the occurrence of haemorrhagic lesions and with higher mRS at discharge ($p=0.037$; OR 1.027; IC 1.002-1.053).

Conclusion: In our cohort, CRP and LMR were associated with a clinical course and brain lesions suggestive of greater severity. These findings may have implication in functional outcome.

Disclosure: Nothing to disclose

EPR2036

Disability improvement in remote ischemic conditioning following acute ischemic stroke

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Background and aims: Remote ischemic conditioning (RIC) is a procedure that supposedly reduces the ischemic injury of an organ. Few studies assessed the role of RIC in acute ischemic stroke (AIS)-related disability.

We aimed to evaluate the efficiency and safety of RIC in AIS patients who are ineligible for reperfusion therapy.

Methods: We performed a double-blind randomized controlled trial. The patients with AIS were assigned to receive 5 cycles of RIC twice daily during the 1st 5 days of hospitalization – an arm tourniquet was inflated either to 180mmHg (intervention group) or 30mmHg (sham group). Clinical severity and disability scales (i.e. NIHSS, mRS, Barthel, IADL, ADL), CT brain infarct volume and complications were recorded at baseline, 90 days and 180 days.

Results: 27 patients were included. Mean age was 65 years old and 60% were men. Although the outcome in terms of disability (median mRS score=0.5 vs. 1, median Barthel score=10 vs. 5, median ADL score=2.5 vs. 1) and infarct volume (median infarct volume=0.29 vs. 0.37) was better in the interventional group than in the sham group, the difference between them was not statistically significant ($p=0.9$, $p=0.7$, $p=0.7$ and $p=0.6$ respectively). RIC did not correlate with local or cerebral complications (e.g. recurrence of stroke, hemorrhagic transformation, convulsions). Prior stroke was associated with better functional outcome ($p=0.04$), suggesting the beneficial role of preconditioning in stroke.

Conclusion: In AIS, RIC is safe and well tolerated. Larger studies are required in order to prove its potential neuroprotective effect.

Disclosure: Nothing to disclose

EPR2037

Neutrophil lymphocyte ratio is associated with the severity of cerebral edema and worse functional outcome in patients with acute ischemic stroke

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Background and aims: Inflammation has an important role in the pathophysiology of acute ischemic stroke. The search for biomarkers to better monitor patients with acute stroke has been of great importance and investigation. Particularly, the neutrophil lymphocyte ratio (NLR) has been associated with functional outcome. Our aim is to determine the association between NLR, cerebral edema (CED) and functional outcome, in patients with acute ischemic stroke treated with intravenous thrombolysis or/and mechanical thrombectomy.

Methods: In this retrospective study, we included all patients with acute ischemic stroke from the anterior circulation treated with intravenous thrombolysis or/and mechanical thrombectomy, between January 2017 and December 2018. We collected demographic, clinical, analytical, and imagological data on all patients. CED was classified from 0 to 3, according to severity. Functional outcome was classified using the modified Rankin scale (mRs). We estimated the odds ratios (OR) and the 95% confidence intervals, between the NLR and CED using ordinal logistic regression, and between NLR and functional outcome using binary logistic regression.

Results: 375 patients were included, median NIHSS 14 (IQR 7-19); 67% were submitted to intravenous thrombolysis and 61% to mechanical thrombectomy. In the multivariate regression model, NLR was associated with an increase of CED (OR=1.47; CI95% 1.18-1.82; $p<0.01$), and worse functional outcome (OR=0.64; CI95% 0.48-0.81; $p<0.01$).

Conclusion: In acute ischemic stroke, systemic inflammation is associated with an increased risk of severe cerebral edema and worse functional outcome. The neutrophil-to-lymphocyte ratio maybe useful in future clinical trials testing immunomodulators efficacy in acute ischemic stroke.

Disclosure: Nothing to disclose

EPR2038

Prevalence of Dehydration at acute ischemic stroke onset and correlation between stroke severity and dehydration sub-type: A prospective study from a tropical country

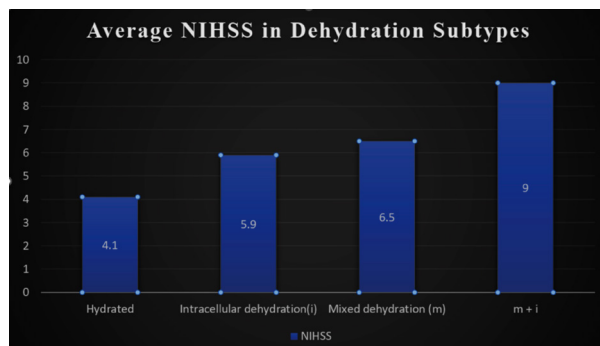
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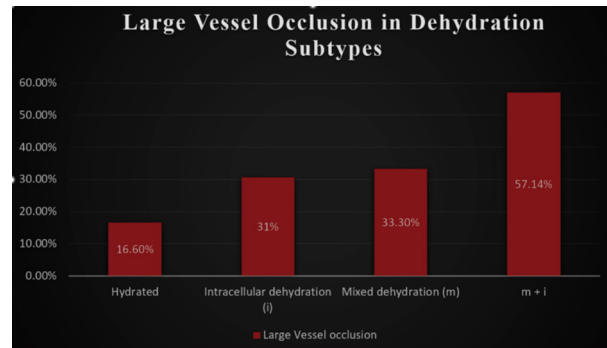
Background and aims: Dehydration can be pathophysiologically categorised into intracellular (ID), extracellular (ED) and mixed (MD) types. Prior studies on dehydration in stroke have not taken this into consideration. The objective was determining the prevalence of dehydration at stroke onset and correlating stroke severity with dehydration subtype.

Methods: Consecutive anterior circulation ischemic stroke patients, who presented within 24 hours of symptom onset to our centre, were included. Patient's clinical features, stroke characteristics, and severity (NIHSS score) were recorded. Patients with renal and pulmonary diseases, uncontrolled diabetes, on diuretics, and intravenous fluids were excluded. Dehydration subtypes were categorised and their surrogate markers, including Urine osmolality/plasma osmolality ratio (>1.5), BUN creatinine ratio (>15), urine specific gravity (>1.020), apart from U.sodium, Serum chloride, sodium, uric acid levels, and IVC collapsibility were recorded.

Results: 177 ischemic stroke admissions were surveyed, of which 72 met the inclusion criteria. 65% were dehydrated, of which 33.3% had ID, 30% had MD and interestingly 36% had positive markers for both MD and ID (ED not separately categorised as no defined surrogate marker). Average NIHSS for hydrated, ID, MD and MD+ID groups were 4.1, 5.9, 6.5 and 9 respectively. Statistically significant correlation was found between presence of dehydration, especially a multitype dehydration and severity of stroke at onset ($p < 0.005$).



Average NIHSS in Dehydration subtypes



Large vessel occlusion percentages in various Dehydration subtypes

Conclusion: Nearly 2/3rds of stroke patients were dehydrated at onset. There was significant correlation between the presence of multi-type dehydration and a more severe stroke. Our study emphasizes that, accumulated Dehydration, as a precipitous trigger for ischemic incidents, needs scrutiny.

Disclosure: Nothing to disclose

EPR2039

CHA2DS2-VASc score in predicting stroke severity, mortality and worse prognosis in a cohort of 566 patients, with or without atrial fibrillation, admitted for ischaemic stroke

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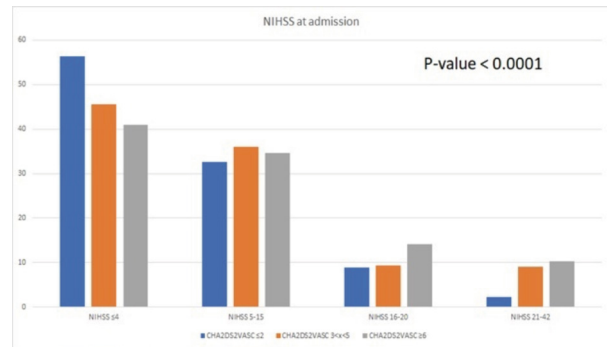
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Background and aims: The CHA2DS2-VASc score is recommended by the International Guidelines. Its predictive abilities in stroke and thromboembolic risks stratification of atrial fibrillation(AF) patients have largely been demonstrated. However, its use as predictor of stroke severity and as prognostic factor is controversial, both in AF and non-AF-patients. Our aim is to investigate if the CHA2DS2-VASc would predict ischaemic stroke severity and prognosis in patients with or without AF.

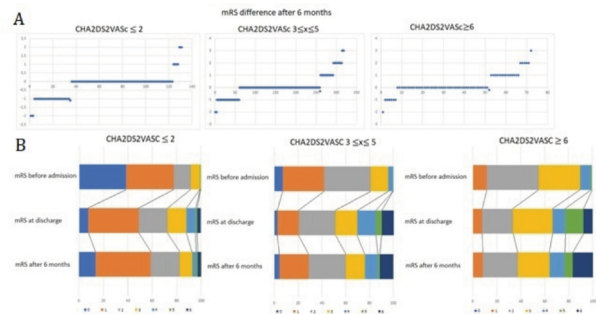
Methods: We performed a retrospective study including 566 patients (AF:26%; non-AF:74%), admitted with ischaemic stroke between 2012 and 2013. We divided our population into 3 groups, depending on their CHA2DS2-VASc (low-L-,middle-M- and high-risk-H-patients). We calculated their NIHSS at admission and their modified-Rankin scale score (mRS) before admission, at discharge and after 6 months (excluding those who died during the hospitalization-7.9%). Finally, for each group, we analysed if any difference between AF and non-AF-patients could be detected.

Results: Patients with higher CHA2DS2-VASc had a greater risk to develop a stroke with higher NIHSS (P-value<0.0001) (fig.1) and a higher mortality rate (L-2.9%;M-9.9%;H-8%);both in AF and non-AF-patients. However, AF-patients had a worse NIHSS compared to the non-AF-patients. They also had increased mortality in the low and middle-risk-group.

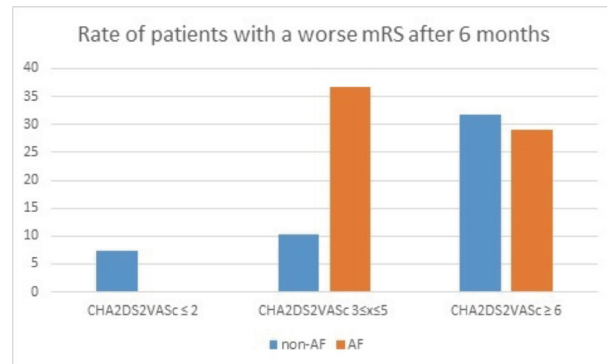
The rate of patients with a worse mRS after 6 months increased over the groups(7%-L, 18.5%-M and 29%-H-risk-group) (fig.2). The same is observed both for AF and non-AF-patients(fig.3).



The patients have been divided into 3 different groups, depending on their CHA2DS2-VASc score (low-blue; middle-orange; high risk patients-grey column) and into 4 groups depending on their NIHSS score. Thus, the correlation between the pre-admission CHA2DS2-VASc score and the NIHSS has been detected



A. Difference between mRS score after 6 months and at discharge for each CHA2DS2-VASc score group. B. Shift analysis of the mRS score in each CHA2DS2-VASc score group



Correlation between worse mRS score at 6 months and presence or absence of comorbid atrial fibrillation in each CHA2DS2-VASc score group

Conclusion: Our data seem to support the use of the CHA2DS2-VASc-score not only as simple tool for cerebrovascular risk but also as a predictor of stroke severity, mortality and worse recovery in AF and, interestingly, also in non-AF-patients.

Disclosure: Nothing to disclose

EPR2040**Anticoagulation treatment in the acute phase of cardioembolic stroke: a retrospective study**

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Background and aims: Although anticoagulation treatment for cardioembolic stroke prevention is recommended, there is no consensus for continuation or disruption anticoagulation in the stroke acute phase. Our aim is to describe treatment variations and compare clinical outcomes in these patients.

Methods: A pilot, retrospective, observational, cohort study of adult patients admitted in a Stroke Center between January 2014 and December 2018 with diagnosis of acute cardioembolic ischemic stroke receiving anticoagulation at admission. Patients who received intravenous thrombolysis were excluded. According to continuation or discontinuation anticoagulation by treating neurologist at admission, we compared safety and clinical outcomes at discharge and at 90 days.

Results: We identified 177 patients, anticoagulation was continued in 106 (59 %) patients. These patients had lower National Institutes of Health Stroke Scale (NIHSS) scores (median 4 vs 14, $P<0.001$), lower hemorrhagic transformation in neuroimaging (14.8% versus 33%, $P=0.025$) but similar thrombotic and major bleeding events at discharge. We found lower mortality and better functional outcome at 90 days in patients in whom anticoagulation was continued (mortality 6% versus 34%, $P=0.01$ and modified Rankin Scale score of 0–2, 54.2% versus 73.7%, $P=0.031$), however the statistical difference disappears after adjusting by NIHSS at admission. Among patients with a severe stroke ($\text{NIHSS}>15$) there was no difference in clinical outcome or mortality between

Conclusion: Our pilot study suggests the continuation of anticoagulation in early phase of cardioembolic stroke is safe, even in severe stroke, and it was associated with better outcomes. Further prospective studies are needed to confirm these findings.

Disclosure: Nothing to disclose

EPR2041**Cancelled**

EPR2042

Causes and rates of switching across direct oral anticoagulants: a real-life setting prospective study, systematic review and meta-analysis

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Background and aims: Crossover between direct oral anticoagulants (DOACs) has been underinvestigated, but happens frequently in clinical practice. The purpose of this study was to evaluate causes, rates and outcomes of DOAC-to-DOAC switch.

Methods: Patients receiving first DOAC prescription at the Anticoagulation-Center, Cardiology-Dept, Bologna-Bellaria Hospital in 2017-2018 were consecutively included and prospectively followed-up. DOAC-to-DOAC switch was the main outcome; causes of switch (cardiovascular-CV-events and non-CV drug-related adverse events), had direct biannual assessment before and after switch. We systematically reviewed (OSF-registered protocol) published studies reporting DOAC-to-DOAC switch, and determined by meta-analysis the pooled odds ratio (OR) for switch depending on index DOAC prescribed.

Results: Among 300 patients enrolled (mean age=79.3, mean follow-up=1.5 years), with no difference in CV risk factors depending on index DOAC, 13% underwent DOAC-to-DOAC switch, minor bleeding and non-CV adverse events being the most frequent causes. Dabigatran carried a 3-fold increase in risk of switch compared to other DOACs. Factors leading to switch resolved in 87% of cases afterwards. Annual rates of CV/non-CV events did not differ before and after switch. Pooling our data with those from 5 retrospective claim-based studies (n=259308), apixaban had consistently lower risk of DOAC-to-DOAC switch compared to dabigatran [OR=0.29 (0.25-0.34)] or rivaroxaban [OR=0.58 (0.50-0.67)], the former carrying a higher risk than the latter [OR=0.2.35 (1.93-2.86)].

Conclusion: DOAC-to-DOAC switch happens in 9%/year, and seems not to impact rates of CV events after switch. Dabigatran might carry a higher risk of DOAC-to-DOAC switch. Further studies are needed to confirm long-term safety and effectiveness of switching paradigm.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 2

EPR2043

Motor imagery by the hand laterality task in Wilson's disease patients

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Introduction: Motor Imagery (MI) refers to mental simulation process in which we imagine to perform an action without actually moving any muscles of body. MI impairments have been reported in several neurological disorders, but it has never been investigated in Wilson's disease (WD).

Methods: To explore MI in WD, we enrolled 19 WD patients attending the Movement Disorders Unit of the University of Naples and 15 healthy controls (HC) of similar sex, age and education. All participants completed the Global Assessment Scale (GAS), constructional, frontal and memory neuropsychological tests and scales for apathy and depression, and MI tasks (i.e., hand laterality judgement and letter rotation). In both tasks, participants had to judge whether a visual stimulus (hand or capital letter) presented in different angular orientations (0°, 90°, 180°, 270°) portrays a left or right laterality (left-right hand or canonical-mirror letter).

Results: Independent-sample t-tests showed that WD achieved significant lower scores on attentional ($p=0.02$) and Raven's matrices ($p=0.01$) tests, compared to HC. ANOVAs on correct response (accuracy) and reaction times (RTs) showed significant effects of orientation [$F(3,96)=7.611$, $p<.001$, $F(3,96)=4.145$, $p<.001$] and orientation-by-laterality, [$F(3,96)=3.199$, $p=0.02$, $F(3,96)=12.064$, $p<0.001$], with responses less accurate and RTs slower in judging left hand at 180° compared to the others orientations (all $p<0.05$), in WD.

Conclusion: Our findings demonstrate a specific alteration of MI skills in WD, thus supporting the simulation view according to which MI would be crucial in understanding intention and actions of others.

Disclosure: Nothing to disclose

EPR2044

Emotional Memory in Multiple Sclerosis Patients

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Background and aims: Emotional memory has been poorly studied in Multiple Sclerosis (MS). This study investigated the ability of MS patients to recognize emotionally charged material and compared this ability with their performance in verbal and visual episodic memory testing.

Methods: 30 MS patients and 30 healthy individuals matched for age, gender and education were included in the study. Participants underwent 2 memory tests (Greek Verbal Learning Test-II, Brief Visuospatial Memory Test-Revised) that assessed verbal and visuospatial learning and an experimental task (Emotional Memory Test, EMT). Addenbrooke's Cognitive Examination – Revised (ACE-R) and Depression Anxiety Stress Scale-21 were administered as measures of overall cognitive ability and presence of psychiatric symptoms respectively. Repeated measures ANOVA was conducted to investigate memory performance of MS patients and stepwise linear regression to clarify the contributing factors affecting EMT scores.

Results: MS patients performed poorly on all memory tests as compared to healthy participants (GVLII-II: $p=0.029$, BVMT-R: $p=0.013$, Emotional Memory Test- Word Recognition: $p=0.018$, Emotional Memory Test – Picture Recognition: $p=0.007$). Patients' performance on the verbal condition of the Emotional Memory Test was predicted by their overall cognitive ability [$R^2=0.363$, $F(2,24)=6.84$, $p=0.004$ ACE-R: $\beta=0.368$, $p=0.037$] but no variable predicted the particularly low performance observed in the visual condition of the test.

Conclusion: Findings support the presence of a specific deficit in visual emotional memory of MS patients, which is not related to clinical characteristics and performance in memory testing.

Disclosure: Nothing to disclose

EPR2045

Nonverbal cognitive deficits in left-hemisphere aphasic patients: relationship with sites of lesion and linguistic measures

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Background and aims: Studies on the relationship between nonverbal and verbal measures in aphasia have yielded contradictory findings. This study examines the relationship between these measures and site of lesion in aphasic stroke patients.

Methods: Participants: 27 aphasic stroke patients (mean age 59.96±10.35) and 35 controls (65.80±9.42) were administered a neuropsychological battery. Patients scoring below a nonverbal cognitive screening cutoff were excluded. Patient lesion areas were measured from MRI scans. Measures and analyses: Number of lesion areas (Table 1), Modified Rankin Scale (Rankin), Barthel Index (Barthel), verbal and nonverbal measures (Table 2) are shown per patient. Patients scoring below 1.5 SD of the mean of controls in nonverbal domains were compared with those scoring above. Performance in verbal and nonverbal domains was correlated with lesion areas and the two disability measures.

Partic code	L.ACA lesions	L.PCA lesions	L.MCA lesions	L. subcort	L.BG	L.int caps	L. ant chor art	L. total	R.ACA lesions	R.PCA lesions	R.MCA lesions	R. subcort	R.BG	R. total
100	6	1	1	1	1	1	1	14						1
110	1	10	1	1	1	1	1	14						1
121	4	1	1	1	1	1	1	6						1
301	3	3	1	1	1	1	1	12						3
302	2	4	1	1	1	1	1	7	3		4			7
303	9							9						0
304	1	9	1	1	1	1	1	12						0
601	3	1	1	1	1	1	1	7						0
604	8	1	1	1	1	1	1	12						0
605	6	1	1	1	1	1	1	9						0
801	6	1	1	1	1	1	1	7		3	1	1	5	1
802	3	1	1	1	1	1	1	5		1				1
904	1	5	1	1	1	1	1	9						0
905	1	6	1	1	1	1	1	8			1	1	2	2
906	2	10	1	1	1	1	1	16		1	2	1	4	4
907	1	5	1	1	1	1	1	7			2	1	3	3
908		6	1	1	1	1	1	7						0
910	4	7	1	1	1	1	1	12			3			3
912	3	1	1	1	1	1	1	6						0
913	1	10	1	1	1	1	1	12	1		2			3
914	1	8	1	1	1	1	1	13						0
915		7	1	1	1	1	1	11						0
916	2	4	1	1	1	1	1	10						0
917	1	2	1	1	1	1	1	5						0
918	2	9	1	1	1	1	1	14						0
920		7	1	1	1	1	1	9				1		1
922	1	2	7	1	1	1	1	14						0

Partic. code: participant code; L: left hemisphere; R: right hemisphere; ACA: anterior cerebral artery; PCA: posterior cerebral artery; MCA: middle cerebral artery; subcort: subcortical; BG: basal ganglia; int caps: internal capsule; ant chor art: anterior choroidal artery. Note: no R internal capsule and R anterior choroidal artery lesions were found in any of the participants.

Table 1. Number of lesions in each vascular territory per stroke patient

110	B	4	>5	<3	<3	3	0	2	1	7	00	18	3	0	9
121	B	3	90	<3	<3	0	2	0	0	15	64	12	6	9	34
301	C	1	95	>5	>5	13	5	6	7	13	45	12	5	4	13
302	A	1	100	>5	>5	9	3	7	7	7	36	10	2	4	11
303	NF	3	3	3.5	3.5	7	1	3	2	10	32	5	7	6	5
304	B	4	55	<3	<3	0	0	0	0	6	58	12	4	7	20
601	G	4	55	<3	<3	0	0	0	2	5	29	6	4	3	8
604	B	4	70	<3	<3	0	0	0	4	4	43	10	5	6	13
605	A,C	4	60	>5	>5	6	1	3	5	12	65	14	5	5	26
801	G	2	95	<3	<3	6	0	0	4	12	54	13	6	6	8
802	B	1	95	<3	<3	9	6	10	5	12	56	14	8	7	38
904	TM	3	75	3.5	3.5	0	3	0	1	11	7	43	9	4	7
905	NF	3	50	<3	3.5	10	3	3	4	14	34	9	5	5	16
906	NF	4	40	3.5	3.5	12	6	4	9	9	54	11	7	8	13
907	A, Dys	4	65	<3	>5	12	15	7	13	12	69	11	8	7	17
908	B	3	55	3.5	3.5	0	3	2	3	10	70	10	7	2	14
910	B	3	60	<3	<3	0	0	0	4	9	56	13	5	7	9
912	A, Ag	2	85	>5	>5	8	0	2	7	5	81	10	3	2	7
913	A	1	95	>5	>5	13	18	10	10	8	54	10	5	2	14
914	G	3	90	<3	<3	0	0	0	0	16	57	14	7	6	33
915	B	3	95	<3	<3	3	2	3	2	13	67	12	7	7	16
916	A	1	100	>5	>5	14	16	9	17	18	68	14	7	8	27
917	F	4	65	3.5	>5	9	2	1	4	12	48	12	4	5	11
918	B	4	55	<3	<3	1	0	1	1	9	39	11	6	7	7
920	A	0	100	>5	>5	13	12	11	11	18	70	12	7	7	28
922	G	4	70	<3	<3	2	0	0	1	3	37	5	1	2	3
CN	-	-	-	-	-	13.91	35.23	17.40	14.03	13.83	64.97	13.20	7.00	7.37	22.91
						(±0.28)	(±9.58)	(±3.11)	(±2.53)	(±3.16)	(±7.44)	(±1.08)	(±1.57)	(±1.90)	(±13.25)

Aphasia type: B = Broca's, C = Conduction, A = Anomic, G = Global, TM = Transcortical Motor, NF = Nonfluent unspecified, F = Fluent unspecified, Ag =agrammatic, Dys = dysarthric, Artic agilty: Articulatory agility, <3 = severe impairment, 3.5 moderate impairment, >5 = mild-no impairment; Phon fluency: phonological fluency; Animal: animals (semantic fluency); Vis mem immed: Visuospatial memory immediate; Vis mem del: Visuospatial memory delayed; Symb point: symbol pointing task (a span task); Pict point: picture pointing task; GAMA: General Ability Measure for Adults. Note: Tests in italics are nonverbal; in bold are test results <1.5 SD from the mean of the controls.

Table 2. Disability measures and test performance in verbal and nonverbal domains per stroke patient

Results: Patients were impaired in most verbal areas compared to controls, as expected. 12 patients scored within the normal range in the 6 nonverbal measures employed (Table 2), but did not differ from those scoring below in number of left or right hemisphere lesions, nor in verbal task performance. Left hemisphere lesions correlated with few verbal tasks (none after correction). The Rankin correlated negatively with all verbal tests and 1 nonverbal, and the Barthel positively with 1 verbal test and 2 nonverbal (Table 3).

	Rankin	Barthel	Artic agilty	Phrase length	Mental Control	Phon fluency	Animal	Digit span	Spatial span	V mem immed	V mem del	Symb point	Pict point	GAMA
L.ACA	.03	-.15	.09	.10	.01	-.04	-.08	.11	-.36	-.16	-.07	-.29	-.09	-.38*
L.PCA	.13	-.02	-.01	.03	.00	-.03	-.18	.10	-.09	-.11	-.09	-.44*	-.19	-.08
L.MCA	.27	-.36	-.29	-.30	-.20	.02	-.08	-.25	-.12	.08	-.02	.20	.29	-.11
L.subcort	.30	-.09	-.39*	-.27	-.37	-.30	-.29	-.10	.01	.27	.27	.03	.26	.20
L.BG	.20	-.10	-.14	-.28	-.19	-.19	-.06	-.15	-.12	.07	.15	.09	.12	.14
L.int caps	.16	-.15	-.22	-.22	-.30	-.12	-.20	-.03	.03	.04	-.11	.08	.18	.16
L. ant chor art	.25	-.09	.10	.05	-.03	.07	-.09	-.00	-.13	-.02	-.02	-.21	-.08	-.07
L. lesions	.39*	-.35	-.27	-.30	-.28	-.07	-.21	-.18	-.27	.03	-.02	-.03	.18	-.18
R.ACA	-.35	.31	.37	.28	.21	.15	.30	.15	-.20	-.26	-.11	-.38*	-.25	-.11
R.PCA	.20	-.35	.06	.22	.24	.09	.30	.18	-.07	.01	-.01	.16	.24	-.06
R.MCA	-.30	.20	.16	.19	.34	.21	.23	.25	-.09	-.09	.16	-.11	-.03	-.22
R.subcort	-.03	-.04	-.15	.12	.32	.28	.11	.21	.37	.19	.05	.29	.38*	.19
R.BG	-.05	-.33	-.25	-.14	.12	-.11	-.15	-.07	.18	-.21	-.01	-.00	-.00	-.12
R.lesions	-.31	.18	.16	.25	.41*	.24	.26	.27	-.02	-.13	.08	-.12	.01	-.16
total														
Rankin	-.58***	-.36	-.57**	-.49**	-.76***	-.52**	-.48*	-.19	-.27	-.23	-.01	-.36		
Barthel	.36	.14	.31	.34	.52**	.34	.44*	.31	.37	.14	.07	.44*		

Artic agilty: Articulatory agility (BDAE); Phrase length: Phrase length (BDAE); Mental Control: Mental Control (BDABE); Phon fluency: phonological fluency; Animal: animals (semantic fluency); Vis mem immed: Visuospatial memory immediate (trials 1-5); Vis mem del: Visuospatial memory delayed; Symb point: symbol pointing task (a span task); Pict point: picture pointing task (a span task); GAMA: General Ability Measure for Adults. * p < 0.05, ** p < 0.01, *** p < 0.001. Note: Tests in italics are nonverbal; in bold are correlations that remain significant after Bonferroni correction.

Table 3. Correlations of verbal, nonverbal and disability measures with number of regions in each vascular territory

Conclusion: Nonverbal cognitive deficits were frequent in the aphasic patients but were unrelated to number of lesions in left or right hemisphere or to verbal task performance. The Rankin and Barthel are sensitive to different verbal and nonverbal domains.

Disclosure: The present study is funded by the European Union (European Social Fund – ESF) and Greek national funds through the Operational Programme “Education and Lifelong Learning” of the National Strategic Reference Framework (NSRF) – Research Funding Programme: THALES – UOA – “Levels of impairment in Greek aphasia: relationship with processing deficits, brain region, and therapeutic implications.”

EPR2046

Non-prescribed usage of psychostimulant drugs by medical students

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Background and aims: Students feel pressure to succeed in the highly competitive medical school environment and misuse stimulant drugs in order to enhance their focus and endurance. The aim of this study is to investigate the frequency and the side effects of stimulant usage.

Methods: A total of 326 people participated to the study. 32 students who were previously diagnosed with ADHD were excluded from analysis. The control group consisted of 93 1st grade and the study group consisted of 101 4th, 5th and 6th grade students. An online survey was used to investigate the habits of stimulant drugs usage, side effects and grade point average of the students.

Results: 16.1% of study group versus 6.8% of controls was using drugs. Although stimulant usage was higher in the study group, it was not statistically significant ($p=0.06$). Among the study group 64% were using methylphenidate, 14% modafinil and 21% were using both. 75% of the study group stated that they experienced various side effects. According to their evaluations, 79% of the students had increased performance. But grade point averages were not differ between stimulant user and not users ($GPA_{non-users}=2.91\pm 0.8$ and $GPA_{users}=3.07\pm 0.8$, $p=0.85$).

Conclusion: Our study has shown that stimulant usage increases in the course of medical education. However stimulants don't have any positive effects on GPA. We advocate more research in this area to expose the extent of the problem and begin to explore potential solutions for study habits and lifestyle choices.

Disclosure: Nothing to disclose

EPR2047

Lower motor neuron signs in the clinical spectrum of Creutzfeldt-Jakob disease: a case report

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Background: Creutzfeldt-Jakob disease (CJD) is a neurodegenerative disease characterized by rapidly progressive dementia. The clinical signs of CJD mainly reflect involvement of the central nervous system, although lower motor neuron involvement is rarely reported.

Methods: Case Report

Results: A 69-year-old man presented with a subacute cerebellar axial ataxia and important cognitive decline, rapidly progressing over 3 weeks. He scored 25/30 on Mini-Mental State Examination. Neurological examination revealed generalized hyperreflexia, a left pyramidal syndrome and ataxic gait, rendering him unable to walk unassisted. 2 months later, amyotrophy of the lower limbs with fasciculations were present. By this time, he also presented generalized myoclonic jerks and rapidly progressed to akinetic mutism 3 months after admission. Brain MRI diffusion-weighted imaging showed left caudate head, putamen and thalamus hyperintensity; CSF examination was positive for 14.3.3 protein; electroencephalogram denoted periodic complexes; and needle electromyography showed diffuse neurogenic potentials with spontaneous activity, suggestive of active denervation. Genetic studies found no mutations in prion gene PRNP and codon 129 polymorphisms analysis showed valine/valine (VV) homozygosity. Post-mortem brain histopathology revealed extensive vacuolization in the neocortex and basal ganglia and evaluation of spinal cord (L2-S1 segment) showed marked atrophy and neuronal loss of anterior horn cells, suggestive of motor neuron disease related to sporadic CJD.

Conclusion: Although rare, lower motor neuron signs can be part of the clinical spectrum of sporadic CJD, with histopathological correlation in neuropathology studies.

Disclosure: Nothing to disclose

EPR2048

Withdrawn

EPR2049

Spatial navigation in early multiple sclerosis

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Background and aims: Cognitive deficits with predominant slowing of information processing speed and impairment of episodic memory are common in early multiple sclerosis (MS). Spatial navigation changes and their associations with brain pathology have not been studied in MS. The aim was to characterize the profile of spatial navigation changes in 2 main navigational strategies (egocentric and allocentric) and their associations with demyelinating and neurodegenerative changes in early MS. **Methods:** Participants with early MS after the first clinical event (n=51) and age-, gender- and education-matched controls (n=42) underwent spatial navigation testing in a real-space human analogue of the Morris water maze, neuropsychological assessment, and MRI brain scan with voxel-based morphometry and volumetric analyses.

Results: The early MS group had lower performance in all spatial navigation tasks ($p \leq 0.038$). Based on the applied criteria, lower performance was present in 22–41% and 14–33% of the participants with early MS. The early MS group with less accurate spatial navigation had lower performance in various neuropsychological tests ($p \leq 0.039$). Smaller volume of the left nucleus accumbens ($\beta = -0.36$; $p = 0.011$) and larger lesion load volume in the cortical, subcortical and cerebellar regions ($\beta \geq 0.29$; $p \leq 0.032$) were associated with less accurate allocentric navigation performance.

Conclusion: Lower spatial navigation performance is present in 14–41% of the participants with early MS, who also have lower performance in other cognitive functions. Lesion load in specific brain regions is associated with allocentric spatial navigation changes in early MS.

Disclosure: This study was supported by the Grant Agency of the Charles University, Prague Grant No. 546317; Ministry of Health, Czech Republic – conceptual development of research organization, University Hospital Motol, Prague, Czech Republic Grant No. 00064203; and Institutional Support of Excellence 2. LF UK Grant No. 699012.

EPR2050

Memory impairment in FTD patients with pathogenic mutations

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Background and aims: A relative sparing of episodic memory compared to semantic/working memory is accepted in FTD patients, but this particular cognitive profile is more controversial in genetic-forms. Our aim was to characterize memory-related profiles of GRN and C9orf72 patients, the most prevalent genetic-forms in Portugal.

Methods: 31 FTD patients, including 18 GRN and 13 C9orf72 mutation carriers, were assessed with a neuropsychological comprehensive battery including Wechsler Memory Scale. Individual raw scores were converted into Z-scores. Differences between groups in working, semantic and verbal/visual episodic memory were examined and group performances in the different memory tasks were further correlated with data from CSF-biomarkers (A β 42, tau, p-tau and NfL).

Results: GRN patients had a mean age-of-onset of 56.39 (SD=5.69) years and the C9orf72 group tend to be older (M=59.45, SD=7.04). Of the total sample 71.4% (22/31), 72% (18/25) and 78% (25/31) had respectively working memory, episodic memory and semantic/autobiographic memory deficits, usually as a compound deficit. Considering episodic memory 61% (16/27) had verbal memory deficits, 49% (13/27) had visual memory deficits and 87% (18/27) had a mixed deficit. Group comparisons through non-parametric Mann-Whitney U test, showed that C9orf72-patients performed better in working memory and episodic memory/learning ($p < 0.05$). Concerning differences in CSF-biomarkers between groups, only higher levels of p-tau in C9orf72-patients were found ($p = 0.007$). A significant correlation between p-tau/tau ratio and visual memory was found in GRN-patients ($r = 0.711$, $p = 0.001$).

Conclusion: This study shows that there is a broad profile of memory impairment in genetic-forms of FTD, including episodic memory, which correlates with biomarkers of neurodegeneration.

Disclosure: Nothing to disclose

EPR2051

Effect of subthalamic nucleus deep brain stimulation on emotional prosody processing in Parkinson's disease: a review and meta-analysis

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Background and aims: Deep brain stimulation (DBS) of subthalamic nucleus (STN) leads to substantial motor improvement of Parkinson's disease (PD). Nevertheless, it is followed by behavioral or emotional changes. Aim of this study was to examine whether STN DBS induces changes in emotional processing (perception, recognition, expression) of vocal stimuli.

Methods: We conducted a literature search in Medline and Web of science between 2000 and 2019 using the keywords "prosody", "emotion", "deep brain stimulation", "Parkinson". We included studies assessing prosody processing of the basic emotions (happiness, sadness, fear anger, surprise, disgust and neutral) in PD patients after STN DBS. Additionally, we conducted a meta-analysis including 5 studies assessing emotional prosody recognition in the same or matched PD patients before and after STN DBS (both on medication, ON stimulation).

Results: Most studies showed no prosody recognition impairment after STN DBS (analysis comparing matched PD patients: random model Hedges' $g=-0.038$, $p=0.852$, $I^2=0$, $P=0.665$; analysis comparing the same PD patients pre- and post-operative: random model Hedges' $g=-0.087$, $p=0.577$, $I^2=0$, $P=0.354$). Moreover, there was no difference in prosody recognition ON or OFF stimulation. Nevertheless, patients perceived emotions more strongly after STN DBS. Concerning prosody emotion expression, fear was less well recognized when expressed postoperative.

Conclusion: Our results suggest that although STN DBS can induce changes in emotional prosody processing, there seems to be no prosody recognition impairment post-operative. Future studies with larger patient samples using standardized testing are needed, in order to derive definite conclusions about the effect of STN DBS on emotional prosody processing.

Disclosure: Nothing to disclose

EPR2052

Neuropsychological and neurological signs associated with the phenomenon of an alien hand in stroke

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Introduction: Alien hand syndrome (AHS) is a rare neurological disorder characterized by involuntary movements of the hand in association with the feeling that it acts on its own will. Typical combinations of an alien hand with other neurological and neuropsychological syndromes are underexplored. The aim of the work was to analyze the relationship between AHS and neurological/neuropsychological signs in patients with acute ischemic stroke (IS).

Methods: 9 acute stroke patients with AHS (mean age of 64.2 ± 4.7 years, range 42-86) were identified in the stroke center over a 10 year period. Neurological, neuropsychological and neuroimaging data were evaluated.

Results: 7 patients had right and 2 patients had left hemisphere IS. Foci of lesions had different topography but all patients ($n=9$) had at least partial involvement of a parietal lobe. Other involved structures included the frontal ($n=3$), temporal ($n=2$) and occipital ($n=3$) lobes, basal ganglia ($n=6$), corpus callosum ($n=1$). AHS was the earliest manifestation of IS and caused fright. It developed along with the feeling of coldness, mild hypoesthesia for pain and impairment of stereognosis and graphesthesia in the same hand. Ideomotor apraxia in both hands was present in all cases while constructional apraxia was identified in the majority ($n=6$), but still not in every patient. Executive dysfunction was not a hallmark of these patients and was found in only 2 cases.

Conclusion: Alien hand syndrome in IS patients is strongly associated with parietal lesions, impairment of elementary and discriminative sensation in the same hand as well as with ideomotor apraxia.

Disclosure: Nothing to disclose

Epilepsy 2

EPR2053

Validation of SeLECT score in prediction of late seizures in ischaemic stroke patients

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Background and aims: Ischaemic stroke is an important cause of structural epilepsy in adults. The SeLECT score is a major prediction model for late post-stroke seizures. The aim of our study is to verify the ability of the SeLECT score and its parameters (severity of the stroke, large-artery atherosclerosis, early seizures, cortical involvement, the involvement of the middle cerebral artery territory) to predict late seizures in ischaemic stroke patients.

Methods: Retrospective analysis of consecutive supratentorial ischaemic stroke survivors with a negative history of epilepsy admitted to 2 major comprehensive stroke centers in the Czech Republic and Austria in a year period (2015). The follow-up information was collected from available medical documentation, structured telephone questionnaire, and patients visits. The median follow-up period was 3.3 years. To assess the risk of late seizures, Cox proportional hazards regression analysis was performed.

Results: 315 patients were included (59% men, average age 69 years, median NIHSS 4, 29.2% received intravenous thrombolysis, in 6.3% mechanical thrombectomy was done). Late seizures occurred in 24 patients (7.6%). The SeLECT score as continuous variable showed hazard ratio 1.576 per point (95% CI 1.229–2.020; $p < 0.001$) with AUC 0.69 (95% CI 0.586–0.794). The hazard ratio of large-artery atherosclerosis was 2.210 (95% CI 0.989–4.942, $p = 0.053$) and cortical involvement of the ischaemic lesion 3.807 (95% CI 1.576–9.195, $p = 0.003$). The rest of the SeLECT score parameters performed insignificantly.

Conclusion: The SeLECT score was a significant predictor of late seizures in ischaemic stroke patients of our cohort. Cortical involvement had the highest hazard ratio of SeLECT score parameters.

Disclosure: Nothing to disclose

EPR2054

Focal cortical dysplasia type IIA and IIB: Is there any clinical difference?

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Background and aims: Focal cortical dysplasia (FCD) type II is divided in 2 subgroups based on absence (IIA) or presence (IIB) of balloon cells. The differences between these 2 entities are not completely understood. The aim of this study was to analyze distinctions between these 2 subgroups regarding clinical features and surgery outcome.

Methods: Cohort study including patients that underwent surgery for drug-resistant epilepsy and had histological proven FCD Type II. Clinical and neuroimaging data and 2-year surgery outcomes (Engel's classification) were obtained.

Results: Six FCD-IIA and 9 FCD-IIB were included. The median age at epilepsy onset was 4 years (IQR 6) in FCD-IIA and 12 years (IQR 20) in FCD-IIB. Regarding seizure characteristics, in FCD-IIA 33% had aura, 83% had impaired awareness, 83% had motor component and 50% had secondary generalization; in FCD-IIB 44% had aura, 67% had impaired awareness, 89% had motor component and 56% had secondary generalization. 83% of FCD-IIA versus 44% of FCD-IIB had daily seizures. Frontal lobe was the most frequent localization in both groups. Surgical outcomes for FCD-IIA were Engel Class I 50%, III 33% and IV 17%; for FCD-IIB were Engel Class I 56%, III 22% and IV 22%. 50% of FCD-IIA patients reduced antiepileptic drugs after 2 years follow-up versus 33% for FCD-IIB.

Conclusion: FCD-IIA patients presented earlier age of epilepsy onset and higher seizure frequency. Seizure semiology was similar despite a higher percentage of impaired awareness in FCD-IIA. Surgery outcomes were similar in both groups, but a higher percentage of FCD-IIA patients reduced antiepileptic drugs during follow-up.

Disclosure: Nothing to disclose

EPR2055

Epilepsy of infancy with migrating focal seizures (EIMFS) due to KCNT1 mutations shows an identifiable temporal sequence and a poor outcome with pharmaco-resistant epilepsy and high mortality with SUDEP

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Background and aims: Assessing data from patients with KCNT1 mutations associated to EIMFS to refine the phenotypic spectrum in particular their long term outcome. **Methods:** We sorted available medical reports of children with KCNT1 mutations and EIMFS followed in the French reference centre for rare epilepsy (2006-2016) and sent a dedicated questionnaire to update their health data for the last 6 months.

Results: 17 patients were included (age: median: 4[25th percentile:2-75th percentile:15] years, sex ratio: 1.4, duration of follow-up: 4[2-15] years). Epilepsy started with sporadic motor seizures in 71% of cases (n=12) at 6[1-52] days. Then, gradually increased to give way to a stormy phase at 57[30-89] days. The remaining patients (29%, n=5) started their epilepsy directly in the stormy phase at 1[1-23] days. On the EEG, interictal suppression patterns were frequent (n=12 patients, 71%). 3 patients received quinidine with no efficacy. 10 patients then entered a 3rd phase called consolidation phase, at 1.3[1-2.8] years. Seizures persisted at least daily (n=8.80%), taking a more frontal aspect. Long-term outcome was poor at 13.6[7.2-16.4] years marked by major mental and motor retardation with an active epilepsy, except for one patient. 8 patients (47%) died at 3[1.5-15.4] years, 3 of them by suspected SUDEP.

Conclusion: Refining the electro-clinical characteristics and the temporal sequence of epilepsy in infancy with migrating focal seizures should help recognizing this epilepsy syndrome. The poor prognosis requires the urgent development of trials targeting the treatment of patients in the stormy phase but also in the consolidation phase.

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EPR2056

IL-8 overexpression in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

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Background and aims: Active inflammation is a feature of pharmaco-resistant Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS). One of its manifestations, experimentally corroborated, is the activation of hippocampal microglia with consequent expression of pro-inflammatory cytokines. These molecules can interfere with normal neurotransmission, and contribute to decrease seizure threshold. IL-8 is a microglia-produced chemokine, with the ability to recruit inflammatory cells. Although studies of IL-8 levels during epilepsy are scarce, serum upregulation, correlating with seizure severity, has been reported. The aim of this study was to quantify IL-8 gene expression in brain tissue of MTLE-HS patients.

Methods: IL-8 gene expression was quantified by Real-time PCR in surgically resected hippocampus and cortex of 18 MTLE-HS (10F, 8M, 39.8±8.6y) patients and 10 controls (2F, 8M, 69.7±7.8y). Relative expression values were calculated using the 2-ΔΔCt method. Patient and Hospital Ethical Committee approval was obtained.

Results: Hippocampal IL-8 expression was higher in MTLE-HS patients in comparing to controls (3.73-fold, p=0.024). IL-8 gene expression was significantly increased in hippocampus of MTLE-HS patients in comparison to cortex of the same patients (4.58-fold; p=0.002); whilst no difference between brain regions were observed (p=0.33) in controls. Cortical IL-8 expression correlated positively with disease duration (rs=0.529; p<0.05).

Conclusion: IL-8 has been associated with Blood-Brain-Barrier disruption and immune cell migration to the Central Nervous System. Hippocampal IL-8 upregulation may thus contribute to the establishment of a vicious cycle of seizure activity – inflammation with disease perpetuation and progressive spreading of inflammation to the adjacent neocortical regions.

Disclosure: Funding: Tecnifar BICE

EPR2057

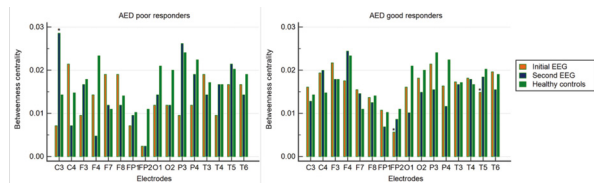
Can we predict drug response by functional connectivity in patients with juvenile myoclonic epilepsy?

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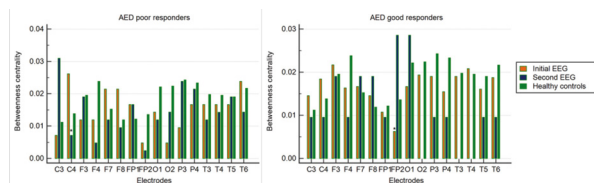
Background and aims: We investigated functional connectivity in patients with newly diagnosed juvenile myoclonic epilepsy (JME), and whether it could play a role as a biomarker predicting antiepileptic drug (AED) response.

Methods: We consecutively enrolled 38 patients with JME and 40 normal controls. The initial EEG was undertaken at the time of diagnosis of JME. The 2nd MRI was done after at least 12 months from the time of the initial EEG. We classified the patients with JME into 2 groups according to AED response at the time of taking the 2nd EEG. We investigated functional connectivity in the patients with JME and healthy controls.

Results: Of the 38 patients with JME, 4 patients were classified as AED poor responders, whereas 34 patients were enrolled as AED good responders. In the analysis of functional connectivity using coherence as a connectivity measure, the global efficiency and local efficiency in the AED poor responders were decreased, whereas the small-worldness index was increased. In the analysis of functional connectivity using phase locking value as a connectivity measure, the global efficiency and local efficiency in the AED poor responders were decreased. However, in the AED good responders, none of the network measures were different from those in healthy controls.



In the analysis of functional connectivity using coherence as a connectivity measure, the betweenness centrality at the Fp2 and T5 electrodes in the AED good responders was decreased compared to that in the healthy controls (0.0058 vs. 0.0109, $p=0.0393$ at Fp2; 0.0145 vs. 0.0202, $p=0.0396$ at T5)



In the analysis of functional connectivity using phase locking value as a connectivity measure, the betweenness centrality at the Fp2 electrode in the AED good responders was decreased compared to that in the healthy controls (0.0064 vs. 0.01357, $p=0.0039$ at Fp2)

Table 3. Differences of the changes in global functional connectivity according to antiepileptic drug response

AED poor responders				AED good responders					
	Initial EEG, mean ± SD	2nd EEG, mean ± SD	p-value	95% CI		Initial EEG, mean ± SD	2nd EEG, mean ± SD	p-value	95% CI
Coherence					Phase locking value				
Average strength	5.7027 ± 0.1597	5.8100 ± 0.2589	0.2081	-0.3724 to 0.1578	Average strength	4.7179 ± 0.2050	4.8217 ± 0.2414	0.1988	-0.2460 to 0.0794
Characteristic path length	2.8725 ± 0.0842	2.8229 ± 0.1236	0.2628	0.0050 to 0.1646	Characteristic path length	3.483 ± 0.1383	3.4207 ± 0.1441	0.1758	-0.1746 to 0.0506
Clustering coefficient	0.3634 ± 0.0091	0.3694 ± 0.0165	0.3290	-0.0223 to 0.0103	Clustering coefficient	0.3013 ± 0.0123	0.307 ± 0.0143	0.1756	-0.0405 to 0.0157
Global efficiency	0.3870 ± 0.0129	0.3955 ± 0.0175	0.2404	-0.0168 to 0.0099	Global efficiency	0.3224 ± 0.0144	0.3269 ± 0.0163	0.2069	-0.0953 to 0.0162
Local efficiency	0.6062 ± 0.0403	0.6317 ± 0.0561	0.2956	-0.0841 to 0.0330	Local efficiency	0.4202 ± 0.0387	0.4338 ± 0.0460	0.2412	-0.0413 to 0.0161
Small-worldness index	0.9681 ± 0.0103	0.9640 ± 0.0155	0.3393	-0.0074 to 0.0107	Small-worldness index	0.9618 ± 0.0069	0.9611 ± 0.0130	0.8385	-0.0096 to 0.0138
AED good responders				AED good responders					
	Initial EEG, mean ± SD	2nd EEG, mean ± SD	p-value	95% CI		Initial EEG, mean ± SD	2nd EEG, mean ± SD	p-value	95% CI
Coherence					Phase locking value				
Average strength	6.1809 ± 0.7428	6.2263 ± 0.6510	0.6602	-0.2539 to 0.1611	Average strength	5.2082 ± 0.6243	5.2361 ± 0.5904	0.7346	-0.1938 to 0.1181
Characteristic path length	2.7181 ± 0.2016	2.6922 ± 0.2457	0.5692	-0.0608 to 0.1324	Characteristic path length	3.2426 ± 0.1381	3.2252 ± 0.2899	0.7158	-0.1442 to 0.0793
Clustering coefficient	0.3919 ± 0.0475	0.3951 ± 0.0422	0.6190	-0.0174 to 0.0100	Clustering coefficient	0.3297 ± 0.0386	0.3317 ± 0.0377	0.7046	-0.0809 to 0.0136
Global efficiency	0.4201 ± 0.0493	0.4223 ± 0.0430	0.7494	-0.0159 to 0.0115	Global efficiency	0.3536 ± 0.0422	0.3549 ± 0.0389	0.8005	-0.0098 to 0.0125
Local efficiency	0.7254 ± 0.1798	0.7311 ± 0.1579	0.8126	-0.0536 to 0.0423	Local efficiency	0.5166 ± 0.1315	0.5198 ± 0.1248	0.8514	-0.0371 to 0.0308
Small-worldness index	0.9486 ± 0.0267	0.9501 ± 0.0213	0.7284	-0.0189 to 0.0071	Small-worldness index	0.9436 ± 0.0292	0.9426 ± 0.0262	0.7966	-0.0663 to 0.0081

However, in the AED good responders, none of the network measures were different from those in the healthy controls.

Conclusion: We newly found that there were significant differences of functional connectivity based on initial EEG according to AED response in the patients with JME. This suggests that brain connectivity could play a role as a new biomarker predicting AED response in patients with JME.

Disclosure: Nothing to disclose

EPR2058

Comparing the effectiveness and tolerability of Perampanel and Brivaracetam: a preliminary retrospective, observational study based on real-world data

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Background and aims: Perampanel (PER) and Brivaracetam (BRV) are 3rd-generation antiepileptic drugs (AEDs). The aim of the present retrospective, double-center study was to compare the effectiveness and tolerability of PER and BRV in patients affected with epilepsy.

Methods: Clinical charts of patients affected by epilepsy admitted to the Epilepsy Centre at the University Hospital of Rome Tor Vergata and the Cardarelli Hospital in Naples were reviewed. Patients started BRV or PER as add-on treatments for controlling seizures and had a follow-up visit of 12 months. We compared seizure freedom, seizure reduction >50%, retention rate, and adverse events reported at the follow-up. Moreover, we considered the effects of both drugs after distributing patients for age (≥60 y.o.), gender, and whether previously treated by Levetiracetam (LEV).

Results: 40 patients treated with BRV and 64 patients treated with PER were included and followed at both sites for 12 months. We found similar effectiveness for both BRV and PER, with similar seizure freedom and seizure reduction >50% at the follow-up. Moreover, PER and BRV discontinuation rates due to inefficiency or adverse events were similar. We also compared the groups of patients who started BRV or PER as 1st add-on treatments and did not observe differences in effectiveness and tolerability. Finally, a better effectiveness of BRV was observed in patients who were not previously treated with LEV.

Conclusion: This retrospective study observed comparable effectiveness and tolerability of PER and BRV as add-on treatments in patients affected with epilepsy, as well as when starting these drugs as first add-on treatments.

Disclosure: Nothing to disclose

EPR2059

Adjunctive Perampanel 4 mg/day for Partial-Onset Seizures (POS): Time to Seizure Onset in Pivotal Phase III Studies

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Background and aims: Although recommended maintenance dosing of perampanel for POS is 8–12mg/day, some patients may respond to 4mg/day. This post-hoc analysis evaluated the efficacy of adjunctive perampanel 4mg/day for treatment of POS, with/without secondarily generalised seizures (SGS), by assessing time to 1st seizure following perampanel administration.

Methods: During Phase III Studies 304 (NCT00699972), 305 (NCT00699582) and 306 (NCT00700310), patients (aged ≥12 years) with POS, with/without SGS, despite 1–3 anti-seizure medications were randomised to once-daily placebo or adjunctive perampanel 2–12mg/day (19-week Double-blind Treatment Period [6-week Titration; 13-week Maintenance]). Time to 1st seizure from Day 1 of placebo or perampanel administration was assessed in the Intent-to-Treat (ITT) Analysis Set using the Kaplan–Meier method. Placebo data were available from Studies 304, 305 and 306; perampanel 4mg/day data came from Study 306 (the only study to include the randomised 4mg/day dose).

Results: ITT Analysis Set included 437/442 (98.9%) placebo-treated patients (182/185 [98.4%] from Study 306) and 168/172 (97.7%) patients who received perampanel 4mg/day. Perampanel 4mg/day was associated with longer time to 1st seizure vs placebo (Figure). Mean time to 1st seizure was 9.3 days with perampanel 4mg/day vs 4.9 and 4.5 days for Study 306 placebo and pooled placebo, respectively (Table).

Table. Summary statistics for time to first seizure analysis in patients who received placebo or once-daily adjunctive perampanel 4 mg/day (ITT Analysis Set)

	Placebo (Study 306) (n=182)	Pooled placebo (Studies 304, 305, 306) (n=437)	Perampanel 4 mg/day ^a (n=168)
Time to first seizure, days			
Mean (SD)	4.9 (7.10)	4.5 (6.33)	9.3 (22.80)
Median (min, max)	3 (1, 73)	3 (1, 73)	3 (1, 135)

^aData from Study 306.

ITT, intent-to-treat; max, maximum; min, minimum; SD, standard deviation.

Table. Summary statistics for time to first seizure analysis in patients who received placebo or once-daily adjunctive perampanel 4 mg/day (ITT Analysis Set)

Figure. Kaplan–Meier plots of time to first seizure in patients who received placebo in (A) Study 306 or (B) Study 304, 305 or 306, vs once-daily adjunctive perampanel 4 mg/day in Study 306 (inset shows Days 0–14; ITT Analysis Set).

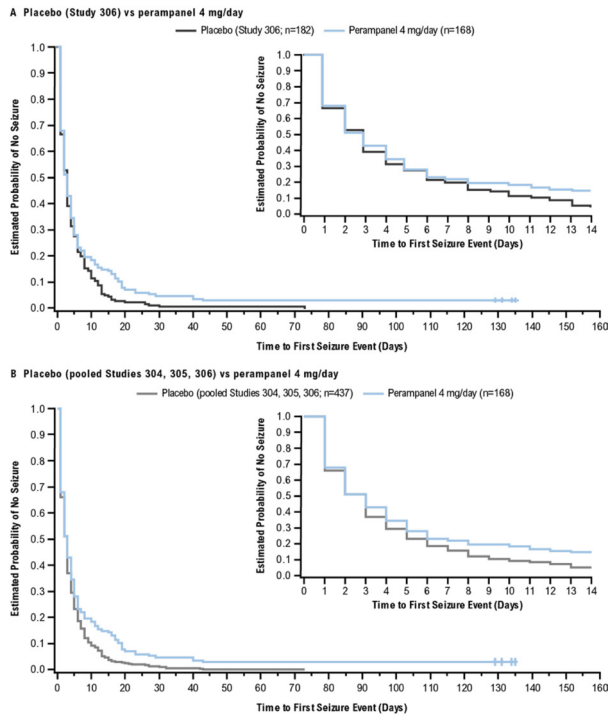


Figure. Kaplan–Meier plots of time to first seizure (ITT Analysis Set)

Conclusion: Adjunctive treatment with once-daily perampanel 4mg/day delayed the time to 1st seizure in patients aged ≥ 12 years with POS, with/without SGS, compared with placebo. These data further support the efficacy of perampanel 4mg/day.

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EPR2060

NF- κ B subunit p65 is transcriptionally up-regulated in the hippocampus of MTLE-HS patients

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Background and aims: Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is the most common form of refractory epilepsy. A better understanding and characterization of signalling pathways dysregulated in MTLE-HS is necessary for the development of novel and more efficient treatments. We aimed to evaluate the gene expression of NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B-cells) subunit p65 (RELA gene) in MTLE-HS patients and to correlate it with clinicopathological features.

Methods: Expression levels of RELA were quantified by Real-time PCR in hippocampus and cerebral cortex of 18 MTLE-HS (10F, 8M, 39.8 \pm 8.6 years) patients and 10 controls (2F, 8M, 69.7 \pm 7.8 years). Relative expression values were calculated using the 2- $\Delta\Delta$ Ct method. Correlations were evaluated using Spearman's test. Patient and Hospital Ethical Committee approval was obtained.

Results: RELA was significantly up-regulated in the hippocampus of MTLE-HS patients in comparison to controls (1.97-fold; $p < 0.001$). RELA expression in the cortex of MTLE-patients correlates positively with disease duration ($r_s = 0.529$; $p < 0.05$).

Conclusion: Inflammation is known to occur in epilepsy. It is considered a consequence and/or a cause of seizure activity. The NF- κ B pathway is one of the major inflammation regulatory mechanisms. In epilepsy, increased NF- κ B activity has been reported. However, NF- κ B up-regulation was only previously observed through increased protein levels in hippocampus of MTLE-HS patients. We demonstrated, for the first time, that p65 expression up-regulation in MTLE-HS occurs at the transcriptional level. The association of cortical p65 gene expression with disease duration may indicate progressive spreading of inflammation to the areas surrounding the epilepsy focus with disease progression.

Disclosure: Nothing to disclose

EPR2061

In silico exploration of candidate CpGs uncovers IRAK2 hypomethylation in brain tissue of epilepsy patients

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Background and aims: Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is the most pharmaco-resistant epilepsy. An epileptogenic phenotype has been described, characterized by persistently dysregulated inflammation-related mechanisms, possibly epigenetically encoded. Genomic cytosine methylation, at CpG dinucleotides (CpGs), is a major epigenetic mechanism of gene expression regulation. Our aim was to evaluate the DNA methylation of specific CpGs, located at regulatory regions of inflammation-related genes in MTLE-HS, selected with an in-silico pipeline.

Methods: 3 publicly available datasets, concerning trans-criptomic (GSE46706) and whole-genome DNA methylation profiling (GSE96615 and GSE111165) were screened for candidate putative differentially methylated CpGs, using a customized statistical approach implemented in R. Methylation percentage of selected candidate CpGs, located at inflammation-related genes including IL1B, IRAK2 and TRAF3, was evaluated using bisulphite pyrosequencing in hippocampus and neocortex of 41 MTLE-HS patients (18M, 23F; aged 39.6±9.8y), comparing to 10 healthy controls (8M, 2F; aged 67.0±10.9y).

Results: We determined significant hypomethylation for two CpGs of the IRAK2 gene. The CpG located at chr3:10215652-10215653 (hg19) was significantly hypomethylated in both hippocampus (6.7±5.1 vs 12.0±2.4, p<0.001) and neocortex (11.0±7.4 vs 22.2±6.9, p<0.001) of MTLE-HS patients vs controls. The chr3:10215713-10215714 (hg19) methylation site showed a similar behaviour in hippocampus (6.8±3.0 vs 10.3±2.3, p<0.001) and neocortex (9.1±5.0 vs 16.5±4.8, p<0.001).

Conclusion: Interleukin-1 receptor-associated kinase 2 (Irak2) is a crucial mediator of TLR/IL-1R-induced signalling, resulting in NFκB activation and pro-inflammatory cytokine expression. NFκB activation and

up-regulation is well documented in epilepsy. However, the epigenetic determinants of this pathway need further exploration.

Disclosure: Nothing to disclose

EPR2062

Epileptic phenotypes, treatment options, and long-term outcomes of autoimmune epilepsies: an Italian multicentre observational cohort study.

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Background and aims: Seizures may be a presenting or prominent symptom of autoimmune encephalitis. They are usually resistant to antiepileptic drugs but may benefit from immunotherapy. This study aims to analyse seizure semiology, management, and outcomes of patients with autoimmune encephalitis.

Methods: The Autoimmune Epilepsies Study Group of the Italian League Against Epilepsy performed a multicentre retrospective observational cohort study over 10 years period (2008–2018), and enrolled patients affected by epileptic seizures with an autoimmune aetiology, defined by the detection of pathogenic antibodies or suspected on the clinical and paraclinical basis.

Results: The series comprised 278 patients (65 children, 213 adults), followed-up for a median time of 24 months (range: 16–54 months). Autoantibodies were detected in 60%. Most patients had focal seizures (85%), usually of temporal or bitemporal origin, drug-refractory in 56% of cases. At disease onset, high seizure frequency and episodes of status epilepticus occurred in 68% and 42%, respectively. In the majority of patients (90%), associated symptoms, like neuropsychological deficits, psychiatric symptoms, movement disorders, and decreased consciousness, were also present. Most patients (86%) received immunotherapy. A favourable response, with seizure freedom or significant ($\geq 50\%$) seizure reduction, was detected in those patients who received early immunotherapy, and in those with cell-surface antibodies ($p < 0.05$). Long-term sequelae as psychiatric symptoms and neuropsychological deficits (45%) were present also in seizure-free patients.

Conclusion: Early detection of seizures of definite or possible autoimmune aetiology, may improve the tailored management of the underlying brain dysfunction, likely leading to an improvement of long-term outcomes.

Disclosure: Nothing to disclose

EPR2063

Limbic encephalitis: a single-centre case series

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Background and aims: To describe the anatomo-electroclinical and prognostic features of patients with limbic encephalitis (LE).

Methods: We reviewed patients referred to our Epilepsy Center from 2004 for a suspicion of autoimmune encephalitis who underwent a comprehensive diagnostic work-up. All cases fulfilling the criteria of LE [Graus et al., 2016] were included.

Results: Out of 16 screened cases, 12 met the criteria of LE (M/F:5/7). The mean age at presentation was 41.8±19.8 years. 9 patients presented with epileptic seizures (3 with status epilepticus), associated with other typical limbic manifestations in 2. 8 patients had focal seizures, 2 faciobrachial dystonic and 2 convulsive seizures. Ictal/interictal EEG showed epileptiform abnormalities in all patients. Brain MRI showed T2-hyperintensities of mesial temporal lobe in 75% of cases. CSF oligoclonal bands were detected in 4. Antibody testing was positive in 4 (33%; 2 with anti-GAD65 and 2 anti-Lgi1 antibodies); 1 patient with anti-GAD65 antibodies had also stiff-limb syndrome. 3 seronegative cases were diagnosed with paraneoplastic LE. 10 patients received 1st-line immunotherapies with improvement in 6; 2 were treated with rituximab/azathioprine with partial seizure control. After a mean follow-up-period of 7.3±4 years seizures/neuropsychological deficits persisted in 8 and 9 cases, respectively (2 with anti-GAD65 antibodies).

Conclusion: We describe 12 LE patients, 4 of whom with anti-GAD65/Lgi1 antibodies, 3 with paraneoplastic LE and 5 seronegative. Faciobrachial dystonic seizures were specifically associated with raised Lgi1 antibodies [Irani et al., 2011]; in these cases early immunotherapy was effective in terms of seizures/cognitive outcome. Among seropositive cases, anti-GAD65 antibodies-related LE showed the worst outcome.

Disclosure: Nothing to disclose

EPR2064

Targeting CD40L-CD40 in Epilepsy

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Background and aims: Previously, we showed that CD40 deficiency downregulates seizure severity, increases seizure latency, and reduces seizure frequency in an experimental model of acute seizures. Therefore, the goal of this research was to determine if upregulation of CD40 and CD40L mediate epilepsy.

Methods: Status epilepticus (SE) was induced in adult male CD40 receptor deficient mice (CD40KO) and its respective wild type mice using pilocarpine model in epilepsy. Silicon probe with 16 microelectrodes was implanted in hippocampus 10 days prior to SE. Simultaneous video and local field potentials (V-LFP) were recorded before, during, and after SE. Clinical and electrical seizures were quantified daily over 4 weeks. Brain concentration of CD40-CD40L, neuronal damage and neuroinflammation was analyzed. In addition, in a group of WT mice, Anti-CD40 (BioXCell InVivoMAb anti-mouse CD40L (CD154) or vehicle (sterile saline) were administered intranasal 2 hours before seizure induction with pentylenetetrazole.

Results: Preliminary results show that concentration of CD40 and CD40L markedly increased in the cortex and hippocampus from Day 1 to Day 22 after SE. Upregulation of CD40L-CD40 was positively correlated with an increase of p38 and phosphorylated-p38, neuronal damage, gliosis and spontaneous seizures. CD40KO mice presented a reduction of spontaneous seizures, gliosis and neuronal damage compare to WT. Also, CD40KO mice showed a reduction of gamma oscillation after seizure. Also, antiCD40L administration limited seizure severity and increased latency for stage 3 seizure compare to vehicle.

Conclusion: These preliminary findings indicate that up-regulation of CD40L-CD40 could mediate epileptogenesis by influencing inflammatory mechanisms that involve and propagate seizure-induced neuronal damage.

Disclosure: Nothing to disclose

Headache and pain 3

EPR2065

Pooled Analysis of Cardiovascular Safety With Fremanezumab Treatment in Patients With Migraine and Concomitant Triptan Use

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Background and aims: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for the preventive treatment of migraine in adults. Given the frequency of triptan use in patients with migraine, it is important to evaluate whether concomitant use of triptans with fremanezumab raises any safety concerns.

Methods: This analysis included data from three phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to receive subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Cardiovascular adverse events (CVAEs) were evaluated in patients with and without triptan use.

Results: Of the total pooled population (N=2,842), 1,123 (40%) used triptans during the studies, with similar proportions using triptans across all treatment groups. Of patients with triptan use, 19 (2%) of patients experienced ≥1 CVAE (Table) with no difference between placebo and fremanezumab-treated patients noted. Occurrences of CVAEs were consistently low across all treatment groups; the only CVAE with >1 occurrence in the placebo and fremanezumab groups was hypertension (Table). The incidence of CVAEs was low and similar in patients without triptan use (n=1,719; 46 [3%]). Among patients without triptan use (not shown), CVAEs with >1 occurrence in any treatment group were palpitations, hypertension, hematoma and hot flush, and all were reported in ≤1% of patients.

Table. CVAEs in Patients With Concomitant Triptan Use

AEs, n (%)	Placebo (N=365)	Quarterly fremanezumab		Monthly fremanezumab	
		675mg/placebo/placebo (N=393)	675mg/225mg/225mg (N=202)	225mg/225mg/225mg (N=163)	
Patients with ≥1 CVAE	6 (2)	6 (2)	5 (2)	2 (1)	
Palpitations	1 (<1)	1 (<1)	0	0	
Tachycardia	1 (<1)	0	0	0	
Heart rate increased	1 (<1)	1 (<1)	1 (<1)	1 (<1)	
Blood pressure increased	1 (<1)	1 (<1)	0	0	
ECG PR prolongation	0	1 (<1)	0	0	
ECG QT prolonged	0	0	0	1 (<1)	
Hypertension	2 (<1)	2 (<1)	1 (<1)	0	
Hypotension	0	0	1 (<1)	0	
Peripheral coldness	0	0	1 (<1)	0	
Raynaud's phenomenon	0	0	1 (<1)	0	

CV, cardiovascular; AE, adverse event; ECG, electrocardiogram.

Conclusion: This pooled analysis demonstrates that fremanezumab treatment over 12 weeks was well tolerated in patients with migraine and concomitant triptan use, with similar CV tolerability to those with no triptan use.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPR2066

Prodromal symptoms in cluster headache: A prospective multicenter study

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Background and aims: Epidemiological data of prodromal symptoms of cluster headaches (CH) are scarce in the literatures. Here, we investigated the prevalence and clinical characteristics of prodromal symptoms of CH.

Methods: This is a prospective multicenter study that enrolled consecutive patients with CH from 11 hospitals. We defined symptoms occurring minutes and hours before an individual attack as pre-attack symptoms, and symptoms occurring days and weeks before an upcoming cluster bout as pre-cluster symptoms. Patients underwent a semi-structured interview about the presence of 21 symptoms/signs in relation to cluster headache. The diagnosis of CH was verified according to ICHD-3 criteria. We excluded patients with probable CH and chronic CH.

Results: In total, 116 patients were enrolled. Pre-attack symptoms were reported by 65.5%, with an average of 2.5 per patients. Most patients experienced pre-attack symptoms within 30 minutes before a cluster attack. The most frequently reported symptoms were a local pain (51.3%) and sensory symptoms (12.9%) in the area of subsequent attack, followed by generalized symptoms (44.7%), neck pain (32.9%), autonomic symptoms (15.8%) and agitation (9.2%). Pre-cluster symptoms were found in 22.4% of participants. 81.9% experienced pre-cluster symptoms within 2 weeks before a cluster bout. The most frequently reported symptoms were a local pain (47.8%). Subjects with pre-attack symptoms were more likely to experience pre-cluster symptoms (p=0.01).

Conclusion: Prodromal symptoms are frequent in CH. Understanding of prodromal symptoms of CH could contribute to the preemptive treatment strategies for the prevention of CH.

Disclosure: Nothing to disclose

EPR2067

The importance of considering the patient's and treating physician's view to generate comprehensive und unbiased real-world evidence data.

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Background and aims: Real-World-Evidence can be collected from different perspectives – the patients' and treating physicians' perspective. Here, we describe the importance of considering the views of both patients and physicians in order to gather comprehensive real-life evidence.

Methods: Between July and December 2019, 2 independent online surveys were conducted in Germany to collect data from a) migraine patients regarding their experience with erenumab (PERISCOPE) and b) migraine-treating physicians regarding their therapy decisions and observations upon erenumab treatment (TELESCOPE). Results were compared regarding the overall therapy outcome, changes in quality of life and influence of quality of life parameters.

Results: The interim analyses of PERISCOPE (90 erenumab patients) and TELESCOPE (30 physicians with 354 erenumab patients) showed that 75% of all physicians already detected improvement after the 1st injection, but only 49% of patients reported a response after their 1st treatment. Further, patients and physicians weighted quality of life parameters differently. However, patients and physicians both reported a reduction of ~7 migraine days after 3 months of treatment. At EAN, the comparison of both full data sets will be presented including 155 erenumab patients (PERISCOPE) and 45 physicians/522 erenumab patients (TELESCOPE).

Conclusion: These analyses indicate differences and overlaps in the patients and physicians perception of therapy outcomes in migraine treatment. The comparison highlights the importance of understanding limitations of the interviewed population and thus shows that only considering both sides will generate comprehensive real-world evidence for treatment options.

Disclosure: This study has been funded by Novartis Pharma GmbH.

EPR2068

Analysis of the patient population for the assessment of long-term safety and tolerability of the monoclonal antibody Erenumab and the frequency of drug holidays in the German treatment algorithm

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Background and aims: In 2018, EMA and FDA approved erenumab for its safety and efficacy. Recently, 4.5-year data from an ongoing open-label treatment phase confirmed the long-term safety profile of erenumab in an international cohort. However, long-term data is still limited for the German population. Further, the impact and relevance of a drug holiday suggested by the German guidelines for migraine therapy by the DMKG (DGN 2018), which is suggested after 6-12 months of treatment should be investigated.

Methods: APOLLON is a 128-week open-label study of erenumab treatment, assessing long-term safety and tolerability data of migraine patients in Germany who previously participated in a head-to-head trial comparing the tolerability of erenumab and topiramate (NCT03828539). At scheduled visit, the treating physician can change the erenumab dose according to the approved label and. Thereby, monthly migraine days 4 weeks to, during and 12 weeks after the medication-free period are documented. In an interim analysis baseline characteristics and the current and planned drug holidays will be analyzed.

Results: At EAN we will present an analysis of the baseline characteristics of the approximately and an analysis of the number and time point of current and planned drug holidays in the treatment scheme.

Conclusion: This analysis will provide insights into the patient population as regards the assessment of long-term safety and tolerability of erenumab and the frequency and timeline for drug holidays during erenumab treatment in the treatment algorithm of approximately 80 German headache centers.

Disclosure: This study has been funded by Novartis Pharma GmbH.

EPR2069

Sentinel headache as a predictor of ischemic stroke

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Background and aims: There are no previous controlled studies of sentinel headache in ischemic stroke. The purpose of the present study was to evaluate the presence of such headache, its characteristics and possible risk factors as compared to a simultaneous control group.

Methods: Eligible patients (n=550) had 1st-ever acute ischemic stroke with presence of new infarction on magnetic resonance imaging with diffusion-weighted imaging (n=469) or on computed tomography (n=81). As a control group we studied in parallel patients (n=192) who were admitted to the emergency room without acute neurological deficits or serious neurological or somatic disorders. Consecutive patients with stroke and a simultaneous control group were extensively interviewed soon after admission using validated neurologist conducted semi-structured interview forms.

Results: Among 550 patients with stroke 94 patients (17.1%) had headache during seven days before stroke and 12 (6.2%) of controls (p<0.001; OR 3.9; 95% CI 1.7-5.8). We defined sentinel headache as a new type of headache or a previous kind of headache with altered characteristics (severe intensity, increased frequency, absence of effect of drugs) within seven days before stroke. had Attacks of arrhythmia during seven days before stroke were significantly associated with sentinel headache (p=0.04, OR 2.3; 95% CI 1.1-4.8).

Conclusion: A new type of headache and a previous kind of headache with altered characteristics during one week before stroke are significantly more prevalent than in controls. Such sentinel headache should prompt urgent examination for stroke prevention.

Disclosure: Nothing to disclose

EPR2070

Abnormal cerebrovascular changes in sporadic hemiplegic migraine

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Background: The pathophysiology of sporadic hemiplegic migraine (SHM) is not well understood. Cortical spreading depression affecting motor excitability and neurovascular coupling may be integral to development of weakness.

Aims: To study hemodynamic responses to a motor activation task in SHM patients using functional near-infrared spectroscopy (fNIRS), during the interictal period.

Methods: A total of 9 right-handed patients and 17 healthy controls were enrolled. Patients were diagnosed with SHM in accordance to IHS criteria, and studied after recovery from the hemiplegic episode. All patients had normal MR brain imaging. Each performed a finger opposition tasks at maximal velocity with simultaneous fNIRS recording.

Results: During motor activation, patients with SHM were less likely to demonstrate increase in oxyhemoglobin (oxyHb) ipsilateral and contralateral to the side of motor activation task than in controls (p=0.002). However, the area of involvement is larger on the side contralateral to motor activation (3 vs. 1 recording site). There were no significant differences found for deoxyhemoglobin (deoxHb) recordings.

Conclusion: Our findings suggest presence of an abnormal interictal hemodynamic response to increased metabolic demands during motor activation in SHM. In addition, these cerebrovascular changes appear to be more pronounced contralateral to the side of activation.

Disclosure: Nothing to disclose

EPR2071

Galcanezumab in patients with treatment-resistant migraine: results from the open-label phase of the CONQUER phase 3 trial

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Background and aims: This study assessed 6-month efficacy and safety of galcanezumab in patients with treatment-resistant migraine.

Methods: During double-blind treatment (Months 1-3), 462 patients (18-75 years) with episodic or chronic migraine and 2-4 previous migraine preventive medication category failures were randomised 1:1 to injections of placebo or galcanezumab 120mg/month (with 240mg loading dose). After completing double-blind treatment, patients could enter an open-label extension (OLE; Months 4-6), in which all patients received galcanezumab 120mg/month. The primary endpoint was mean change from baseline in number of monthly migraine headache days. Key secondary endpoints included response rate ($\geq 50\%$ reduction in monthly migraine headache days) and mean change in Migraine-Specific Quality of Life Questionnaire Role Function-Restrictive domain score (MSQ-RFR).

Results: Of 451 patients who completed double-blind treatment, 449 entered the OLE, with 432 (96%) completing. From a baseline of approximately 13 monthly migraine headache days, the mean decrease at Month 6 was >5 days. At Month 6, approximately 54% of patients met the $\geq 50\%$ response criterion. Of the 87 galcanezumab-treated patients with $\geq 50\%$ response at double-blind treatment end, 52% maintained that response throughout OLE. Mean MSQ-RFR scores improved from baseline (score=45) to Month 6 by approximately 27 points on a 100-point scale.

Treatment-emergent adverse events occurring in $>2\%$ of patients were nasopharyngitis (4%), injection-site pain (4%), and injection-site erythema (3%). 5 patients (1%) discontinued due to an adverse event. There were no clinically meaningful changes in any safety parameters.

Conclusion: Galcanezumab was effective, safe, and well tolerated during the CONQUER open-label extension in patients with treatment-resistant migraine.

Disclosure: This research was supported by Eli Lilly and Company.

EPR2072

Eptinezumab Reduced Acute Medication Use in Patients with Chronic Migraine and Medication-Overuse Headache: Subgroup Analysis of PROMISE-2

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Background and aims: Eptinezumab is a monoclonal antibody that inhibits CGRP for the prevention of migraine. This analysis evaluated the impact of eptinezumab on acute headache medication use in patients enrolled in the pivotal PROMISE-2 clinical trial who were given a dual diagnosis of chronic migraine (CM) and medication-overuse headache (MOH).

Methods: In PROMISE-2, patients with CM were randomized to eptinezumab 100mg, 300mg, or placebo for 2 intravenous doses administered every 12 weeks. MOH was diagnosed by trained investigators at screening based on 3 months of medication history and in alignment with ICHD-3b criteria. Endpoints included days/month of any acute medication use (days of ≥ 1 medication class), total acute medication use days/month (sum of days for each medication class), and days/month with triptan use over Weeks 1-12 and 13-24. Classes of acute medication included triptan, ergot, opioid, simple analgesic, and combination analgesic.

Results: Of 1072 patients treated in PROMISE-2, 431 (40.2%) were diagnosed with MOH (100mg, n=139; 300mg, n=147; placebo, n=145). During the 28-day baseline period, the mean days of any acute medication use was ~ 16.4 , total acute medication use was ~ 20.4 , and triptan use was ~ 8.9 across treatment arms. Over Weeks 1-12, mean days/month of any acute medication use was 8.8 (100mg), 9.9 (300mg), and 11.8 (placebo); total acute medication use was 10.8, 12.2, and 14.8; and triptan use was 4.3, 4.4, and 6.4. Similar or lower rates were observed over Weeks 13-24.

Conclusion: In patients diagnosed with both CM and MOH, eptinezumab treatment reduced acute headache medication use.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark

EPR2073

Wavelet-transform coherence analysis to assess the dynamic changes of the brain during NTG-induced migraine attacks

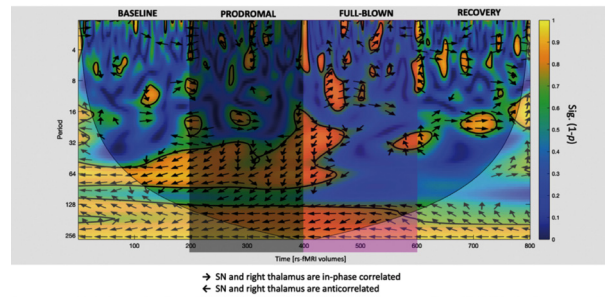
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Background and aims: Migraine is a cyclical disorder where the attack evolves over the span of hours to days. Resting state functional MRI (rs-fMRI) has been widely used to study the brain functional connectivity changes during migraine attacks, helping to better understand the complex mechanisms underlying this disorder. In this pilot study, we aimed to investigate the functional connectivity of the migraine brain using dynamic rs-fMRI analysis. To this end, the Wavelet Transform Coherence (WTC) approach, which allows to estimate the changes in the dynamic interactions between rs-fMRI signals from distinct brain areas, was applied to study the coherence between the salience network (SN) and the thalamus rs-fMRI signals during the different phases of a nitroglycerin (NTG)-induced episodic migraine attack.

Methods: 5 episodic migraineurs underwent 3T MRI examination consisting in 4 rs-fMRI repetitions matched with the different phases of an attack: baseline, prodromal, full-blown attack, recovery. Subjects' rs-fMRI data were processed to extract the SN and thalamic time-courses. The extracted time-series were treated with WTC to obtain a wavelet coherence map from which the time-in-phase coherence between SN and thalamic signals was assessed.

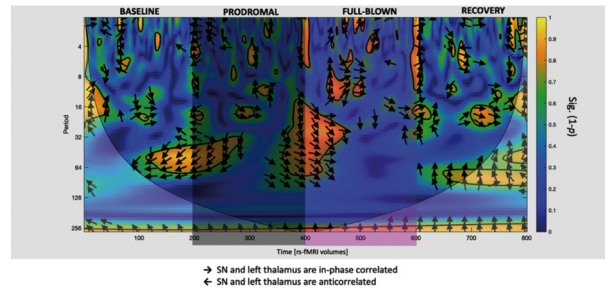
Results: Results revealed that in all subjects both right and left thalamic rs-fMRI signals were significantly ($p < 0.05$) anti-correlated with the SN time-course during the prodromal phase, while they showed significant in-phase correlation with SN during the full-blown attack.

WCT: Salience Network vs. right Thalamus



Wavelet coherence map showing the WTC results between the SN and the right thalamus rs-fMRI time-courses.

WCT: Salience Network vs. left Thalamus



Wavelet coherence map showing the WTC results between the SN and the left thalamus rs-fMRI time-courses.

Conclusion: Overall, these results suggest that the temporal dynamic alterations of brain functional circuitries implicated in pain processing are differently involved during the attack and may play a key role in modulating the migraine experience.

Disclosure: Nothing to disclose

EPR2074

Efficacy of Galcanezumab In Patients with Migraine and History of Failure to at least Three Preventive Treatment Categories: Subgroup Results from CONQUER Study

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Background and aims: CONQUER (NCT03559257) was a Phase 3, multicenter, randomized controlled trial in patients with episodic (EM) or chronic (CM) migraine who had 2–4 preventive category failures. We report efficacy outcomes from pre-specified subgroup of patients with three or more (≥ 3) preventive category failures, given the large unmet need in this population.

Methods: Eligible patients in CONQUER were aged 18–75 years, had 4–29 migraine headache days/month, and 2–4 migraine preventive medication category failures in past 10 years (reasons: inadequate efficacy and/or safety/tolerability). Patients were randomized 1:1 to monthly subcutaneous injections of galcanezumab_120mg (loading dose: 240mg) or placebo during the 3-month double-blind treatment period. Evaluated endpoints include overall mean change from baseline (CFB) of monthly migraine headache days across Month 1–3, overall proportion of patients achieving $\geq 50\%$ reduction in monthly migraine headache days (Months 1–3) and mean CFB on the migraine-specific quality of life role function-restrictive (MSQ RF-R) domain (at Month 3).

Table 1. Baseline demographics and disease characteristics among patients with failures to three or more preventive categories* in CONQUER Study.

	Episodic migraine (N=100)	Chronic migraine (N=86)	Total Population (N=186)
Galcanezumab_120mg, n (%)	56 (56.0)	43 (50.0)	99 (53.2)
Placebo, n (%)	44 (44.0)	43 (50.0)	87 (46.8)
Demographics			
Age, years, mean (SD)	46.0 (11.5)	45.5 (12.5)	45.8 (11.9)
Gender (female), n (%)	83 (83.0)	72 (83.7)	155 (83.3)
Disease Characteristics			
Duration of migraine, years, mean (SD)	21.4 (13.8)	24.5 (15.5)	22.8 (14.7)
Migraine headache days/month, mean (SD)	9.9 (2.7)	18.8 (4.7)	14.0 (5.8)
Migraine attacks/month, mean (SD)	5.8 (1.7)	6.2 (2.3)	6.0 (2.0)
Headache days/month, mean (SD)	11.1 (2.5)	21.0 (4.5)	15.7 (6.1)
MSQ Role Function-Restrictive, mean (SD)	48.4 (16.9)	38.4 (18.9)	43.8 (18.5)
Acute Medication overuse, n (%)	36 (36.0)	63 (73.3)	99 (53.2)

MSQ, migraine-specific quality of life questionnaire; SD, standard deviation. *Following is the list of preventive categories: propranolol or metoprolol; topiramate; valproate or divalproex; amitriptyline; flunarizine; candesartan; botulinum toxin A or B (if documented that botulinum toxin was taken for chronic migraine); medication locally approved for prevention of migraine.

Table 1

Results: Of the 462 randomised patients, 186 (40.3%) had history of ≥ 3 preventive category failures (Table 1). For these patients, galcanezumab_120mg led to a significantly larger overall mean (SE) reduction in monthly migraine headache days versus placebo ($p < 0.001$) for both populations: EM: galcanezumab_120mg: -3.6 (0.6); placebo: -0.7 (0.7); CM: galcanezumab_120mg: -6.7 (1.2);

placebo: -1.6 (1.1). Galcanezumab was also superior to placebo for $\geq 50\%$ response and for improvements in MSQ RF-R score (Table 2).

Table 2. Efficacy measures in patients with failures to three or more preventive categories* in CONQUER Study.

Endpoint	Treatment	Episodic migraine		Chronic migraine		All Population	
		LS mean change (SE) / estimated rate (SE)	LS mean change difference (SE) / odds ratio (95% CI)	LS mean change / estimated rate (SE)	LS mean change difference (SE) / odds ratio (95% CI)	LS mean change (SE) / estimated rate (SE)	LS mean change difference (SE) / odds ratio (95% CI)
Monthly migraine headache days	Placebo	-0.7 (0.7)	---	-1.6 (1.1)	---	-1.0 (0.7)	---
	GMB 120	-3.6 (0.6)	-3.0 (0.8) [†]	-6.7 (1.2)	-5.1 (1.3) [†]	-5.5 (0.7)	-4.5 (0.7) [†]
$\geq 50\%$ response	Placebo	16.5 (4.1)	---	8.4 (3.9)	---	12.7 (2.9)	---
	GMB 120	41.1 (4.9)	3.5 (1.7, 7.3) [†]	41.5 (6.9)	7.8 (2.4, 24.8) [†]	41.0 (4.0)	4.8 (2.6, 8.7) [†]
MSQ Role Function-Restrictive ^b	Placebo	14.5 (3.6)	---	4.7 (3.4)	---	12.0 (2.8)	---
	GMB 120	22.7 (3.4)	8.2 (4.0) [*]	25.2 (3.6)	20.5 (4.2) [†]	27.3 (2.7)	15.3 (3.0) [†]

CI, confidence interval; MSQ, migraine-specific quality of life questionnaire; LS, least squares; SE, standard error; [†] $p < 0.05$; ^{*} $p < 0.001$. Following is the list of preventive categories: propranolol or metoprolol; topiramate; valproate or divalproex; amitriptyline; flunarizine; candesartan; botulinum toxin A or B (if documented that botulinum toxin was taken for chronic migraine); medication locally approved for prevention of migraine. ^bAt Month 3.

Table 2

Conclusion: In patients with ≥ 3 migraine preventive medication category failures, galcanezumab led to significant improvements in key efficacy outcomes over placebo.

Disclosure: The study was sponsored by Eli Lilly and Company, Indianapolis, Indiana, USA.

Headache and pain 4

EPR2075

Improvements in Quality-of-Life, Productivity, and Satisfaction With Fremanezumab in Migraine Patients ≥ 60 Years of Age: Pooled Results of 3 Randomised, Double-blind, Placebo-controlled Phase 3 Studies

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Background and aims: Migraine is a leading cause of disability and negatively affects patients' quality of life. The impact of fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide (CGRP), on health-related quality of life (HRQoL) in a subgroup of patients ≥ 60 years of age was evaluated in this pooled analysis.

Methods: This analysis in patients ≥ 60 years of age with episodic migraine (EM) or chronic migraine (CM) included data from three phase 3 studies (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to receive subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Mean changes from baseline in Migraine-Specific Quality of Life (MSQoL) and Work Productivity and Activity Impairment (WPAI) questionnaire scores and proportions of Patient Global Impression of Change (PGIC) responders (rating, 5–7) over 12 weeks were evaluated.

Results: Overall, 246 patients ≥ 60 years of age were included in these analyses. Over 12 weeks, greater improvements from baseline were observed with both fremanezumab dosing regimens versus placebo across all MSQoL domains and WPAI percent work time missed due to health and percent impairment while working due to health domains (Table). Proportions of responders on the PGIC scale were also significantly higher with both quarterly (59%) and monthly (64%) fremanezumab versus placebo (40%, $P < 0.01$).

Table. Change From Baseline in WPAI and MSQoL in Patients ≥ 60 Years of Age During 12 Weeks of Double-blind Treatment

	Placebo (n=80)	Quarterly fremanezumab (n=74)	Monthly fremanezumab (n=92)
Change from BL in WPAI domains, LSM (SE)*			
Percent work time missed due to health	-5.0 (1.66)	-4.3 (1.65)	-3.4 (1.58)
Percent impairment while working due to health	-4.1 (3.16)	-17.0 (3.08) ^b	-12.9 (3.00) ^b
Percent overall work impairment due to health	-5.7 (3.59)	-17.9 (3.52) ^b	-14.1 (3.42)
Change from BL in MSQoL domains, LSM (SE)			
Role-function restrictive	9.6 (2.07)	15.9 (2.13) ^c	18.9 (1.97) ^d
Role-function preventive	10.8 (1.86)	13.5 (1.93)	14.2 (1.79)
Emotional function	13.7 (1.92)	20.3 (1.98) ^b	18.8 (1.84) ^c

WPAI, Work Productivity and Activity Impairment; MSQoL, Migraine-Specific Quality of Life; LSM, least-squares mean; SE, standard error.

*Assessed in patients who were working; placebo, n=32; fremanezumab quarterly, n=32; fremanezumab monthly, n=35.

^b $P < 0.01$ versus placebo.

^c $P < 0.05$ versus placebo.

Conclusion: This pooled analysis demonstrates that both fremanezumab treatment regimens over 12 weeks improved HRQoL, productivity, and satisfaction, as measured by MSQoL, WPAI, and PGIC, respectively, in patients ≥ 60 years of age with EM or CM.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPR2076

Resting State Functional Connectivity Changes of the Hypothalamus in Migraine Patients: A Cross-Sectional and Longitudinal Study

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Background and aims: Previous studies support the role of the hypothalamus in migraine pathophysiology. The aim of our study was to explore cross-sectional and longitudinal resting state functional connectivity (RS FC) changes of the hypothalamus in patients with migraine.

Methods: Using a 3.0 Tesla scanner, RS functional magnetic resonance imaging (MRI) and 3D T1-weighted scans were acquired from 92 headache-free episodic migraine patients and 73 controls. 23 migraineurs and 23 controls were reexamined after 4 years. RS FC analysis was performed using a seed-region correlation approach and SPM12.

Results: At baseline, compared to controls, migraineurs showed a decreased RS FC between the left and right hypothalamus and the right cerebellum, frontal, temporal and occipital areas, bilaterally. At baseline, the decreased RS FC between the right hypothalamus and the ipsilateral lingual gyrus correlated with higher migraine attack frequency. After 4 years, migraine patients developed an increased RS FC between the hypothalamus and the orbitofrontal cortex, bilaterally, while RS FC between the right hypothalamus and the ipsilateral lingual gyrus decreased. RS FC between the right hypothalamus and the ipsilateral orbitofrontal cortex correlated with lower migraine attack frequency at year 4.

Conclusion: The hypothalamus modulates the activity of pain and visual processing areas in migraine patients. The recurrent experience of migraine attacks might disrupt the functional interaction between the hypothalamus and high-order visual processing areas. An increased RS FC between the hypothalamus and brain areas belonging to the descending pain-inhibitory pathway might reduce migraine attack frequency over time.

Disclosure: Nothing to disclose

EPR2077

Efficacy of Fremanezumab Treatment in Patients ≥ 60 Years of Age With Episodic or Chronic Migraine: Pooled Results of 3 Randomised, Double-blind, Placebo-controlled Phase 3 Studies

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Background and aims: Preventive treatment of migraine may be challenging in older patients as some preventive medications may cause cognitive or cardiac side effects in this population. Fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ a) that selectively targets calcitonin gene-related peptide, has proven efficacy for preventive treatment of migraine in adults. Efficacy of fremanezumab was evaluated in a subgroup of patients ≥ 60 years of age in this pooled analysis.

Methods: This analysis in patients ≥ 60 years of age with episodic migraine (EM) or chronic migraine (CM) included data from 3 phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Changes from baseline in monthly migraine days, headache days of at least moderate severity, and days with acute headache medication use, as well as the proportion of patients achieving $\geq 50\%$ reduction in monthly migraine days, were evaluated over 12 weeks.

Results: Overall, 246 patients ≥ 60 years of age were included in these analyses. Reductions from baseline in monthly migraine days, headache days of at least moderate severity, and days with acute headache medication use over 12 weeks were significantly greater with quarterly and monthly fremanezumab versus placebo (all $P \leq 0.0103$; Table). The proportion of patients achieving $\geq 50\%$ reduction in monthly migraine days was significantly greater in patients receiving monthly fremanezumab versus placebo ($P = 0.0372$; Table).

Conclusion: This pooled analysis demonstrates that fremanezumab treatment was efficacious over 12 weeks in patients ≥ 60 years of age with EM or CM.

Disclosure: This study was funded by Teva Pharmaceuticals.

Table. Efficacy in Patients ≥ 60 Years of Age During 12 Weeks of Double-blind Treatment

	Placebo (n=80)	Quarterly fremanezumab (n=74)	Monthly fremanezumab (n=92)
Change from BL in monthly average number of migraine days			
LSM (SE)	-2.3 (0.57)	-4.3 (0.59)	-4.6 (0.54)
LSMD (SE) change from baseline	—	-2.0 (0.74)	-2.3 (0.70)
P value	—	0.0073	0.0011
Change from BL in monthly average number of days headache days of at least moderate severity			
LSM (SE) change from baseline	-2.1 (0.53)	-3.9 (0.55)	-4.2 (0.51)
LSMD (SE) change from baseline	—	-1.8 (0.69)	-2.1 (0.65)
P value	—	0.0103	0.0012
Change from BL in monthly average number of days of acute headache medication use			
LSM (SE)	-1.3 (0.55)	-3.7 (0.56)	-4.0 (0.52)
LSMD (SE) versus placebo	—	-2.4 (0.71)	-2.6 (0.66)
P value	—	0.0009	0.0001
$\geq 50\%$ reduction from BL in monthly average number of migraine days	=		
n (%)	20 (25)	27 (36)	37 (40)
OR (95% CI)	—	1.74 (0.87, 3.48)	2.01 (1.04, 3.88)
P value	—	0.1200	0.0372

BL, baseline; LSM, least-squares mean; SE, standard error; OR, odds ratio; CI, confidence interval.

EPR2078

SLEEP, PAIN, AND MIGRAINE: A blinded crossover study of experimental pain after sleep restriction

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Background and aims: There is an obvious link between insufficient sleep and migraine. Our objective was to explore whether sleep restriction increases pain perception more in episodic migraine than in headache-free controls. To our knowledge, this is the first study comparing the effect of sleep restriction on pain perception between migraineurs and controls.

Methods: Heat detection (HDT), heat pain (HPT), and heat pain tolerance (HPTT) thresholds were measured in interictal migraineurs and headache-free controls after 2 consecutive nights of habitual sleep (HS), and after 2 consecutive nights of partial sleep restriction (SR) (4 hours per night). 20 migraineurs (9 with aura, 15 females) and 29 controls (22 females) were included in the analyses. Investigators were blinded for diagnosis and sleep condition during recording and analysis of data.

Results: We did not find any significant between-group differences in effect of SR on thermal thresholds ($p=0.64$ for HDT, $p=0.59$ for HPT, $p=0.79$ for HPTT). HPT in migraineurs was $39.3^{\circ}\text{C}\pm 2.9$ after HS, 38.6 ± 2.8 after SR, and in controls 39.3 ± 3.1 after HS, and 39.2 ± 2.3 after SR. Notably, HPT was 0.7°C lower after SR in the migraine subgroup, although non-significantly ($p=0.41$).

Conclusion: Our hypothesis, that sleep restriction would increase pain sensitivity in episodic migraine more than in controls, was not confirmed in this study. Sleep restriction does not seem to have a large effect on experimental thermal pain thresholds in the interictal phase. More sensitive pain measures, increased sleep restriction, specific sleep-stage disruption, or larger groups may be necessary to further explore the hypothesis.

Disclosure: The research is funded by the Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, NTNU

EPR2079

Reversible cerebral vasoconstriction syndrome: triggers and minor brachiocephalic vascular abnormalities

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Background and aims: Reversible cerebral vasoconstriction syndrome (RCVS) manifests by thunderclap headache with focal/universal cerebral symptoms and multiple segmental spasm of cerebral arteries which resolves within 3 months. Aim of study was to reveal main triggers, minor brachiocephalic vascular abnormalities (MBVA) in patients with RCVS

Methods: 172 patients with verified RCVS were examined (age 37.3 ± 11.3 years, women 133, men 39, $p<0.001$). Detailed neurological examination, brain MRI (1.5T/3T), MR arteriography and MR venography were performed in patients

Results: Primary RCVS was detected in 66 (38.4%) patients: 18 men and 48 women. Main triggers were: stress in 13 men and 39 women, physical or sexual activity in 8 men and 10 women. 2ndary RCVS was in 106 patients (61.6%): 18 men and 88 women, provoked by sympathomimetics (nasal spray) 9 men and 15 women; oral contraceptives in 45 women, alcohol consumption in 2 men and 9 women, cannabis in 3 men; paroxetine (2 men, 4 women) and triptan (3 women) administration. MBVA were revealed in 126 patients: vertebral artery hypoplasia: 68 women and 16 men, absence of posterior communicating arteries: 28 women and 7 men, anterior cerebral artery asymmetry: 12 women and 3 men, internal carotid artery trifurcation: 27 female, 6 males; venous sinus asymmetry: 36 women and 8 men

Conclusion: RSVS was more often in women comparing with men. Patients with RCVS had minor brachiocephalic artery abnormalities in 73.3% and venous sinus asymmetry in 25.6%. No significant difference in triggers in patients with primary and secondary RCVS was revealed.

Disclosure: Nothing to disclose

EPR2080

Effect of circadian phase on the discomfort and post injection complaints in preventive onabotulinumtoxin A injections for migrainesA. Packard¹, C. Smotherman²¹Neurology, University of Florida, Jacksonville, USA,²CHEQR, University of Florida, Jacksonville, USA

Background and aims: Determine circadian timing of the quarterly onabotulinumtoxin A (TBA) injections for chronic daily headaches/migraines associated with the lowest discomfort and minimal follow-up pain.

Methods: 61 patients receiving their initial TBA injection for migraine prevention were enrolled in the study and randomly assigned to morning or afternoon clinics. Patients self-reported level of discomfort prior to TBA injections by marking discomfort level on 100mm visual analog pain scale, VAPS. 155 units of BTA was administered by following the standardized PREEMPT injection protocol and the post-injection discomfort level was marked by the patient on the VAPS. The final patients' discomfort level was marked on the same VAPS 24-hours after TBA administration. Groups of morning versus afternoon patients were compared using the non-parametric Wilcoxon's Rank Sum Tests.

Results: 62% patients were injected during morning clinic and 38% were injected during afternoon clinic. There was no difference in gender, race and age variables between morning and afternoon patients. Increased in-pain was more frequent following the morning injections compared to the afternoon injections (78% vs 50%, $p=0.021$). 24 hour post-injection pain level was also significantly increased in patients that received morning injections compared to the afternoon injections (64% vs. 28%, $p=0.024$).

Conclusion: Performing TBA injections for migraine prevention during the morning clinic was associated with more treatment related discomfort both immediately following, as well as 24 hours after the injection. Scheduling patients with regular circadian rhythm for afternoon TBA injections might be beneficial in terms of decreasing treatment related discomfort and increasing therapeutic compliance.

Disclosure: Nothing to disclose

EPR2081

Patient-Reported Outcomes in Patients with Migraine and Prior Prophylactic Treatment Failure: A Subgroup Analysis from the BECOME StudyP. Pozo-Rosich¹, C. Lucas², C. Gaul³, D. Watson⁴,P. Martelletti⁵, S. Ritter⁶, J. Snellman⁷¹Headache Unit, and Headache and Neurological Pain Research Group, Vall d'Hebron University Hospital, andUniversitat Autònoma de Barcelona, Barcelona, Spain, ²Pain Clinic, Service de Neurochirurgie, Hôpital Salengro, CHRU de Lille, Lille Cedex, France, ³Migraine and HeadacheClinic Königstein, Königstein im Taunus, Germany, ⁴Hamilton Medical Group, Aberdeen, Scotland, UnitedKingdom, ⁵Department of Clinical and Molecular Medicine, Sapienza University of Rome, Sant'Andrea Hospital, Via diGrottarossa, Rome, Italy, ⁶Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, ⁷Novartis Pharma AG,

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Background and aims: In this subgroup analysis from the BECOME study, we report the patient-reported outcomes (PROs) in patients with migraine and prior prophylactic treatment failure (PPTF 1, 2, 3, ≥ 4 medication categories) due to lack of efficacy and/or poor tolerability.

Methods: The BECOME study assessed disease characteristics of all patients with migraine visiting headache specialist centres (Part 1), and burden of disease using PROs and healthcare resource utilisation questionnaires in patients with ≥ 1 PPTF and ≥ 4 monthly migraine days (Part 2). Here, we assessed the impact of migraine on a patient's ability to work and perform regular activities using Work Productivity and Activity Impairment-headache (WPAI-headache), on general anxiety and depression using Hospital Anxiety and Depression Scale (HADS), and on daily functioning using the Migraine-Specific Quality of life (MSQ) questionnaire.

Results: Overall, 2419 patients were included in Part 2 analysis. The WPAI-headache scores indicated a high level of impairment due to migraine on absenteeism (15.6%), presenteeism (48.6%), and overall work impairment (52.6%) domains (Table). HADS scores indicated a possible presence of anxiety associated with migraine (mean[95%CI]: 8.0[7.8,8.2]). Migraine substantially limited and restricted patients' social and work-related activities (MSQ-RFR score 43.8[43.0,44.6]), and affected their emotional function (MSQ-EF: 50.5[49.4,51.6]). The burden of disease generally increased with higher PPTF, indicating a more difficult-to-treat population (except for HADS scores in ≥ 4 PPTF subgroup).

Conclusion: This subgroup analysis of the BECOME study confirms the burden of migraine on work productivity, anxiety, and quality of life in migraine patients, and an incremental increase with the number of PPTFs.

Table. PRO scores of the BECOME study population set for Part 2 (N=2419) by number of PPTF

	All N=2419 n=1587	1 PPTF N=1034 n=682	2 PPTF N=690 n=462	3 PPTF N=324 n=206	≥4 PPTF N=371 n=237
WPAI percent work time missed	15.6 (14.3, 16.9)	14.7 (12.7, 16.6)	15.0 (12.6, 17.4)	16.3 (12.5, 20.1)	18.8 (15.1, 22.4)
WPAI percent impairment while working	48.6 (47.2, 49.9)	47.1 (45.0, 49.2)	46.7 (44.1, 49.3)	52.8 (49.3, 56.3)	52.9 (49.6, 56.1)
WPAI percent overall work impairment	52.6 (51.2, 54.0)	50.7 (48.5, 52.9)	50.9 (48.2, 53.6)	56.5 (52.8, 60.1)	58.0 (54.6, 61.4)
WPAI Percent activity impairment	56.4 (55.3, 57.4)	53.6 (51.9, 55.3)	55.5 (53.4, 57.5)	60.7 (58.0, 63.5)	61.9 (59.4, 64.4)
HADS overall score	14.6 (14.3, 15.0)	14.3 (13.8, 14.8)	14.7 (14.1, 15.3)	15.5 (14.6, 16.4)	14.8 (13.9, 15.6)
HADS anxiety score	8.0 (7.8, 8.2)	7.9 (7.6, 8.2)	8.1 (7.8, 8.5)	8.2 (7.6, 8.7)	7.8 (7.4, 8.3)
HADS depression score	6.7 (6.5, 6.8)	6.4 (6.1, 6.7)	6.6 (6.2, 6.9)	7.3 (6.9, 7.8)	6.9 (6.5, 7.4)
MSQ-RFR score	43.8 (43.0, 44.6)	46.7 (45.4, 48.0)	44.8 (43.3, 46.3)	39.1 (37.0, 41.2)	38.1 (36.1, 40.1)
MSQ-RFP score	59.2 (58.2, 60.1)	61.7 (60.3, 63.1)	59.9 (58.2, 61.7)	55.7 (53.2, 58.2)	53.8 (51.4, 56.2)
MSQ-EF score	50.5 (49.4, 51.6)	54.2 (52.5, 55.8)	50.0 (48.0, 52.1)	46.9 (44.1, 49.8)	44.0 (41.2, 46.8)

All values are mean (95% CI), unless otherwise indicated
 CIs were calculated using Wald formula/method
 CI, confidence intervals; EF, emotional function; HADS, hospital anxiety and depression; HIT-6, headache impact test; HRCoL, health-related quality of life; mMIDAS, modified migraine disability assessment; MSQ, migraine specific quality-of-life; N, total number of patients in Part 2 or PPTF subgroups; n, number of patients responding to the respective questionnaire; PPTF, prior prophylactic treatment failures);
 PRO, patient-reported outcomes; RFR, role function restrictive; RFP, role function preventive; WPAI, work productivity and activity index
 WPAI scores range between 0 and 100, where higher scores indicate greater impairment
 MSQ scores range between 0 and 100, where higher scores indicate better HRCoL
 HADS scores range between 0 and 21, where higher scores indicate more severe distress
 Note: Data for the PRO measures including HIT-6 and mMIDAS were previously reported

PRO scores of the BECOME study population set for Part 2 (N=2419) by number of PPTF

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the e-poster presentation.

EPR2082

Treatment with Onabotulinumtoxin A versus Erenumab for Patients with Acquired/Post-traumatic Chronic Migraine

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Background and aims: Traumatic brain injury frequently is complicated by chronic headache which often has features of chronic migraine. We currently lack any evidence-based prophylactic therapy for chronic posttraumatic headache. In this study we assessed the relative efficacy, safety and tolerability of onabotulinumtoxinA versus erenumab for headache prophylaxis in patients with acquired/post-traumatic chronic migraine.

Methods: We randomized patients with chronic post-traumatic headache of at least 6 months duration and possessing the clinical phenotype of chronic migraine to treatment with open-label onabotulinumtoxin A versus erenumab. We evaluated the safety, tolerability and efficacy of each treatment, defining efficacy as a 50% or greater decline in monthly headache frequency at month 6 of treatment relative to the pre-treatment baseline month.

Results: We treated 172 patients (onabotulinumtoxin A n=87; erenumab n=85). There were no significant adverse events, and no patient discontinued treatment consequent to lack of tolerability. More patients achieved the primary treatment endpoint in the erenumab group (43/83: 52%) than in the onabotulinumtoxin A group (37/84: 44%), but the difference did not reach statistical significance.

Conclusion: Both onabotulinumtoxin A and erenumab appear to be safe and well-tolerated treatments for acquired/posttraumatic chronic migraine, and with either treatment over a period of 6 months approximately half of patients will experience a meaningful reduction in monthly headache frequency.

Disclosure: Consultant and speakers bureau: Amgen, Allergan My parent institution has received revenue from Amgen and Allergan for research I have performed. Amgen and Allergan advertise in and so provide revenue for a healthcare magazine (Migraineur) for which I serve as editor-in-chief.

EPR2083

Impact of an Employer-Provided Migraine Coaching Program on Patient Burden and Engagement

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Background and aims: This retrospective study assessed the impact of a migraine telemedicine coaching program offered by a healthcare company as a complimentary service within its corporate health management program for its Swiss-based employees and their family members.

Methods: Of 339 participants who registered for the program from June 2018 until October 2019, 141 enrolled into a study for retrospective analysis of their data. All participants received six monthly sessions of individualized telecoaching comprised of educational modules and action plans from a specialized nurse by phone and through a specially developed module on the Migraine Buddy smartphone application. The study participants were evaluated through a series of questionnaires including Migraine Disability Assessment (MIDAS), Patient Activation Measure (PAM), and the commonly used coaching lessons and implemented action plans.

Results: Seventy-nine participants completed the program at 6 months. The mean age (standard deviation, SD) at baseline was 41.5 (8.8) years with 70.0% females, 64.1% had a confirmed diagnosis of migraine, and 56.8% were not being treated by a physician despite 74.0% having MIDAS grade ≥ 2 . The total mean (SD) MIDAS score and the PAM score significantly improved from baseline to 6 months (table). The most used coaching lessons focused on progressive muscle relaxation, sleep, general disease understanding, stress management, and nutrition while top action plans addressed sleep, hydration, nutrition, disease understanding and daily routine.

Parameter	# of Patients who completed baseline and 6 months assessments	Mean (SD)	P-value
MIDAS	73	Baseline= 15.0 (13.6) At 6 months= 6.9 (8.2) Change from baseline= -8.1 (5.5)	<.001
PAM	78	Baseline= 63.8 (10.9) At 6 months= 69.6 (12.8) Change from baseline= 5.8 (1.9)	.003

MIDAS and PAM scores

Conclusion: The results demonstrate that an employer-sponsored educational and counseling support that empower to leverage all options, medical & lifestyle, can significantly decrease migraine-related disability and promote disease management among employees.

Disclosure: This study was funded by Novartis Pharma AG.

EPR2084

Erenumab in real life: a multicentric italian observational study

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Background and aims: Erenumab is a monoclonal antibody targeting the calcitonin gene-related peptide receptor. Randomized, placebo-controlled trials demonstrated that erenumab is effective in the prevention of Episodic (EM) and Chronic Migraine (CM). However, real life clinical evidence is still missing.

Methods: An observational multicentre study was designed. Patients were treated with erenumab 70mg every four weeks. If no clinical response was observed after 12 weeks, a dose increase to 140mg was attempted. Data about outcome, adverse events, abortive medication consumption and disability (Migraine Disability Assessment Score Questionnaire – MIDAS; Headache Impact Test – HIT-6) were collected.

Results: 108 consecutive patients were enrolled (22 EM; 86 CM). Baseline clinical and demographic characteristics are shown in Table 1. A significant reduction from baseline to week 4, 12, 24 and 36 in headache days, analgesics consumption, pain intensity (numerical rating scale) and MIDAS score per month was found (Table 2). The percentage of non-responders (<30% headache days reduction), partial-responders (<50%), responders (>50%) and super-responders (>75%) at week 4, 12, 24 and 36 is shown in Figure 1. When analysing data from non responders and partial responders at week 12, a significant reduction from baseline in analgesics consumption (p=0.001), pain intensity (p=0.001) and MIDAS (p<0.0001) was found.

Table 1: subjects baseline demographic and clinical features.

	SUBJECTS (n=108)
AGE, years (mean, SD)	47.15 (9.5)
FEMALE, number (%)	83 (76.9%)
DISEASE DURATION, years (mean, SD)	27.9 (9.8)
PREVIOUS PROPHYLAXIS, number (mean, SD)	5 (1.08)
ADD-ON PROPHYLAXIS, number (%)	44 (40.7%)
MEDICATION OVERUSE, number (%)	84 (77.8%)

Table 1: subjects baseline demographic and clinical features.

Table 2: between-subjects ANOVA results documenting a statistically significant reduction in headache days, analgesics consumption, pain intensity and disability.

	BASELINE	WEEK 4	WEEK 12	WEEK 24	WEEK 36	p
TOTAL HEADACHE DAYS/MONTH	21.0 (1.2)	12.0 (1.6)	10.8 (1.5)	8.8 (1.3)	8.4 (1.3)	<0.001
Mean (SD)						
MILD HEADACHE DAYS/MONTH	11.6 (1.4)	6.9 (1.1)	7.0 (1.3)	6.6 (1.0)	3.9 (0.6)	=0.02
Mean (SD)						
SEVERE HEADACHE DAYS/MONTH	9.3 (1.3)	5.0 (0.8)	3.9 (1.0)	2.0 (0.6)	3.6 (0.7)	=0.001
Mean (SD)						
TOTAL ANALGESICS/MONTH	22.4 (2.7)	10.3 (1.4)	9.0 (1.3)	6.8 (0.9)	8.0 (1.0)	=0.002
Mean (SD)						
NSAIDs/MONTH	11.6 (3.2)	3.7 (0.9)	3.8 (1.3)	2.7 (0.8)	2.1 (0.7)	=0.02
Mean (SD)						
TRIPTANS/MONTH	11.2 (1.9)	6.5 (1.2)	5.3 (1.1)	3.9 (0.8)	5.5 (0.9)	=0.03
Mean (SD)						
NRS	7.4 (0.2)	5.6 (0.3)	5.1 (0.3)	4.9 (0.3)	4.9 (0.3)	=0.001
Mean (SD)						
MIDAS	76.0 (9.7)	N/A	28.0 (6.1)	23.8 (5.4)	N/A	=0.001
Mean (SD)						
HIT-6	62.3 (1.8)	N/A	54.6 (1.4)	52.4 (1.6)	N/A	=0.009
Mean (SD)						

Abbreviations: SD: standard deviation; NSAIDs: Nonsteroidal anti-inflammatory drugs; NRS: numerical rating scale; MIDAS: Migraine Disability Assessment Score Questionnaire; HIT-6: Headache Impact Test; N/A: not available.

Table 2: between-subjects ANOVA results documenting a statistically significant reduction in headache days, analgesics consumption, pain intensity and disability.

Figure 1: responders rates at week 4, 12, 24 and 36 of treatment.

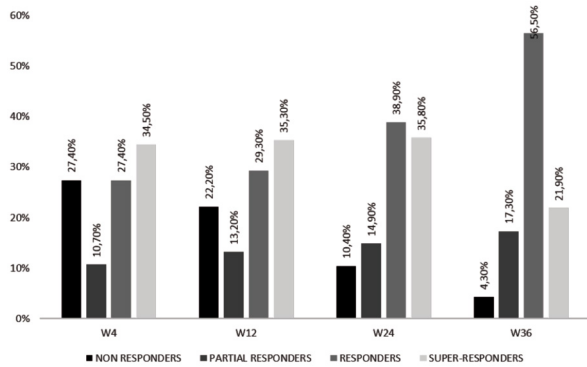


Figure 1: responders rates at week 4, 12, 24 and 36 of treatment.

Conclusion: The data confirm erenumab efficacy in migraine prophylaxis. Over 70% of patients documented a significant progressive and sustained improvement, from week 4 to week 36, in headache days, analgesics consumption, pain intensity and migraine related disability.

Disclosure: Nothing to disclose

Infectious diseases 1

EPR2085

Tuberculoma simulates a brain neoplasm in an immunocompetent patient: a diagnostic challenge

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Background and aims: Tuberculoma is a granulomatous inflammatory process that can simulate a malignant tumor in the brain. This entity is uncommon even more in immunocompetent patients. Our goal is to present a clinical case of cerebral tuberculoma resembling a brain tumor.

Methods: We present a 44-year-old man from Mauritania. He had mild oppressive fronto-temporal headache associated with vertiginous sensation and unsteady gait for a month. The magnetic resonance showed an isolated expansive ring-enhancing lesion in left cerebellar hemisphere with perilesional edema. The cerebrospinal fluid was normal. This patient developed clinical deterioration requiring external ventricular shunt and subsequent surgical intervention by craniotomy and total excision. The histopathological diagnosis was tuberculoma and screening showed indeterminate bilateral pulmonary millimeter nodules only. No immunodeficiencies were observed.

Results: Mycobacterium tuberculosis usually spreads hematogenously from a primary pulmonary infection. It can produce subpial, subependymal or borderline gray/white foci in the brain. Exceptionally, these foci can grow without breaking into the subarachnoid space and develop tuberculomas without meningeal involvement. This presentation is uncommon in immunocompetent patients.

Conclusion: Tuberculoma should be included in the differential diagnosis of an expansive isolated cerebral lesion. Epidemiological history is important even in immunocompetent patients.

Disclosure: Nothing to disclose

EPR2086

Listerial abscesses, the key is in the blood

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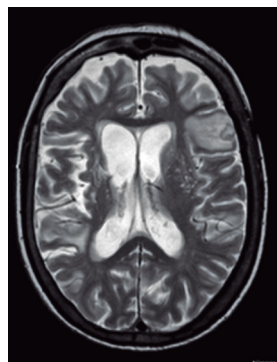
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Background and aims: *Listeria monocytogenes* (LM) is a cause of CNS infection, especially in immunocompromised population. The most common manifestation is meningoencephalitis -typically- rhombencephalitis, whereas cerebral abscesses are exceptional. We present one case and a literature review from 1968 to 2019.

Methods: Study case and systematic literature review

Results: A 77-year-old woman, under treatment with methotrexate and corticosteroids by polymyalgia rheumatica, presents at emergency department due to fever, disorientation and aphasia. She had consumed homemade goat cheese in the last month. Lumbar puncture demonstrated lymphocytic pleiocytosis. Only blood cultures were positive for LM. MRI showed a left frontal abscess. After 6 weeks of treatment with ampicillin, she was discharged, without sequelae, and neuroimaging improvement. There are 80 cases described in the literature, with a mortality rate about 20%. Despite LM is an opportunistic agent, in 25.3% of cases there was not any predisposing condition. As in our case, in 79.3% of cases the blood cultures were positive for LM, compared to 40.3% in CSF. The most common location was lobar (53.5%), followed by basal ganglia (21%) brainstem location (19%). In 21% of cases, multiple abscesses were found, half of them occurring in immunosuppressed patients.



T2 sequence showing left frontal abscess

Conclusion: The spread to central nervous system of LM, including abscesses is a rare condition, associated in most cases with immunosuppression. Due to the hematogenous dissemination of LM, blood cultures have a higher diagnostic profitability compared to CSF culture, being able to avoid brain biopsy

Disclosure: Nothing to disclose

EPR2087

Neurological presentations of HIV infection: a retrospective observational study in Hong Kong

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Background and aims: Human immunodeficiency virus (HIV) infection can present in various ways, and the nervous system is frequently involved. The prevalence of neurological presentations of HIV in our locality is unknown.

Methods: This is a retrospective observational study that included adult HIV patients admitted to Princess Margaret Hospital (1 of the 2 hospitals with HIV specialist care in Hong Kong) during January to December 2018. Data including demographics, past history, initial presentation, neurological diagnoses, etc. were analysed.

Results: 113 HIV patients were identified (male 81%, with 52% men having sex with men; mean age at diagnosis 42, range 20-86). 19 patients presented with neurological conditions, most commonly cryptococcal meningitis (32%), followed by tuberculous meningitis (21%), cerebral toxoplasmosis and varicella zoster virus meningoencephalitis (both 16%). 1 patient presented with bilateral Bell's palsy as a manifestation of acute retroviral syndrome. On the other hand, 5 patients developed neurological conditions after commencement of antiretroviral therapy (ART) - progressive multifocal leucoencephalopathy in 2, cerebral toxoplasmosis in 2, and epidural mass in spinal cord due to tuberculosis in 1. They were either due to unmasking immune reconstitution inflammatory syndrome, or poor adherence to ART. At 1 year follow-up, majority survived with good outcomes.

Conclusion: The prevalence of neurological conditions among HIV patients in our cohort is 21% (17% as the initial presentation). This is not as frequent compared to less developed areas like India (26%) and sub-Saharan Africa (45%).

Disclosure: Nothing to disclose

EPR2088

Neurosyphilis: clinical and socio-demographic profile in a tertiary hospital in Madrid

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Background and aims: Neurosyphilis is the clinical result of infection of the nervous system by *Treponema Pallidum* and can occur at any time after the initial infection.

It is uncommon now, as compared with the era before the introduction of penicillin, but there has been a resurgence of syphilis in low- and middle-income countries and in certain populations in developed countries.

We present a series of 33 patients with neurosyphilis, describing their clinical, serological, neuroimaging and socio-demographic characteristics.

Methods: Retrospective and descriptive study including all patients presenting to Neurology and Infectious Diseases departments with neurosyphilis between 2004 and 2019.

Results: We identified 33 patients with neurosyphilis. Mean age of onset was 50 years, 84% were males and 72% were Spanish. 45% presented a concomitant infection by human immunodeficiency virus. The most frequent forms were ocular syphilis (39%), followed by meningovascular syphilis (18%), and cognitive deterioration and neuropsychiatric alterations (12%). VDRL in cerebrospinal fluid was positive in 40% of patients. Most patients (93%) were treated with high dose IV penicillin G between 10 to 14 days, with partial or total improvement in 66%.

Conclusion: -Neurosyphilis is the result of infection of the nervous system by *Treponema Pallidum* and can occur at any time in the course of infection. It's incidence has increased over recent years.

- Diagnosis of neurosyphilis is based on clinical features, laboratory test and cerebrospinal fluid analysis.

-Neurosyphilis has undergone a very important clinical and epidemiological change in recent years, so clinical suspicion is essential for the diagnosis.

Disclosure: Nothing to disclose

EPR2089

Bacterial Meningitis Complicated by Cerebral Venous Thrombosis

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Background and aims: Cerebral venous thrombosis (CVT) has been described as an uncommon complication of community-acquired bacterial meningitis, but this has not systematically been studied.

Methods: We evaluated clinical characteristics and outcome of CVT in adults with community-acquired bacterial meningitis in a prospective nationwide cohort study of bacterial meningitis from 2006 to 2018 in the Netherlands.

Results: CVT occurred in 26 of 2565 episodes with bacterial meningitis (1%) in 26 patients. The diagnosis of CVT was made on presentation day in 15 patients (56%) and during admission in 11 patients after a median of 6 days (IQR 2-7). Sinusitis or otitis was present in 16 of 24 patients (67%). Patients with CVT presented more often in coma, as defined a score on the Glasgow Coma Scale <8, than those without CVT (53 vs. 18%; P=0.001) and the clinical course was more often complicated by focal neurologic deficits (58 vs. 22%; P<0.001). The transverse sinus was most frequently thrombosed (18 of 26; 69%) and *Streptococcus pneumoniae* was the most common causative pathogen, occurring in 17 of 26 patients (65%). Eleven patients (44%) received anticoagulant therapy with heparin and none of them developed intracerebral hemorrhage. Unfavorable outcome, as defined as a score on the Glasgow Outcome Scale <5, occurred in 14 of 26 patients (54%) and 4 patients (15%) died.

Conclusion: CVT is a rare complication of bacterial meningitis and is associated with coma, ENT infections, and focal neurologic deficits.

Disclosure: Nothing to disclose

EPR2090

Cerebrospinal fluid sex steroid hormone levels in pneumococcal meningitis

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Background and aims: Unfavourable outcome in bacterial meningitis is related to excessive inflammation and higher inflammatory markers have been reported in female than male patients. We investigated the association between cerebrospinal fluid (CSF) sex steroid hormone levels and outcome, disease severity and inflammatory parameters in pneumococcal meningitis.

Methods: We identified adults with culture-proven pneumococcal meningitis included in a prospective cohort study (2006-14). We measured oestradiol and testosterone in leftover CSF using liquid chromatography-tandem mass spectrometry and sex hormone-binding globulin (SHBG) using an enzyme-linked immunoassay. Outcome was graded using the Glasgow Outcome Scale score (5 indicating favourable, 1-4 unfavourable outcome).

Results: 60 patients were included: 20 males, 20 premenopausal (<50 years) and 20 postmenopausal (>50 years) women. Median age was 65, 38 and 70 years, respectively. 21 (35%) patients had an unfavourable outcome and 11 (18%) died. Median SHBG was 0.65nmol/L in men, 0.45 in premenopausal and 1.10 in postmenopausal women (p=0.52), while median testosterone was 0.24nmol/L, 0.05 and 0.13, respectively (p<0.001). Median oestradiol was 7.50pmol/L in males, 11.00 in premenopausal and 12.50 in postmenopausal females (p=0.27). Only SHBG differed between cases with favourable vs unfavourable outcome (1.00 vs 0.40, p=0.03). Oestradiol was positively correlated with C-reactive protein (rs=0.47, p=0.01) and erythrocyte sedimentation rate (rs=0.48, p=0.04), while testosterone was negatively correlated with the latter (rs=0.39, p=0.03). We found no correlation between hormone levels and illness severity (Dutch Meningitis Risk Score).

Conclusion: In this exploratory study, lower SHBG was associated with unfavourable outcome whereas oestradiol was positively and testosterone negatively correlated with serum inflammation parameters.

Disclosure: This study has been funded by a Research Grant (2018) of the European Society of Clinical Microbiology and Infectious Diseases and by a Research Training Fellowship (2019) of the European Academy of Neurology.

EPR2091

Causes, clinical presentation and outcome of Meningitis, Meningoencephalitis and Encephalitis cases in Switzerland, a retro- and prospective analysis of 258 patients

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Background and aims: We aimed to identify most frequent causes, clinical presentation and long-term outcome of acute cases of meningitis (M), meningoencephalitis (ME) and Encephalitis (E) treated in the Inselspital, University Hospital Bern, Switzerland.

Methods: We performed a retrospective review of clinical patient records for all patients treated in the Inselspital for the diagnosis of M/ME/E during the period of 1.1.2016 until 31.10.2018. Patients were contacted prospectively for a telephone follow-up interview and were asked to fill out and return questionnaires.

Results: We included 258 patients: 85 (33%) had M, 127 (49%) ME and 46 (18%) E. Most frequently infectious causes were identified: 48% in M and 40% in ME/E, with Enterovirus (39%) and tick borne virus (57%) being the most frequently identified infectious agent respectively. 7% of all ME/E cases were of autoimmune origine. In 43% of M and 32% of ME/E patients the etiology remained unknown. In a telephone interview, undertaken more than a year (Median 14/17 months respectively) after recovering from the acute disease, still 29% of M and 65% of ME/E patients reported persisting neurological sequelae such as headache (22%/28% resp.), memory problems (26%/29% resp.), cognitive deficits (17%/23% resp.) as well as epileptic seizures (28%) in ME/E amongst other signs and symptoms. 17% of M and 41% of ME/E patients indicated to suffer from excessive daytime sleepiness.

Conclusion: Long-term sequelae after M/E and also after M are found in a significant portion of survivors.

Disclosure: Nothing to disclose

Movement disorders 3

EPR2092

Fall risk assessment with in- and off-laboratory mobility measures in patients with neurological gait disorders – the PAss FaMous study

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Background and aims: Falls are frequent among patients with neurological gait disorders (Stolze et al., 2005). Besides the assessment of socio-demographic and clinical risk factors via questionnaires and clinical scoring systems, technical based movement quantification procedures have reached scientific impact in order to quantify gait stability and fall risk. The study examined the predictive power of in- and off-laboratory measures for fall prediction.

Methods: For the Prospective Assessment of Falls and Mobility–study (PAss FaMous-study, DRKS-ID: DRKS00007762) 396 patients were examined by a standardized fall risk assessment, in-laboratory-based gait analysis (GAITrite[®]), and an off-laboratory tracking of physical activity (ActivPal[®]). A follow-up of 6 months with prospective recordings of falls via fall calendar and telephone interview was established. After testing for possible differences via ANOVA models, binary logistic regression procedures for model I “fall status”, model II “fall frequency” and model III “fall severity” were performed.

Results: The regression model I showed a correct prediction in 82% of the cases, model II and model III in 88%. Significant factors were dependent on the underlying model. (Table 1)

Conclusion: For the identification of falls and high fall frequency, the assessment of the fall history in combination with dynamic stability parameters of the walking behavior appears to be useful. Mobility measures are relevant for the prediction of frequent falling and severe falling. Frequent falling shows associations to the daily intensity of locomotion. For the identification of severe falling, pattern parameters of physical activity are more important.

Disclosure: Nothing to disclose

	model information	parameter information						
	correct prediction	coefficient	SE	df	p-value	Exp(b)	low	high
Model I ,Fall status'	0.82							
retrospective fall status		1.46	0.27	1	0.001	4.296	2.528	7.299
MOCA		0.14	0.06	1	0.030	1.148	1.014	1.300
FGA		-0.10	0.05	1	0.045	0.901	0.815	0.997
gait velocity		-0.04	0.02	1	0.010	0.957	0.925	0.989
stride time		0.67	0.02	1	0.003	1.069	1.023	1.118
CV of stride time		0.47	0.15	1	0.001	1.607	1.203	2.146
phase synchronization index		-0.18	0.15	1	0.46	0.839	0.706	0.997
Model II ,frequent falls'	0.88							
retrospective fall status		1.61	0.35	1	0.001	5.024	2.510	10.058
MOCA		0.15	0.08	1	0.050	1.166	1.000	1.359
ABC-d		-0.03	0.01	1	0.007	0.971	0.950	0.992
SF-12		0.16	0.08	1	0.050	1.174	1.004	1.374
base of support		0.13	0.06	1	0.020	1.143	1.021	1.279
CV of stride time		0.53	0.18	1	0.002	1.704	1.207	2.405
phase synchronization index		-0.25	0.11	1	0.018	0.781	0.636	0.959
ambulatory bout #		-0.01	0.01	1	0.007	0.990	0.983	0.997
daily intensity		0.52	0.22	1	0.020	1.681	1.085	2.605
sedentary bout duration	-0.01	0.01	1	0.044	0.998	0.995	1.000	
Model III ,severe falls'	0.88							
gait velocity		-0.03	0.01	1	0.012	0.969	0.945	0.993
ambulatory bout alpha		-23.45	1.45	1	0.024	0.100	0.002	0.121

EPR2093
Cancelled

EPR2094

Genetic screening for autosomal recessive genes and phenotypic features in young onset Parkinson's disease: A Greek Cohort.

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Background and aims: Young onset Parkinson's disease (PD) with onset ≤ 45 years old, has been associated with several causative genes. We aimed to determine the incidence of the most common autosomal recessive PD genes (PRKN, PINK1, DJ1) in a cohort of 68 unrelated young onset PD patients in Greece.

Methods: Assessment included Sanger Sequencing for PARK, PINK1, DJ1 genes, Multiplex ligation-dependent probe amplification (MLPA) for dosage PRKN mutations and Whole Exome Sequencing in selected cases.

Results: Pathogenic PRKN variants were identified in 5 cases (2 homozygous/ 3 compound heterozygous). Mean age at onset was 38, dystonia was reported in 5/5 and family history in 2/5 patients. Cognition was not affected, psychiatric problems were prominent, while hyposmia and REM sleep behavior disorder (RBD) were scarce. 2 patients were mutation carriers with likely pathogenic heterozygous PRKN mutations (exon 2 deletion and c.101_102del AG). Pathogenic PINK1 mutations, including a novel pathogenic mutation p.Y295X in a homozygous state, were found in 3 patients (2 homozygous / 1 compound heterozygous). The mean age at onset was 35.7, 1st symptom was rest tremor in 2/3 cases, and a positive family history was reported in 2/3 patients. Cognition was not severely affected, olfaction was intact, RBD was reported in 2/3 cases, insomnia in 3/3 and freezing of gait (2/3) was very pronounced in one patient.

Conclusion: Our genetic screen revealed a prevalence of common recessive PD genes in 14.7% of young onset PD cases, suggesting the existence of additional pathogenic variants besides those currently screened in clinical routine.

Disclosure: Nothing to disclose

EPR2095

DAT SPECT and MIBG myocardial scintigraphy imaging profiles and clinical stages in Parkinson's disease and dementia with Lewy Bodies.

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Background and aims: DAT SPECT and MIBG are widely used tools in the diagnosis of Parkinson's disease (PD) and dementia with Lewy Bodies (DLB). This study aimed to reveal their correlation to Hoehn-Yahr (H-Y) stage and disease duration in PD and DLB.

Methods: The subjects were idiopathic 63 PD and 23 DLB patients who underwent DAT SCAN. Among these patients, 58 PD and 18 DLB patients also received MIBG. Specific binding ratio (SBR) and delayed heart-to-mediastinum (H/M) ratio were evaluated.

Results: SBR value was significantly reduced (cut off: 4.5) in 97% of the PD and 100% of the DLB patients, and H/M ratio was significantly reduced (cut off: 2.2) in 78% of the PD and 89% of the DLB patients. SBR value was significantly correlated with H-Y stage in both PD and DLB patients (PD: $R^2=0.072$, $p=0.033$, DLB: $R^2=0.34$, $p=0.0047$) but not with disease duration, which indicates that SBR value evaluates motor severity. H/M ratio was significantly correlated with H-Y stage and disease duration in PD patients (H-Y stage: $R^2=0.091$, $p=0.021$, duration: $R^2=0.13$, $p=0.0048$) whereas no correlation was observed between H/M ratio and these parameters in DLB patients. H/M ratio in H-Y 1 stage seemed to be lower (1.4 ± 0.2) in DLB patients compared to that of PD patients (2.2 ± 0.8).

Conclusion: DAT scan is suitable for evaluation of motor severity in both PD and DLB patients. Our preliminary result of MIBG may reflect that pathological changes in the cardiac sympathetic nerves are more profound in DLB patients compared to PD patients with early motor stage.

Disclosure: Nothing to disclose

EPR2096

The role of the cerebellum in cortical myoclonus: a neurophysiological study

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Background: The putative involvement of the cerebellum in the pathogenesis of CM syndromes has been long hypothesized, as pathological changes in patients with CM have commonly been found in the cerebellum rather than in the suspected culprit, the sensorimotor cortex. The hypothesis is that the increased cortical excitability seen in CM is due to loss of the cerebellar inhibitory control via cerebello-thalamo-cortical connections. Here, we explore this hypothesis by modulating cerebellar excitability by means of transcranial Direct Current Stimulation (tDCS), and assessing its effect on sensorimotor cortex excitability in patients with CM.

Methods: 7 patients with CM underwent the following neurophysiological tests: short intracortical inhibition (SICI), somatosensory evoked potentials (SEP) and long-latency reflexes (LLR), tested before and after anodal cerebellar tDCS applied on the cerebellum. Data were compared with those obtained in 7 healthy controls (HC).

Results: The amplitude of N20-P25 and P25-N33 components of SEP was increased in patients after tDCS, but not in HC. A similar trend was observed in LLR, with a significant increase in amplitude before and after tDCS in patients. Baseline SICI was reduced in patients compared to HC. Whereas tDCS caused a further SICI reduction in patients, it did not change SICI in HC.

Conclusion: According to our data, anodal cerebellar tDCS increases sensorimotor cortex excitability in CM. Overall, the present results suggest a role of the cerebellum in the pathophysiology of CM, and that CM patients might have abnormal homeostatic plasticity within the sensorimotor cortex, possibly responsible for this paradoxical response.

Disclosure: Nothing to disclose

EPR2097

Correlation of dopaminergic denervation and the progression of autonomic dysfunctions in different clinical subtypes of Parkinson's disease: Analysis of the PPMI data

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Background and aims: Autonomic dysfunctions occur in the early stage of Parkinson's disease (PD), and impacts the quality of life throughout the progression of the disease. In this study, we evaluated the serial progression of autonomic dysfunctions in different subtypes of a prospective PD cohort.

Methods: From the Parkinson's Progression Markers Initiative (PPMI) database, 325 PD patients (age 61.2 ± 9.7 , M:F = 215:110) were enrolled. Patients were subgrouped into tremor dominant (TD), indeterminate, and postural instability gait disorder (PIGD) subtypes. The progression of autonomic dysfunctions, and dopaminergic denervation from I-123 FP-CIT SPECT images of each group were analyzed and compared at baseline, 12 months, 24 months, and 48 months of follow up periods.

Results: The SCOPA-AUT score of the indeterminate group was significantly higher than that of the TD group ($P < 0.05$) at baseline, and was significantly higher than both TD and PIGD subtypes ($P < 0.05$) at 48 months. The indeterminate group had the most significant correlation between the aggravation of dopaminergic denervation in I-123 FP-CIT SPECT images, and the increase of SCOPA-AUT scores during 48 months of follow up ($r = 0.56$, $P < 0.01$).

Conclusion: Autonomic dysfunctions were most severe in the indeterminate subtype throughout the 48 months follow up period, with a significant correlation with dopaminergic denervation. The indeterminate subtype may present autonomic dysfunctions as the main symptom, and the severity of autonomic dysfunctions may be monitored with I-123 FP-CIT SPECT.

Disclosure: Nothing to disclose

EPR2098

Remote and frequent assessment of Huntington's disease in clinical trials: Strategies for assessing and accounting for the practice effect

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Background and aims: Digital monitoring tools enable remote assessment of Huntington's disease (HD) signs and symptoms in patients' daily lives at a higher frequency than clinician-administered tests. Studies have shown that most gold-standard tests are influenced by practice effects; i.e. the improvement in performance resulting from the repetition of a task. During initial digital testing sessions, changes in performance may be confounded by test-taking strategies, difference in manual dexterity or test/device knowledge. It is key to distinguish between a subject's familiarisation period with the test, and subsequent longitudinal changes related to disease progression and continued practice to avoid confounding the interpretation of clinical results.

Methods: This study assessed the impact of task repetition on performance and established the number of practice test iterations required to accurately estimate true performance changes. 7 motor and cognitive smartphone-based assessments were completed daily or weekly by individuals with manifest HD ($n = 36$), premanifest HD ($n = 20$) and healthy controls ($n = 20$) in the Digital-HD Study. A 2-phase learning curve model characterised individual practice and longitudinal effects. Based on the model's estimation of familiarisation period duration and performance changes, the impact on each task and disease group performance was established.

Results: While subjects experienced practice effects for cognitive tasks, some motor tasks were free of such effects. When practice occurred, less than 10 test iterations were required for the subject to reach a stable test performance.

Conclusion: Practice effects can be characterised using high-frequency remote patient monitoring, and mitigation strategies implemented to facilitate accurate interpretation of clinical trial results.

Disclosure: Study sponsored by UCL and supported by F. Hoffmann-La Roche Ltd; the authors thank Sarah Child, of MediTech Media, for providing editorial support for this abstract.

EPR2099

Withdrawn

EPR2100

Analysis of mortality in patients with advanced Parkinson's disease treated with Deep Brain Stimulation of the Subthalamic Nucleus (STN-DBS).

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Background and aims: STN-DBS in advanced Parkinson's disease (PD) has shown to improve the quality of life of patients and, in some studies, greater survival.

Methods: Clinical-demographic variables and causes of mortality of advanced PD patients treated with STN-DBS in our center are analyzed.

Results: 72 patients were recruited. 61,1% men. Mean age of diagnosis was 51.1 years with a median age at surgery of 65 years and a mean of 10 years from the diagnosis to the surgery.

18 patients have died, 12 (66.7%) men, without gender being an influencing factor in mortality. In those who died, the mean age of diagnosis was 56.5 years (SD 6.9) and the median age at surgery was 69 years (IQR 65-73), being this one significantly higher ($p=0.007$) than the median age at surgery in the living patients (62 years, IQR 52-69). There were no differences in the median number of years from the diagnosis to the surgery between groups. The median age of death was 76 years (IQR 68-78) with a mean time since surgery of 5.5 years (SD 3.8). 9 patients (50%) died of aspiration pneumonia, 2 of heart attack, one of mesenteric ischemia, another of neoplasia and one due to postoperative cerebral hemorrhage.

Conclusion: Pneumonia is the most frequent cause of death in patients with advanced PD regardless of treatment. The results show that the median age at the time of surgery is significantly higher in the group that died, probably due to chronobiological evolution. Patients over 70 years can benefit from DBS without surgery significantly increasing the risk of mortality.

Disclosure: Nothing to disclose

EPR2101

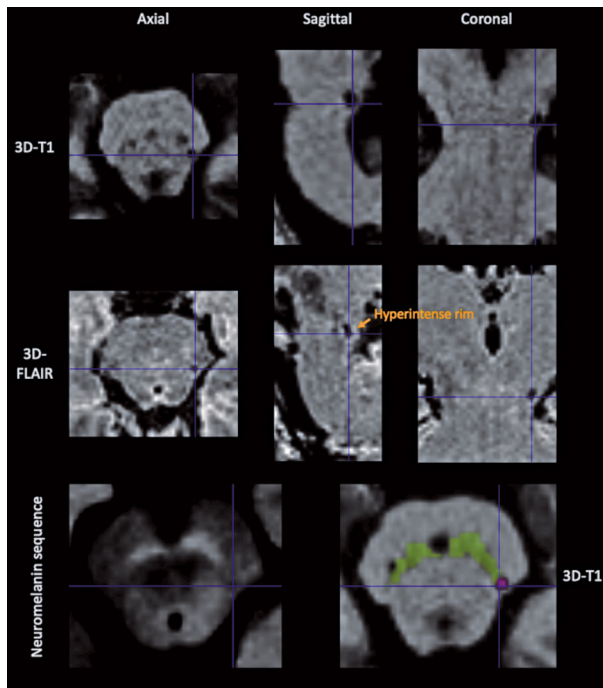
Nigro-striato-pallidal lacunes, white matter hyperintensities and radio-clinical correlations in Parkinson's disease: an MRI-based observational case-control study

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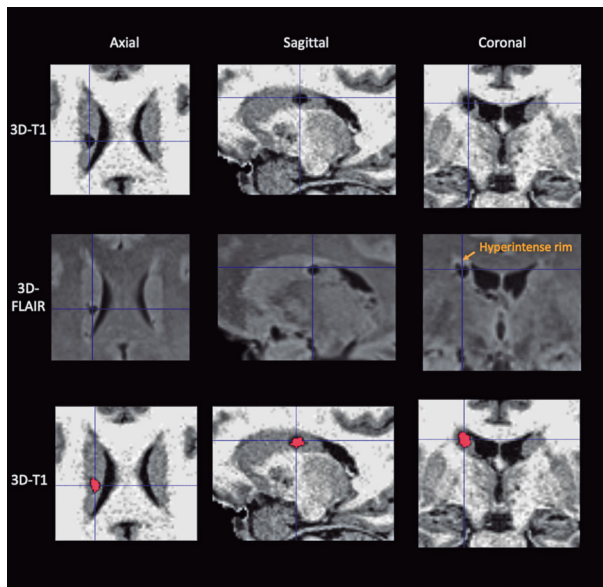
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Background and aims: Vascular parkinsonism is poorly defined, often diagnosed when extrapyramidal signs occurs following a symptomatic stroke. Accumulation of 'asymptomatic' small vessel lesions is often considered of 'fortuitous discovery' and has received little consideration. This study aimed to quantify nigro-striato-pallidal lacunes and white matter hyperintensities (WMH) on MRI in Parkinson's disease (PD) and in matched healthy subjects, and to explore the correlations between these lesions and the clinical signs of PD.

Methods: Retrospective MRI study using blinded comparison of number and volume of lacunes in basal ganglia, as well as WMH, between 68 PD and 34 control subjects comparable in age and sex from the ICEBERG cohort. Radio-clinical correlations between UPDRS-III symptoms and MRI lesions were explored.



Technique for manual acquisition of a lacune located on the tail of the substantia nigra in a PD patient of the study



Example of manual acquisition of a lacune located on the right caudate nucleus in a PD patient of the study

Results: Cardiovascular risk factors were of similar distribution in the 2 groups. In PD, there were more lacunes (often larger) in substantia nigra ($p < 0.001$), putamen ($p = 0.003$) and caudate ($p = 0.045$) than in controls, but only on the left side (90% of PD subjects were right-handed). Prevalence of pallidal lesions or WMH was comparable. There were significant correlations between the presence and volume of nigro-striatal lacunes and resting tremor.

Conclusion: In the dominant hemisphere, nigro-striatal lacunes were more prevalent in PD than in a comparable

group of healthy subjects and correlated with resting tremor. If PD symptoms could be worsened by cumulative small vessel nigro-striatal lesions, this could modify the therapeutic management of the disease: stricter control of cardiovascular risk factors would be necessary and the introduction of an antiplatelet medication could be discussed.

Disclosure: Principal investigator has been granted with the Medical Research and Study Fund (Paris Hospitals).

EPR2102

Variability of the APOE, TREM2, SLC1A2 and LINGO1 genes in the occurrence of essential tremor in a Tunisian population

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Background and aims: Essential tremor (ET) is the most common movement disorder. Despite its prevalence, to our knowledge there is no study on genetic predisposition of this pathology in Tunisia. Our aim was to investigate the role of polymorphisms in different genes in the occurrence of ET in Tunisian population.

Methods: Samples from 110 Tunisian ET patients and 158 healthy controls (HC) were used and the genotyping of 10 polymorphisms in LINGO1, SLC1A2, APOE and TREM2 genes was established by Sanger sequencing, PCR-PFLP and PCR-ARMS.

Results: SLC1A2 rs3794087 ($p=0.0001$ -OR=6.39 [4.31-9.48]) and LINGO1 rs13313467 ($p=0.040$ -OR=1.56[1.01-2.41]) polymorphisms increased the risk of ET. The stratification of patients according to clinical parameters suggested that the 3 LINGO1 polymorphisms favor the development of cognitive disorders. The binding analysis of these 3 variants allowed us to determine a single block with significant linkage disequilibrium. The haplotype study has shown that the GCC haplotype was more frequent in patients who developed cognitive disorders, considered as a risk factor of their occurrence ($p=0.002$) and the ACC haplotype seemed to play a protective role ($p=0.002$).

Conclusion: Our study showed associations between SLC1A2 and LINGO1 and the occurrence of ET and the latter with cognitive disorders. It is assumed that the neuronal degeneration would be influenced by the synergistic action of the different mutations on these genes. Indeed, mutations of SLC1A2 would cause excitotoxicity by EAAT2 deficiency involved in the process of apoptosis of Purkinje cells while LINGO1 amplifies this action and further inhibits the GABAergic effect of the remaining cells on neurons.

Disclosure: Nothing to disclose

EPR2103

Exposure-response efficacy model of amorphine sublingual film for the treatment of “OFF” episodes in patients with Parkinson’s disease

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Background and aims: A longitudinal exposure-response model characterized the relationship between apomorphine exposure and efficacy with apomorphine sublingual film (APL-130277; APL) using the MDS-UPDRS Part III score in patients with Parkinson’s disease (PD) and “OFF” episodes.

Methods: MDS-UPDRS data from 4 APL phase 2 and 3 studies and exposure data from a population pharmacokinetic model from 9 studies were analyzed using nonlinear mixed effects modeling methodology as implemented in NONMEM[®] (version 7.3). Final model simulations estimated apomorphine concentration with clinical response.

Results: Overall, 13,171 MDS-UPDRS measurements from 631 nonunique patients were analyzed. The model comprised placebo and nonlinear drug-effect components and predicted a maximal decrease of 20 points from baseline in MDS-UPDRS score, consistent with the phase 2 and 3 clinical data. A cutoff of at least -9.5 points in MDS-UPDRS score corresponded with a FULL “ON” response. Simulations indicated that average apomorphine concentrations of 3.18-3.39 ng/mL corresponded with these outcomes, consistent with the predicted apomorphine maximum concentration of 3.13ng/mL for a 10mg APL dose; however, apomorphine concentrations required for FULL “ON” vary due to interpatient variability. Increasing the APL dose from 10 to 35mg resulted in a faster time to FULL “ON” (18 to 12 minutes) and a greater MDS-UPDRS response with a longer duration of effect (2.4 to 3.9 hours).

Conclusion: The model demonstrated that as apomorphine exposure increased, time to FULL “ON” decreased, while duration and magnitude of response increased, thus supporting the recommended 10-35-mg dose range of APL and the importance of dose optimization.

Disclosure: Supported by funding from Sunovion Pharmaceuticals Inc.

Movement disorders 4

EPR2104

The organisational impact of upcoming treatments in Huntington's disease (HD) in Europe: Resource capacity gaps and access to care implications

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Background and aims: HD is a genetic, progressive neurodegenerative disease. While no disease-modifying-therapies (DMTs) are available, several approaches are being considered in clinical development. The investigational drugs most advanced in clinical development are administered intrathecally, requiring additional resources in HD clinics. The impact of upcoming DMTs for HD on healthcare systems and the implications of potential resource capacity gaps on access to care were investigated. **Methods:** 27 HD specialist centres from 6 European countries were involved in a prospective study assessing their capacity to perform intrathecal drug administrations. Data on current resource availability, utilisation, skills and equipment were collected through interviews with >140 healthcare professionals. Resources available in each HD centre were compared to the predicted amount of future resources that the estimated eligible patient population would require.

Results: Only 26% of participating HD teams currently have the required resources to perform intrathecal injections: a skilled “proceduralist” (e.g. trained neurologist, anesthesiologist, interventional radiologist), 1 or more nurses assisting in the procedure, and the appropriate space. When considering all resources available in the hospital (e.g. neurology department, infusion suites), only 22% of HD-specialist clinics are estimated to have enough capacity to serve the eligible population for intrathecally administered DMTs. When simulating the additional referral-in of patients from non-HD-specialised clinics, only 7% of HD clinics have enough capacity.

Conclusion: To ensure adequate care, capacity-constrained healthcare systems will need to plan adequately and ensure providers have sufficient training and resources to deliver new intrathecally administered DMTs, while coping with an increased demand for diagnosis, treatment and follow-up.

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EPR2105

Voice Handicap Index in patients with Parkinson's disease

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Background and aims: Voice and speech problems are common in Parkinson's disease (PD). In particular, impairments in phonation, articulation and prosody are the commonest characteristics. Voice Handicap Index (VHI) is a questionnaire for measuring the psychosocial handicapping effects of voice disorders.

The purpose of our study is to evaluate the self-perception of voice anomalies and psychosocial discomfort using the VHI in patients with PD.

Methods: 93 patients (74 men and 19 women) with PD participated in the study with mean age 62.8±7.9 years and disease duration of 8.2±4.8 years. Patients with dementia or laryngeal problems were excluded. Motor symptomatology was assessed by means of the Unified Parkinson's Disease Rating Scale-part III. Patients were classified in stages according to the Hoehn and Yahr scale. Patients were asked to fill the VHI, that is a 30 questions scale divided in 3 subscales (functional-physical-emotional). VHI total score from 0-30 indicates minimal amount of handicap, 31-60 moderate and 60-120 severe.

Results: All patients completed the questionnaire. Average VHI total score was 18.5. 5 patients (5.3%) had severe voice handicap (average score 72.2), 16 (17.2%) had moderate handicap (average score 47.2) and 72 (78.4%) had minimal voice handicap (average score 8.3). The functional subscale had the highest average score (7.1). Particularly, questions No1 and 2 (“difficult for people to hear and understand me”) had the highest scores.

Conclusion: Voice impairment is common in PD, but it usually produces mild handicap concerning especially difficulty “to be heard”. VHI is a useful tool to assess self-perception of voice impairment before starting precision voice treatment strategy.

Disclosure: Nothing to disclose

EPR2106

Withdrawn

EPR2107

Dopamine transporter, age and motor complications in Parkinson's disease: a clinical and SPECT study

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Background and aims: Previous molecular imaging studies comparing dopamine function in vivo between early-onset Parkinson's disease (EOPD) and late-onset PD (LOPD) patients have shown contradictory results, presumably due to the aging-related decline in nigrostriatal function.

1) To investigate baseline dopamine transporter availability in EOPD (<55y) and LOPD (>70y) patients, specific z-scores values of putamen and caudate [123I]FP-CIT uptake were calculated using the respective age-matched controls in order to correct for early presynaptic compensatory mechanisms and age-related dopamine neuron loss.

2) To examine the associations of such baseline SPECT measures with the emergence of late-disease motor complications

Methods: 105 de novo PD patients who underwent [123I]FP-CIT-SPECT at time of diagnosis were divided into 3 tertile groups according to the age at disease onset (EOPD, n=35; LOPD, n=40). Z-scores values were compared between the 2 groups and their predictive power for motor complications (during a mean follow-up of 7 years) were evaluated using Cox proportional hazard models.

Results: Despite a less severe motor phenotype, EOPD patients exhibited more reduced [123I]FP-CIT binding in the putamen and had a higher and earlier risk for developing motor complications than LOPD. Lower [123I]FP-CIT uptake in putamen and caudate increased the risk of motor complications.

Conclusion: Our findings suggest that a lower dopamine transporter binding in EOPD predicts the later development of motor complications but it is not related to the severity of motor symptoms. Understanding the mechanisms by striatal compensatory strategies contribute to the future disease progression will be crucial for the interpretation of [123I]FP-CIT-SPECT in PD.

Disclosure: Nothing to disclose

EPR2108

Parkin mRNA expression levels in Peripheral Blood Mononuclear Cells in Parkin-related Parkinson's disease

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Background and aims: Parkin is an ubiquitin E3 ligase that monoubiquitinates and polyubiquitinates proteins to regulate a variety of cellular processes. Mutations in parkin (PRKN gene) are the 2nd most prevalent known monogenic cause of Mendelian Parkinson's disease (PD). Loss of Parkin's E3 ligase activity is thought to play a pathogenic role in both inherited and sporadic PD. How mutations in Parkin in a heterozygous or homozygous or compound heterozygote state may affect its transcription in patient-derived biological material has not been systematically studied.

Methods: PRKN mRNA expression levels were measured with Real-time Polymerase Chain Reaction (RT-PCR) in Peripheral Blood Mononuclear Cells (PBMCs). PBMCs were derived from PRKN-mutation carrier PD patients (PRKN-PD; n=12) and healthy controls (n=21). 6 of the PRKN-PD subjects were heterozygous, 4 were compound heterozygous, and 2 were homozygous for pathological mutations.

Results: A statistically significant decrease in PRKN expression levels was present in heterozygous PRKN-PD (mean 592.9±SEM 316) compared to healthy controls (2131±371; p=0.014). Similarly, a statistically significant decrease was found between biallelic PRKN-PD (31.93±15) compared to healthy controls (p<0.001). In fact most biallelic patients have mRNA expression level values close to detection limit, with two samples being below that threshold.

Conclusion: Assessment of PRKN mRNA levels in PBMCs may be a useful way to screen for biallelic mutations in the PRKN gene. Suspicion for certain mutations in a heterozygous state may also be raised based on very low PRKN mRNA levels.

Disclosure: Nothing to disclose

EPR2109

Oral Venglustat in Parkinson's Disease Patients With a GBA Mutation: Part 1 Baseline Characteristics and Results and Part 2 Study Design of the MOVES-PD Trial

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Background and aims: Glucocerebrosidase gene (GBA) mutations increase the risk of rapidly progressing Parkinson's disease (PD). MOVES-PD (NCT02906020) is a phase 2, randomised, double-blind, placebo-controlled trial assessing efficacy, safety, and pharmacokinetics/pharmacodynamics of venglustat, a glucosylceramide synthase inhibitor, in PD patients with GBA mutations. Here, we report patient characteristics from MOVES-PD Part 1 and describe the Part 2 study design.

Methods: Part 1 was a placebo-controlled, dose-escalation study in patients from Japan and the rest of the world (ROW). GBA sequencing was done pre-enrolment. Montreal Cognitive Assessment (MoCA) and Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS-UPDRS; Parts II/III) scores were collected at baseline. Part 2 is an ongoing 52-week study (target enrolment: 216 patients, randomised 1:1 to placebo or venglustat using the dose selected in Part 1). Efficacy and safety will be assessed.

Results: Of Japanese (n=12) and ROW (n=17) patients enrolled in Part 1, 75.0% and 41.2% had severe GBA mutations (most commonly L444P), respectively, with the remaining carrying mild GBA mutations (eg, E326K, G193W, N370S, R496C). 50% (Japan) and 71% (ROW) of patients had baseline MoCA scores ≥ 26 , indicating no cognitive impairment. Mean baseline MDS-UPDRS Part II/III scores ranged from 43.3–49.0 (Japan) and 30.5–65.8 (ROW). Venglustat decreased glucosylceramide levels in cerebrospinal fluid and had a favourable safety profile in Part 1 patients.

Conclusion: Target engagement by venglustat occurred in patients with a range of GBA mutations and cognitive/motor functionality at baseline. Part 2 will assess venglustat safety and efficacy in a larger cohort of PD patients with GBA mutations.

Disclosure: STUDY SUPPORT: Sanofi.

EPR2110

A Gait Data-Driven Approach to Identify Different Clinical Subtypes of Parkinson's Disease: a Proposal for a New Classification

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Background and aims: Gait disorders are characteristics of Parkinson's Disease (PD). Spatio-temporal and kinematic parameters can be routinely quantified by gait analysis. Numerous attempts have been made to identify different clinical subtypes with poor agreement and temporal inconsistency. The principal aim of this study was to identify different clinical subtypes based on cluster analysis of gait parameters applied to a cohort of PD patients.

Methods: We retrospectively analyzed data of PD patients who underwent gait analysis. They all performed 10 trials walking at their self-selected speed along a 6-m walkway during their "on" pharmacological state if treated. A non-hierarchical cluster analysis using k-means method was performed using average values of forty selected spatio-temporal and kinematic parameters for the optimum solution based on the Calinski-Harabasz criterion.

Results: We enrolled 39 patients. 3 different subtypes were identified by cluster analysis: a 1st subtype (A) including the majority of enrolled subjects; a 2nd subtype (B) characterized by pronounced instability, with prominent reduced stance phase, cadence and step length as well as enlarged step width as compared to the other groups; a 3rd phenotype (C) with significant kinematic modifications consisting in pronounced hip flexion-extension and pelvic tilt while walking compared to A and B. No differences were detected in terms of age, disease duration and severity, treatment and cognitive profile among the 3 identified groups.

Conclusion: A gait data-driven approach may be adopted to practically categorize PD patients in different clinical subtypes. This could be helpful to personalize rehabilitative programs since earlier stages of disease.

Disclosure: Nothing to disclose

EPR2111

Opicapone in Clinical Practice in Parkinson's disease Patients with Motor Fluctuations: Findings from the OPTIPARK Study

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Background and aims: Opicapone (OPC) proved effective in treating end-of-dose motor fluctuations in Parkinson's Disease (PD) patients in 2 large multinational trials (BIPARK-I and II) [1,2]. This real-world study evaluated OPC 50mg in a heterogeneous population of PD patients treated in clinical practice.

Methods: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany and the UK under clinical practice conditions. PD patients with motor fluctuations received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change (CGIC) after 3 months. Secondary efficacy endpoints included Patient's GIC (PGIC) and Unified Parkinson's Disease Rating Scale (UPDRS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs).

Results: 495 patients took \geq OPC dose (Safety Set; Table 1) and 393 completed 3 months' treatment. Of 477 patients with post-baseline efficacy data (Full Analysis Set), 71.3% and 76.8% experienced very much/much/minimal improvement on CGIC and PGIC after 3 months, respectively (Table 2). There were significant improvements on UPDRS II and III scores (Table 3). TEAEs considered at least possibly related to OPC were reported for 45.1% of patients, the most frequently reported (\geq 5% patients) being dyskinesia (11.5%) and dry mouth (6.5%). 94.8% of TEAEs were of mild or moderate intensity. Serious TEAEs considered at least possibly related to OPC were reported for seven (1.4%) patients.

Table 1. Baseline characteristics (Safety Set)

Characteristic	N=495
Male gender, n (%)	315 (63.6)
Age, mean (SD) years	67.7 (9.0)
Disease duration, mean (SD) years	8.5 (5.0)
Duration of motor fluctuations, mean (SD) years	2.5 (3.2)

SD, standard deviation

Table 1

Table 2. CGIC and PGIC results after 3 months (Full Analysis Set)

Category	CGIC	PGIC
	N=477	N=393
Not assessed	3 (0.6)	0
Very much improved	31 (6.5)	30 (7.6)
Much improved	174 (36.5)	159 (40.5)
Minimally improved	135 (28.3)	113 (28.8)
No change	88 (18.4)	58 (14.8)
Minimally worse	28 (5.9)	25 (6.4)
Much worse	15 (3.1)	6 (1.5)
Very much worse	3 (0.6)	2 (0.5)

CGIC, Clinician's Global Impression of Change; LOCF, Last Observation Carried Forward; PGIC, Patient's Global Impression of Change; LOCF applied to CGIC

Table 2

Table 3. Changes from baseline in UPDRS scores (Full Analysis Set)

Scale	N	Mean (SD) change from baseline to 3 months	p-value
UPDRS II (activities of daily living) score at OFF stage	389	-3.0 (4.6)	<0.0001
UPDRS II (activities of daily living) score plus III (motor function) score at ON stage	393	-6.4 (10.4)	<0.0001
UPDRS III (motor function) score at ON stage	391	-4.6 (8.1)	<0.0001

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; p-values obtained through Student's t-test

Table 3

Conclusion: OPC 5-mg was effective and generally well tolerated in PD patients with motor fluctuations treated in clinical practice.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.
2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPR2112

Efficacy and safety of high doses of Safinamide in advanced Parkinson's disease patients in a real-world experience

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Background and aims: Standard doses of safinamide (50-100mg) have proved efficacious as an add-on treatment to levodopa in fluctuating Parkinson's disease (PD). Glutamatergic modulation with safinamide 100mg seems to increase with higher doses, whose safety has been proved in preclinical trials.

Methods: Retrospective analysis of electronic records of PD patients treated with safinamide >100mg (April 2019-December 2019).

Results: 15 PD fluctuating patients, with insufficient motor control with safinamide 100mg, 10 (66.6%) male, median age 74 (IQR 16), disease duration 13 years (IQR 10), Hoehn-and-Yahr stage 3 (IQR 2), who were switched to 150mg (4) or 200 (11) mg safinamide, and followed a median of 3 months (IQR 5) were analysed. 4 patients were also treated with DBS (26.7%). Mean UPDRS IV items of dyskinesia duration (2.5±1.3 vs. 2.2±1.1), functional impact (1.6±1.2 vs. 1.1±1.1), pain (0.6±1 vs. 0.3±0.7) and off duration (2±0.8 vs. 1.3±0.5) did not change significantly. However, 9 patients (60%) had a Clinical Global Impression of improvement (CGI 1-3): in 8 cases regarding off duration, in 3 cases regarding dyskinesia duration, in 4 in dyskinesia functional impact and in 2 in pain due to dyskinesia. In 1 patient levodopa doses were decreased. 3 patients (20%) had mild-moderate adverse events leading to suspension of the drug in 2 (both due to dyskinesia worsening). 1 patient discontinued safinamide 200mg due to levodopa/carbidopa intestinal infusion.

Conclusion: In our experience with advanced PD patients, safinamide >100mg was overall well tolerated, and had a clinical benefit in a subset of patients.

Disclosure: Nothing to disclose

EPR2113

Longitudinal changes of retinal morphology in Wilson's disease assessed by optical coherence tomography: Results from 47 patients over 5 years

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Background and aims: To longitudinally investigate the changes in retinal morphology of Wilson's disease (WD) patients compared to healthy controls (HC) analyzing the influence of laboratory findings, disease severity, and therapy.

Methods: Spectral-domain OCT was used to assess the retinal morphology of 47 patients with WD and 44 HC measuring the peripapillary retinal nerve fiber layer (pRNFL) thickness as well as the thickness of all retinal layers in macular volume scans. The longitudinal data were gathered over 5 years, with at least 2 assessments for each individual. Generalized Estimating Equation (GEE) and mixed effects linear models were used to study retinal layer changes over time within and between controls and patients.

Results: At baseline, WD patients presented about 2.8 and 4.2µm³ lower values compared to controls for mRNFL and GCIPL, respectively (p<0.05, corrected for age). The longitudinal analysis of WD patients revealed an annual thickness loss of -0.07µm, -0.1 µm, p<0.05 in RNFL and GCIPL layer, respectively. The expected discrepancy between control and WD patients over time was associated with almost 2.4µm more pronounced thinning of RNFL and GCIPL layers in WD compared to HC (p<0.05). The analysis of clinical findings further revealed a significant association only for the non-motor WD symptoms, indicating 0.7µm RNFL thickness reduction per non-motor symptoms increment.

Conclusion: Our data corroborate previous findings of reduced RNFL and GCIPL values in WD patients and, for the first time, demonstrate it in a longitudinal analysis. A more detailed investigation of the longitudinal changes over 5 years will be presented.

Disclosure: Nothing to disclose

EPR2114

Premotor compensatory mechanisms in Parkinson's disease with LRRK2-R1441H mutation

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Background and aims: Increased dopamine metabolism has been suggested as a compensatory mechanism in the premotor phase of PD. Little is known about the delay between compensatory mechanisms and motor symptoms onset. Here, we report the longitudinal investigation of PET scan brain imaging in a family with LRRK2-R1441H mutation including one participant who converted nine years after inclusion.

Methods: 4 family members were included: 2 patients with PD (aged 67 and 59, PD duration 11 and 8 years) carrying the mutation (LRRK2+PD+), 1 unaffected sibling carrying the mutation (age 61, LRRK2+PD-) and 1 unaffected non-carrier (age 61, LRRK2-PD-). Subjects underwent clinical evaluation and PET-scan for dopamine transporter binding (11C-PE2I) and L-DOPA uptake (18F-DOPA) repeatedly at two years interval.

Results: At baseline, LRRK2+PD+ patients had -77% and -82% decrease of 11C-PE2I binding, and -81% and -70% decrease of 18F-DOPA uptake in the most affected putamen relative to normal data. The LRRK2+PD- participant had -57% decrease of 11C-PE2I binding in the left putamen (right binding in the normal range), whereas 18F-DOPA uptake was not altered (-21%) but decreased progressively over time, reaching -51% at the time of conversion, 9 years after inclusion. PET imaging parameters of the LRRK2-PD-subject were typical normal values and remained stable during follow-up.

Conclusion: This observation confirms the early upregulation of L-DOPA metabolism compensating dopaminergic nerve terminal loss up to 9 years before conversion to clinical PD. This is the 1st report associating evolution of distinct presynaptic markers and clinical evaluation over 9 years before PD diagnosis.

Disclosure: Nothing to disclose

EPR2115

Depression is associated with impulse-compulsive disorders in Parkinson's disease. Results of the COPPADIS Study Cohort.

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Background and aims: Depression and impulse control disorders (ICDs) are both common in Parkinson's disease (PD) patients, and their coexistence is frequent. Our objective was to determine the relationship between depression and impulsive-compulsive disorders in a large cohort of PD patients.

Methods: PD patients recruited from 35 centers of Spain from the COPPADIS cohort from January/2016, to November/2017, were included in the study. The QUIP-RS was used for screening ICDs (cutoff points: gambling ≥ 6 , buying ≥ 8 , sex ≥ 8 , eating ≥ 7) and compulsive behaviors (CBs) (cutoff points: hobbyism-punding ≥ 7). Mood was assessed with the BDI-II and major, minor and subthreshold depression were defined.

Results: Depression was more frequent in PD patients with impulse-compulsive disorder than in those without: 67% (71/106) vs 47.9% (246/514); $p < 0.0001$. Major depression

was more frequent in this group as well: 22.6% (24/106) vs 14.8% (76/514); $p = 0.035$. Depression was also more frequent in both patients with ICDs (64.5% [49/76] vs 49.3% [268/544]; $p = 0.009$) and CBs (62.7% [35/59] vs 49.6% [276/556]; $p = 0.038$). Considering types of impulse-compulsive disorders individually, depression was more frequent in patients with gambling (90% [9/10] vs 50.5% [306/606]; $p = 0.012$), eating (66.7% [28/42] vs 50% [289/578]; $p = 0.026$), and hobbyism-punding (70.5% [31/44] vs 49.4% [282/571]; $p = 0.005$). To suffer from impulse-compulsive disorder was associated with depression (OR=2.109; 95%CI 1.261-3.526; $p = 0.004$) after adjustment to age, gender, disease duration, equivalent daily levodopa dose, Hoehn&Yahr stage and non-motor symptoms burden.

Conclusion: Depression is associated with impulse-compulsive disorders in PD. Specifically, with gambling, eating and hobbyism-punding.

Disclosure: Nothing to disclose

MS and related disorders 4

EPR2116

Fingolimod improves the functional recovery of the optic pathway in focal demyelination model of rat optic chiasm

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Background and aims: Fingolimod (FTY720) possesses beneficial effects on remyelination in the central nervous system (CNS). In the present study, the effects of FTY720 and sodium valproate (VPA) as histone deacetylase inhibitor (HDAC) on the conductivity of visual signals, extent of demyelination area, and expression levels of HDAC1 and S1PR1 have been evaluated in the optic chiasm of lysolecithin (LPC)-induced demyelination model.

Methods: In order to induce demyelination model, LPC (1%, 2 μ L) was injected into the rat optic chiasm. Latency of visual waves was measured by visual evoked potential (VEP) recording. The extent of demyelination area was assessed using Fluoromyelin staining. Gene expression analysis was performed to evaluate the expression levels of HDAC1, S1PR1, Olig2, and MBP in the optic chiasm.

Results: Analysis of electrophysiological data showed that FTY720 improved the functional recovery of the visual pathway. FTY720 enhanced myelin repair and up-regulated the expression levels of Olig2 and MBP. Additionally, the expression levels of HDAC1 and S1PR1 were significantly reduced in animals treated with FTY720. In contrast to FTY720 treated animals, administration of VPA could not significantly improve the functional recovery of optic pathway following LPC injection.

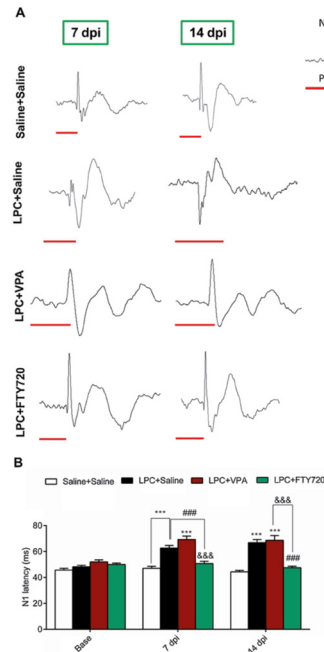


Fig. 1. FTY720 improved the functional recovery of the optic pathway in LPC-induced demyelination model. A) Sample traces of VEP waves. Scale bar=10 μ V, 50ms. B) Quantitative analysis of N1 latency. n=6.

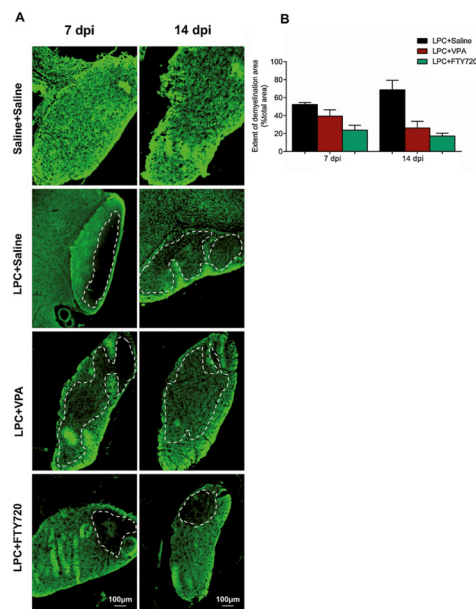


Fig. 2. FTY720 reduced demyelination level in the optic chiasm. A) Fluoromyelin staining. Scale bar: 100 μ m. B) Quantitative analysis of fluoromyelin staining results. Dashed line indicated the extent of demyelination area. n=3.

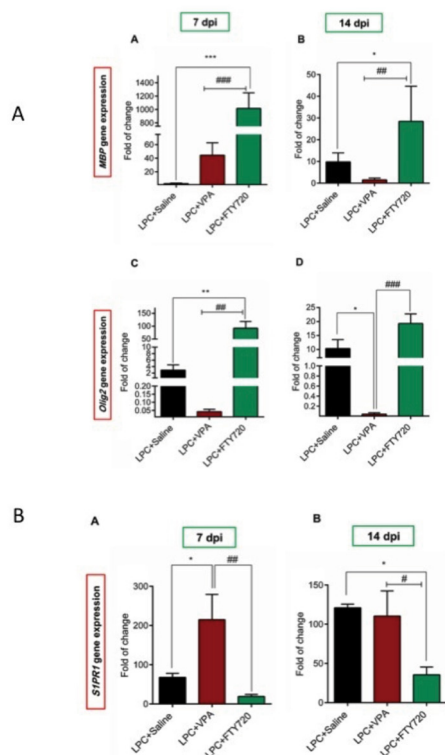


Fig. 3. A) The effect of FTY720 on expression levels of MBP and Olig2 on days 7 and 14 post lesion. B) The effect of FTY720 application on expression levels of S1PR1 on days 7 and 14 post insult. n=6.

Conclusion: Cumulatively, the results of the present study demonstrate that FTY720 application improves the functional recovery of the optic pathway by reducing demyelination levels and down-regulating of S1PR1 and HDAC1.

Disclosure: Nothing to disclose

EPR2117

Updated Safety of Cladribine Tablets in the Treatment of Patients with Multiple Sclerosis: Integrated Safety Analysis and Post-Approval Data

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Background and aims: Integrated analysis of pooled long-term safety data allowed comprehensive characterisation of the cladribine tablets (CT) 10mg (3.5mg/kg cumulative dose over 2 years [CT3.5]) safety profile in patients with relapsing multiple sclerosis (RMS). By integrating final data from the PREMIERE registry, and reporting post-approval safety data from worldwide sources, this analysis provides an update to the serious treatment emergent adverse event (TEAE) profile of CT3.5.

Methods: The monotherapy oral cohort (CT3.5, N=923, patient-years [PY]=3936.69; placebo [PBO], N=641, PY=2421.47) comprised patients from the CLARITY, CLARITY Extension and ORACLE-MS trials, and PREMIERE. Adjusted incidences per 100PY were calculated for AEs, cumulative to the end of PREMIERE (October 2018). Serious and non-serious AEs from post-approval sources are summarised.

Results: Patient characteristics were balanced between treatment groups (mean age [37.8 years, CT3.5; 37.2 years, PBO], proportion of females [66.3%, CT3.5; 66.1%, PBO] and proportion of patients with prior disease modifying drug experience [19.9%, CT3.5; 20.4%, PBO]). Incidences per 100PY for ≥ 1 serious TEAE and serious TEAEs of special interest for CT3.5 and placebo in the monotherapy oral cohort from the clinical program are shown in Table 1. Post-approval, the Periodic Benefit-Risk Evaluation Report listed 1622 AEs; 275 were serious; none represented a new safety signal.

Table 1. Serious TEAEs of special interest in the monotherapy oral cohort from the clinical program						
Incidences per 100PY System organ class Preferred term	Cladribine tablets 3.5 mg/kg (n=923)			Placebo (n=641)		
	n	Total PY	Adj-AE/100 PY	n	Total PY	Adj-AE/100 PY
≥1 serious TEAE	133	3498.1	3.80	68	2226.2	3.05
Blood and lymphatic system disorders	10	3912.7	0.26	0	2421.5	0
Lymphopenia	4	3925.4	0.10	0	2421.5	0
Infections and infestations	23	3857.2	0.60	10	2395.8	0.42
Herpeszoster	2	3929.7	0.05	0	2421.5	0
Pneumonia	6	3907.4	0.15	3	2415.2	0.12
Pulmonary tuberculosis	1	3933.6	0.03	0	2421.5	0
Tuberculosis	1	3936.7	0.03	0	2421.5	0
UTI	4	3923.4	0.10	1	2419.9	0.04
Neoplasms benign, malignant and unspecified	26	3865.7	0.67	8	2398.7	0.33
Malignant tumours	10	3918.9	0.26	3	2414.8	0.12
Uterine leiomyoma	6	3905.7	0.15	2	2413.1	0.08

Serious was defined as resultant in death, life-threatening, required inpatient hospitalisation, congenital anomaly or birth defect, or was otherwise considered as medically important.
Adj-AE per 100PY, adjusted adverse events incidences per 100 patient-years; PY, patient-years; TEAE, treatment-emergent adverse event; UTI, urinary tract infection.

Table 1

Conclusion: No new major safety findings were identified in this finalised integrated dataset comprising final data from PREMIERE. This profile is consistent with previously published integrated safety analyses. No new safety signals were identified in the real-world post-approval data of CT.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR2118

Siponimod Slows Physical Disability Progression and Decline in Cognitive Processing Speed in SPMS Patients with Active Disease: A Post Hoc Analysis of the EXPAND Study

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Background and aims: Siponimod significantly reduced confirmed disability progression (CDP) and cognitive processing speed (CPS) decline in the broad secondary progressive multiple sclerosis (SPMS) population (EDSS 3.0–6.5) in the EXPAND study. Siponimod received a positive CHMP opinion for the treatment of adult SPMS patients with active disease. Here, we assess the efficacy of siponimod on CDP and CPS in SPMS patients with active disease from the EXPAND study.

Methods: Analysis included 779 patients with active disease (presence of relapses in the 2 years before screening and/or ≥1 gadolinium-enhancing T1 lesion at baseline); 516 received siponimod 2mg and 263 received placebo in the EXPAND core part. Outcomes: time-to-3- and 6-month (3m/6m) CDP in all active disease patients and 6mCDP in further subgroups of patients with active disease based on prior treatment (any disease-modifying therapy [DMT], interferon at anytime and recent interferon use); and clinically meaningful (≥4-point change on Symbol Digit Modalities Test) sustained improvement/worsening in CPS in all active disease patients.

Results: Siponimod significantly reduced the risk of 3mCDP by 31% (p=0.0094) and 6mCDP by 37% (p=0.0040) versus placebo in all active patients and consistently in subgroups of patients switching from any DMT, interferon at anytime or recent interferon use (p<0.05 for all). Siponimod improved the chance of sustained improvement in CPS by 51% (p=0.0070) and reduced the risk of sustained worsening by 28% (p=0.0166) versus placebo (Table).

Efficacy parameter	Siponimod 2 mg N=516	Placebo N=263	HR (95% CI)	p-value
Disability progression				
3mCDP ^a				
SPMS patients with active disease	24.9% (128/515)	34.6% (91/263)	0.69 (0.53; 0.91)	0.0094
6mCDP ^a				
SPMS patients with active disease	19.0% (98/515)	28.1% (74/263)	0.63 (0.47; 0.86)	0.0040
Subgroups of patients with active disease				
Any DMT	20.3% (80/394)	29.1% (59/203)	0.67 (0.48; 0.94)	0.0203
Interferon at any time	21.2% (65/306)	29.9% (48/154)	0.68 (0.47; 1.00)	0.0496
Recent interferon	17.6% (36/205)	31.7% (33/104)	0.52 (0.32; 0.83)	0.0063
Cognitive processing speed				
SPMS patients with active disease				
Sustained ^b worsening in CPS ^c	27.3% (140/512)	38.2% (100/262)	0.72 (0.56; 0.94)	0.0168
Sustained ^b improvement in CPS ^c	34.2% (175/ 512)	22.9% (80/ 262)	1.51 (1.12; 2.04)	0.0070

^aBased on EDSS score
^bA change that continued until the end of the core part of the study, or occurred at the last assessment
^cMeasured by a ≥ 4 -point change on Symbol Digit Modalities Test
Data are presented as % (n/N); n is number of patients with events; N is number of patients included in the analysis
Number of patients in the subgroups: 597 in any DMT group; 460 in interferon at any time group; 309 in recent interferon group
CDP, confirmed disease progression; CI, confidence interval; CPS, cognitive processing speed; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HR, hazard ratio; m, month; SPMS, secondary progressive multiple sclerosis

Table. Efficacy of siponimod on disability progression and cognitive processing speed in patients with active disease

Conclusion: In patients with active SPMS, siponimod significantly delayed disability progression in the entire group, and in subgroups defined by prior treatment, and showed significant benefits on CPS.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation.

EPR2119

Perceptual and visuospatial functions in multiple sclerosis

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Background and aims: Perceptual and visuospatial (PVS) functions are affected in a significant number of patients with multiple sclerosis (MS), they have been less evaluated than other functions. The interpretation of the findings is often difficult due to the frequent affectation of the afferent visual pathway, which could limit the validity of the results of the studies. The involvement of PVS functions has been associated with the progressive forms of MS or has even taken as a marker of diffuse cerebral involvement of progression. Objective was to describe PVS and relate them with clinical variables

Methods: 185 patients with MS were included; mean age 42±10 years, 130 women, mean disease duration 10±7 years, 172 Relapsing-Remitting forms, 8 2ndary-progressive and 5 Primary Progressive. Expanded Disability Status Scale (EDSS) score 2.0 (median). All participants were evaluated with the Hopper Visual Organization Test (HVOT) and the Judgement Orientation Line Test (JOLT).

Results: 9.7% of patients had impaired perceptual functions (HVOT) and 16.75% had impaired visuospatial functions (JOLT). PVS functions perform was negatively correlated with disease duration. Visuospatial functions were not related to EDSS but patients with high level of disability performed significantly worse than patients with low and without disability. No significant differences were found in JOLT associated with the evolutionary type of the disease but patients with progressive forms performed significantly worse in HVOT.

Conclusion: The impairment of PVS functions in MS is significantly higher in subjects with progressive forms and moderate/high neurological disability. Disease duration is an important factor to determinate the affectation of these functions.

Disclosure: Nothing to disclose

EPR2120

Multimodal Evoked Potentials in Primary Progressive Multiple Sclerosis: Identification of Patients at Risk for Disease Progression

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Background and aims: To enhance power, clinical trials in primary progressive multiple sclerosis (PPMS) need patients at risk for progression. Quantitatively scored multimodal evoked potentials (mmEP) measure altered signal conduction and predict clinical disability in PPMS (Schlaeger et al. 2014).

To evaluate an EP-score cut-off as predictor of disease progression in PPMS patients from the Swiss Multiple Sclerosis Cohort.

Methods: 35 PPMS patients (median age: 51.6 years; EDSS: 4.0 [range 2.0-7.0]) had EDSS over 2 years and baseline mmEP (upper and lower limb sensory and motor EP). A modified quantitative EP-score (mqEPS; height-corrected N20-, P40- and cortico-motor-latencies) was used in logistic regression with 2-year EDSS-progression as outcome (increase of EDSS by 1.0 if EDSS <5.5, by 0.5 otherwise).

Results: Progression occurred in 12 subjects (34%). Progressors were younger ($p=0.034$) and had higher mqEPS ($p=0.006$). Significant predictors were age (OR=0.9; CI 95%: 0.82-0.99) and mqEPS (OR=1.28; CI 95%: 1.04-1.57); in a multivariate model, only mqEPS remained significant. Excluding 2 non-progressing subjects with outlying EDSS (6.5 and 7.0), mqEPS predicted progression with an OR=1.81 (CI 95%: 1.12-3.08; $p=0.016$). The cut-off mqEPS=4.0 showed a good sensitivity (75%) and high specificity (90%) translating into an event rate of 64%.

Conclusion: High mqEPS predicts disease progression in PPMS in particular if EDSS <6.5. Event rates may be substantially increased if patients are selected by mmEP. The mqEPS cut-off needs further validation in an independent sample.

Disclosure: the EP-SMSC study has been financially supported by the Swiss Multiple Sclerosis Society

EPR2121

Malignancy Rates With Long-term Use of Ozanimod in Relapsing Multiple Sclerosis Trials

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Background and aims: By modulating sphingosine 1-phosphate receptor subtype 1, ozanimod reduces circulating lymphocytes, potentially increasing susceptibility to malignancy. Herein we evaluate malignancy rates with long-term exposure to ozanimod in clinical trial participants with RMS.

Methods: SUNBEAM (NCT02294058; ≥ 12 months) and RADIANCE (NCT02047734; 24 months) were multicenter, randomised, double-blind, phase 3 trials comparing oral ozanimod HCl 1 and 0.5mg/day with intramuscular interferon β -1a 30 μ g/week in adults (18–55 years) with RMS. Participants who completed any ozanimod RMS clinical trial were eligible to enrol in an open-label extension trial (DAYBREAK; NCT02576717) of ozanimod HCl 1mg/d. Malignancy rates with ozanimod are compared descriptively in controlled phase 3 trials (SUNBEAM and RADIANCE) and in participants who received ozanimod in any RMS trial.

Results: In pooled controlled phase 3 studies, 882 participants received ozanimod HCl 1mg and 892 received 0.5mg (mean [SD] combined exposure, 17.9 [5.97] months; 2686.8 person years [PY] on study). The incidence of treatment-emergent malignancy (4 nonmelanoma skin cancers, 4 noncutaneous malignancies) was 0.5% and incidence rate was 298.2/100,000 PY (Table). With longer term exposure to ozanimod in any RMS trial ($n=2787$; data cutoff 31/1/2019; mean [SD] exposure, 37.1 [14.7] months; 8688.3 PY on study), overall incidence of malignancy (11 nonmelanoma and 1 melanoma skin cancer, 13 noncutaneous malignancies) was 0.9% and incidence rate was 289.3/100,000 PY. No lymphomas were reported.

Table. Treatment-Emergent Malignancies by Preferred Term in Participants With RMS Who Were Exposed to Any Dose of Ozanimod HCl (0.5 and/or 1 mg)

	Phase 3 Population (N=1774)		Overall RMS Population (N=2787)	
	Incidence, n (%)	Study Duration-Adjusted IR/100,000 PY ^a	Incidence, n (%)	Study Duration-Adjusted IR/100,000 PY ^a
Treatment-emergent malignancies	8 (0.5)	268.2	25 (0.9)	288.3
Cutaneous	4 (0.2)		12 (0.4)	
Basal cell carcinoma	3 (0.2)	111.8	9 (0.3)	104.0
Keratoacanthoma	1 (0.06)	37.2	1 (0.04)	11.5
Squamous cell carcinoma	0	0	1 (0.04)	11.5
Malignant melanoma	0	0	1 (0.04)	11.5
Noncutaneous	4 (0.2)		13 (0.5)	
Breast cancer ^b	Overall: 3 (0.2) Females only: 3/1174 (0.3)	Overall: 111.7 Females only: 168.7	Overall: 5 (0.2) Females only: 5/1888 (0.3)	Overall: 67.7 Females only: 88.4
Cervix carcinoma	0	0	1 (0.04)	11.5
Testicular seminoma (pure) stage I ^c	1 (0.06)	37.2	1 (0.04)	11.5
Bile duct cancer	0	0	1 (0.04)	11.5
Clear cell renal carcinoma	0	0	1 (0.04)	11.5
Glioblastoma	0	0	1 (0.04)	11.5
Malignant neoplasm	0	0	1 (0.04)	11.5
Pancreatic carcinoma metastatic	0	0	1 (0.04)	11.5
Papillary thyroid cancer	0	0	1 (0.04)	11.5
Treatment-emergent malignancies, excluding NMSC	4 (0.2)	148.9	14 (0.5)	161.7

^aIR/100,000 PY, incidence rate per 100,000 person years, calculated as number of persons having the malignancy of interest/person years × 100,000, where person years = (date first malignancy of interest - date of first dose of study drug + 1)/365.25; for subjects not having the malignancy of interest, the time on study is the study duration (last date on study - first dose date of study drug + 1)/365.25.
^bBreast cancer includes cases using preferred terms of invasive breast cancer, breast cancer, and breast neoplasm.
^cDiagnosed on study day 51.
NMSC, nonmelanoma skin cancer; RMS, relapsing multiple sclerosis.

Table

Conclusion: In RMS participants with longer ozanimod exposure, rates of malignancy were similar to those with ≤24 months' exposure in controlled phase 3 trials and consistent with rates in MS patients and the age-matched general population.

Disclosure: The DAYBREAK study and all parent studies were sponsored by Celgene, a wholly-owned subsidiary of Bristol-Myers Squibb.

EPR2122

Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients With Relapsing and Primary Progressive Multiple Sclerosis

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Background and aims: Ongoing safety reporting is crucial to understanding the long-term benefit-risk profile of ocrelizumab in multiple sclerosis (MS). Safety/efficacy of ocrelizumab have been characterised in Phase II (NCT00676715) and III (NCT01247324/NCT01412333/NCT01194570) trials in relapsing-remitting MS, relapsing MS (RMS) and primary progressive MS (PPMS). We report ongoing safety evaluations from ocrelizumab clinical trials and open-label extension periods up to September 2019 and selected post-marketing data.

Methods: Safety outcomes are reported for the ocrelizumab all-exposure population in Phase II/III and ongoing Phase IIIb trials. The number of post-marketing ocrelizumab-treated patients is based on estimated number of vials sold and US claims data. To account for different exposure lengths, rates per 100 patient years (PY) are presented.

Results: In clinical trials, 4,611 patients with MS received ocrelizumab (14,329 PY of exposure) as of January 2019. Reported rates per 100 PY (95% confidence interval) were: adverse events (AEs), 252 (249–254); serious AEs, 7.33 (6.89–7.79); infections, 76.7 (75.3–78.2); serious infections, 1.99 (1.77–2.23); malignancies, 0.46 (0.35–0.58); and AEs leading to discontinuation, 1.08 (0.92–1.27). As of October 2019, over 125,000 patients with MS have initiated ocrelizumab globally in the post-marketing setting. Updated ocrelizumab all-exposure population data using a September 2019 cut-off and selected post-marketing data will be presented.

Conclusion: Reported rates of events remain generally consistent with the controlled treatment period in RMS/PPMS populations. Rates of serious infections and malignancies remain within the range reported for patients with MS in real-world registries. Regular reporting of long-term safety data will continue.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPR2123

Therapeutic effects of Leukadherin1 on mobility defects and demyelinated areas in an animal model of multiple sclerosis

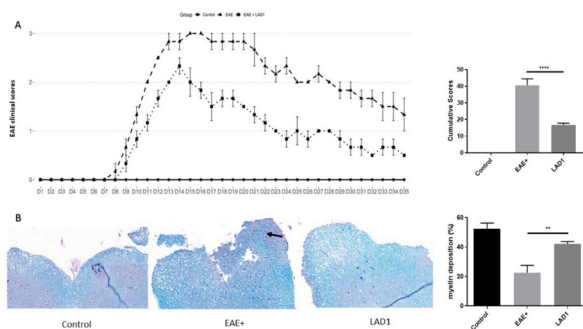
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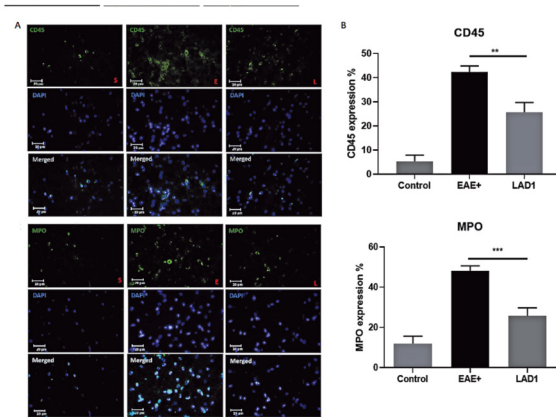
Background and aims: Peripheral immunity cells participate in the development and exacerbation of multiple sclerosis (MS). These cells infiltrate MS lesions and produce extensive amounts of inflammatory cytokines and reactive oxygen species. Myeloperoxidase (MPO), the main mediator of oxidative stress in neutrophils, is reported to be elevated in MS lesions. Leukadherin1, a specific CD11b/CD18 agonist, has been shown to inhibit transmigration of inflammatory cells to tissue injury sites. Therefore, we evaluated effects of leukadherin1 on an animal model of MS.

Methods: C57Bl/6 mice were immunized with 100ug MOG 35-55 emulsion to induce experimental autoimmune encephalitis (EAE). On the immunization day and 2 days later, animals were subjected to intraperitoneal injection of pertussis toxin. 3 days after injection, all animals in the treated group received daily 1mg/kg leukadherin1 intraperitoneally. Clinical signs of EAE were observed daily from day 7 onwards. The specific lumbar spinal tissues were isolated on day 35 in order to observe infiltrations of CD45+ leukocytes and MPO+ neutrophils. Furthermore, the extent of demyelinated areas was assessed as a hallmark of disease severity.

Results: Leukadherin1 exhibited promising improvements in EAE clinical scores and reduced demyelinated areas in comparison with the untreated EAE group ($p=0.0018$). Moreover, spinal tissues of treated animals showed reduced number of infiltrated CD45+ leukocytes and MPO+ neutrophils ($p=0.0015$ and $p=0.0005$, respectively).



(a) Leukadherin1 resulted in significant decrease in EAE scores starting from day 10 ($p=0.0122$) until the end of day 35 ($p<0.0001$). Cumulative scores were also reduced ($p<0.0001$). (b) The micrographs present stained tissues and demyelinated area with the arrow. Quantified demyelinated area showed significant difference between groups ($p<0.0001$).



(a) Spinal sections were double immunolabeled for DAPI and cell type-specific markers (green) MPO (neutrophils), CD45 (leukocytes). (b) Quantitative analysis CD45+ and MPO+ cells revealed that leukadherin1 decreased the number of infiltrative leukocytes and microglia ($p<0.01$ & $p<0.001$, One-way ANOVA, post-hoc).

Conclusion: Our study showed beneficial effects of leukadherin1 on clinical and pathological features of a multiple sclerosis model in mice. We suggest leukadherin1 as a potential therapeutic agent to be evaluated in further clinical trials.

Disclosure: Nothing to disclose

EPR2124

Efficacy of Diroximel Fumarate in Relapsing-Remitting MS Patients Who Are Newly Diagnosed or Previously Treated With Interferons or Glatiramer Acetate

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Background and aims: Diroximel fumarate (DRF) is a novel oral fumarate recently approved in the United States for relapsing forms of multiple sclerosis (MS). EVOLVE-MS-1 (NCT02634307) is an ongoing, open-label, Phase 3 study of long-term safety, tolerability, and treatment effect of DRF in adults with relapsing-remitting MS (RRMS).

Methods: 2-year efficacy outcomes as of 30 November 2018 were assessed in subgroups of patients from EVOLVE-MS-1 who were newly diagnosed with RRMS (≤1-year since diagnosis and treatment-naïve; n=109) or previously treated with interferon-β or glatiramer acetate (IFN/GA) as their most recent disease-modifying therapy (n=327; Table 1).

Results: Median (range) DRF exposures were 96 (2-99) weeks for newly diagnosed and 69 (0-99) weeks for IFN/GA switch patients. Adjusted annualized relapse rate was 0.13 (95% CI 0.07-0.23) in newly diagnosed and 0.17 (95% CI 0.12-0.23) in IFN/GA switch patients, representing an 88.6% (95% CI 79.8-93.6; p<0.0001) and 73.2% (95% CI 63.1-80.6; p<0.0001) reduction, respectively, from the 12 months before study entry (Figure 1). Mean (SD) Expanded Disability Status Scale scores remained stable at Wk96 versus baseline (newly diagnosed: 2.00 [1.06, n=60] vs 2.02 [1.13, n=108]; IFN/GA switch: 2.55 [1.55, n=100] vs 2.64 [1.51, n=310]). More patients were Gd+ lesion-free at Wk96 versus baseline (newly diagnosed: 86.9% vs 54.1% [n=61]; IFN/GA switch: 93.9% vs 78.6% [n=98; Figure 2]). Patient-reported outcomes remained relatively stable or improved.

Conclusion: DRF demonstrated improvements from baseline on clinical and radiological endpoints and may be an effective treatment option in newly diagnosed and IFN/GA switch patients.

Support: Biogen/Alkermes

Table 1. Baseline Demographics and Disease Characteristics in Newly Diagnosed and IFN/GA Switch Patients from EVOLVE-MS-1

	Newly Diagnosed ^a (n = 109)	IFN/GA Switch ^b (n = 327)	Overall (n = 888)
Mean (SD) age, y	36.0 (10.8)	43.6 (10.4)	42.4 (10.8)
Female, n (%)	78 (72)	242 (74)	637 (72)
US region, n (%)	31 (28)	184 (56)	395 (45)
Prior DMT, n (%)	0	327 (100)	674 (75.9)
Median (range) duration of prior GA/IFN treatment ^c , y		1.8 (0–20.9)	N/A
Mean (SD) time since diagnosis, y	0.4 (0.5)	8.5 (6.9)	7.5 (7.3) ^d
Mean (SD) no. relapses previous year	1.2 (0.7)	0.6 (0.8)	0.7 (0.8)
Mean (SD) EDSS score	2.0 (1.1)	2.6 (1.5)	2.7 (1.5)
Mean (SD) no. Gd+ lesions	1.9 (5.1)	1.0 (3.2) ^e	1.2 (3.7) ^f
Patients with Gd+ lesions, n (%)	48 (44)	79 (24)	268 (30)

DMT = disease modifying therapy; EDSS = Expanded Disability Status Scale; GA = glatiramer acetate; Gd+ = gadolinium-enhancing; IFN = interferon; N/A = data not available

^aNewly diagnosed patients were diagnosed within one year of screening and without any prior DMT (immunomodulator, immunosuppressant, or intravenous immunoglobulin use [investigational or approved]; steroids were not included).

^bIFN/GA switch patients received IFN/GA as their most recent DMT, with no restrictions on the lengths of the gap between the prior medication end date and the study medication first dose date.

^cn = 160; if there was more than one treated IFN/GA period, only the most recent treatment period was summarized.

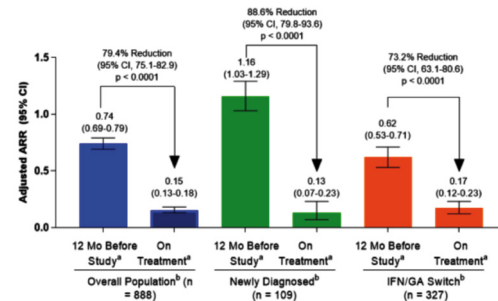
^dn = 887

^en = 325

^fn = 885

Table 1. Baseline Demographics and Disease Characteristics in Newly Diagnosed and IFN/GA Switch Patients from EVOLVE-MS-1

Figure 1. Newly Diagnosed and IFN/GA Switch Patients in EVOLVE-MS-1 Had a Reduction in ARR on DRF Treatment Compared With the 12 Months Before Study Entry



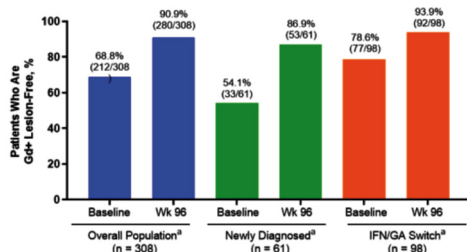
ARR = annualized relapse rate; DRF = diroximel fumarate; GA = glatiramer acetate; IFN = interferon

^aAdjusted ARR comparison between patient-reported relapses in the 12 months before study entry and protocol-defined relapses occurring at any time on treatment was based on a Poisson regression model.

^bRelapse was evaluated in all patients who received ≥ 1 dose of DRF (overall population) and in subgroups of patients who were newly diagnosed with multiple sclerosis or who received IFN/GA as their most recent disease-modifying therapy.

Figure 1. Newly Diagnosed and IFN/GA Switch Patients in EVOLVE-MS-1 Had a Reduction in ARR on DRF Treatment Compared With the 12 Months Before Study Entry

Figure 2. More Newly Diagnosed and IFN/GA Switch Patients Were Gd+ Lesion-Free at Week 96 Compared With Baseline



DRF = diroximel fumarate; Gd+ = gadolinium-enhancing; GA = glatiramer acetate; IFN = interferon

^aRadiological outcomes were assessed in patients who received 1 dose of DRF and completed ≥ 1 post-baseline efficacy assessment (overall population) and in subgroups of newly diagnosed and IFN/GA switch patients. Baseline included those with Week 48 and Week 96 data (n = 308 for the overall population, n = 61 for newly diagnosed patients, and n = 98 for IFN/GA switch patients).

Figure 2. More Newly Diagnosed and IFN/GA Switch Patients Were Gd+ Lesion-Free at Week 96 Compared With Baseline

Disclosure: This study was funded by Biogen (Cambridge, MA, USA) and Alkermes (Waltham, MA, USA); medical writing support was provided by Excel Scientific Solutions (Fairfield, CT, USA) and funded by Biogen.

EPR2125

The effect of self-assessed fatigue and cognitive impairment on health care consumption, work capacity and utility: A study in 5475 patients in Germany.

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Objectives: To investigate the effect of self-assessed fatigue and cognitive impairment on direct health care consumption, work participation and utility in People with multiple sclerosis (MS) in Germany.

Methods: The study included 5,475 German participants in a large European burden of illness study in 16 countries that investigated - in addition to resource consumption - fatigue, cognitive impairment and the effect of MS on work using visual analogue scales (0-10). The analysis controlled for gender, age, disease duration, education, disability and use of DMTs.

Results: The level of severity of fatigue and cognitive impairment was significantly and independently correlated with all resource utilisation. Total inpatient and outpatient costs increased significantly with symptom severity ($p < 0.0001$), as did individual resources. Utility decreased by 0.034 and 0.028 for each VAS point in severity of fatigue and cognitive impairment, respectively. With each VAS point increase in severity of symptoms, the probability of working was reduced by 10.6% for cognitive impairment ($p < 0.0001$) and 4.9% for fatigue ($p = 0.005$). Work hours decreased in linear fashion with each point of increasing severity for both symptoms, while sick leave increased accordingly ($p < 0.0001$). Both symptoms significantly affected productivity at work ($p < 0.0001$).

Conclusion: This study shows that fatigue and cognitive impairment have a significant impact regardless of physical disability on both productivity and working capacity as well as on the quality of life and resource utilization.

Disclosure: Funded by Biogen

EPR2126

Leptomeningeal contrast enhancement in adult patients with MOG-antibody associated CNS demyelinating disease: a multi-center study

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Background and aims: Leptomeningeal contrast enhancement (LMCE) in Multiple Sclerosis (MS) patients has been reported using 3-dimensional-FLAIR-sequences post-gadolinium (3D-FLAIRE) and has been associated with cortical pathology and the presence of ectopic B-cell follicle-like structures. We investigated the presence of LMCE in anti-MOG-positive-patients with CNS demyelinating disease (MOG-group), using 3D-FLAIRE, as an indirect indicator of the pathogenetic role of sustained compartmentalized immune response within the CNS of these patients.

Methods: We evaluated 11 MOG-group patients (MOG-IgG1 serum detection with cell-based-assay) and 14 Relapsing-Remitting MS (RRMS) patients age and sex matched as controls, from 3 Departments of Neurology. LMCE foci were assessed using 3D-FLAIR and T1-weighted sequences pre- and post-gadolinium on 3 Tesla scanner. None had a relapse or received corticosteroids within one month preceding study entry.

Results: Characteristics of our MOG-group were: a) female 72.7% (n=8), b) mean age at MRI acquisition 45.2 years (range 23–75years), c) mean disease duration 47.7 months (range 2-153months). LMCE, identified as foci of hyperintensities on 3D-FLAIRE and not on T1-weighted-contrast-enhanced sequences, was detected in 27.3% (n= 3) all with supratentorial distribution. LMCE in one brain region was observed in 2 patients (parietal n=1, frontal n=1), while the 3rd patient had 3 LMCE foci (parietal, temporal, occipital). In the RRMS-group LMCE was detected in 7.1% (n=1), in the parietal lobe.

Conclusion: To our knowledge, this is the 1st study showing LMCE using 3D-FLAIRE sequence in adults with MOG-antibody associated CNS demyelinating disease; this finding may be indicative of the presence of ectopic B-cell follicle-like structures in the meninges associated with meningeal inflammatory infiltrates.

Disclosure: Nothing to disclose

MS and related disorders 5

EPR2127

Safety of Alemtuzumab in RRMS Patients in the Period Following Lymphocyte Repopulation: Clinical Trial and Postmarketing Experience

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Background and aims: In the CARE-MS trials (NCT00530348, NCT00548405), alemtuzumab significantly improved efficacy outcomes versus subcutaneous interferon beta-1a over 2 years in RRMS patients. Efficacy was maintained in 2 consecutive extension studies (NCT00930553, NCT02255656 [TOPAZ]), wherein patients could receive additional alemtuzumab courses as needed or receive other disease-modifying therapy (DMT) per investigator discretion. Alemtuzumab selectively depletes circulating CD52-expressing B and T lymphocytes, followed by a distinctive pattern of lymphocyte repopulation. Here, we report incidences of adverse events (AEs) of special interest occurring during the postrepopulation period (18–36 months post treatment) using clinical trial and postmarketing data.

Methods: Safety measures in clinical trials included monthly patient questionnaires, complete blood counts, serum creatinine, urinalysis with microscopy, and quarterly thyroid function tests. All patient- and investigator-reported AEs, serious AEs, and medical events of interest were recorded.

Results: Over 9 years in pooled CARE-MS alemtuzumab-treated patients (N=811), incidences of thyroid disorders, immune thrombocytopenia, autoimmune nephropathies, and acute acalculous cholecystitis were 47.6%, 2.7%, 0.4%, and 0.4%, respectively. Among 25,292 patients treated with alemtuzumab in the postmarketing setting as of 31 March, 2019, additional events occurring post repopulation included autoimmune hepatitis (AIH; 10.7 in 10,000) and haemophagocytic lymphohistiocytosis (HLH; 2.7 in 10,000).

Conclusion: AEs occurring after lymphocyte repopulation in RRMS patients treated with alemtuzumab have included thyroid disorders, immune thrombocytopenia, autoimmune nephropathies, and acute acalculous cholecystitis in clinical trials, and rare postmarketing cases of AIH and HLH.

Disclosure: STUDY SUPPORT: Sanofi and Bayer HealthCare Pharmaceuticals.

EPR2128

Long-term Efficacy of Siponimod Treatment for up to 5 Years in Patients with Secondary Progressive Multiple Sclerosis: Analysis of the EXPAND Extension Study

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Background and aims: In the EXPAND-Core study, siponimod significantly reduced 3-/6-month (m) confirmed disability progression (3mCDP/6mCDP) and cognitive decline in secondary progressive multiple sclerosis (SPMS) patients. We assessed long-term efficacy of siponimod on disability, cognitive processing speed (CPS) and relapses in SPMS patients from the Core and Extension parts of the EXPAND study.

Methods: This analysis included patients who received ≥ 1 dose of randomised treatment (siponimod 2mg/placebo; 36m Extension data cut-off [April 2019]; total study duration ≤ 5 years). Efficacy analyses included time-to-3mCDP/time-to-6mCDP, time-to-6m confirmed meaningful worsening in CPS (6mCW; ≥ 4 points in SDMT) and annualised relapse rate (ARR) for the continuous (CSG: siponimod in Core/Extension) and switch groups (PSG: placebo in Core/switched to siponimod in Extension).

Results: Of the 1224 (74% of 1651 randomised) patients entering the Extension, 878 (72%) were ongoing. Patients in CSG versus PSG were less likely to experience 3mCDP ($p=0.0064$) and 6mCDP ($p=0.0048$). Time-to-6mCDP was prolonged by 54% for the 25th percentile and risk for 6mCDP reduced by 22% in CSG versus PSG; median time-to-6mCDP not reached for CSG. Decline in CPS on SDMT was delayed ($p=0.0014$) and risk for 6mCW reduced by 23% in CSG versus PSG (Table). ARR was reduced by 52% in CSG versus PSG ($p<0.0001$); the effect was similar for

relapses without complete recovery, requiring steroids/hospitalisations.

Parameter	Continuous siponimod group (N=1099)	Placebo-siponimod group (N=546)	p-value	Relative risk reduction %; HR (95% CI)	Delay in time-to-event %
	KM estimate ^a				
Time-to-6mCDP on EDSS ^b % of patients without event up to Month 48	58.65 (55.34; 61.96)	52.40 (47.56; 57.21)	0.0048 ^b	22% 0.78 (0.66; 0.92)	-
Time to 6mCDP on EDSS for the 25 th percentile Months	21.0	13.6	-	-	54%
Time-to-6mCW on SDMT ^c % of patients without event up to Month 48	68.28 (65.16; 71.39)	58.45 (53.67; 63.24)	0.0014 ^b	23% 0.77 (0.65; 0.92)	-
Time-to-6mCW on SDMT for the 25 th percentile Months	29.6	18.3	-	-	62%

^aKM estimates relate to the end day of the interval. The Greenwood formula is used for the CIs of the KM estimates. The numbers provided in parentheses are CI values. CIs are point-wise rather than simultaneous intervals; ^bUsing a log-rank test stratified by treatment group

³mCDP, 3-month confirmed disability progression; 6mCDP, 6-month confirmed disability progression; 6mCW, 6-month confirmed worsening; CI, confidence interval; CPS, cognitive processing speed; EDSS, Expanded Disability Status Scale; HR, hazard ratio; KM, Kaplan-Meier; SDMT, Symbol Digit Modalities Test

Table. Efficacy results

Conclusion: Benefits on disability, cognitive processing speed and relapses of CSG over PSG gained during the controlled period are sustained for up to 5 years, demonstrating the sustained treatment effect and advantage of early treatment initiation with siponimod in patients with SPMS.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

EPR2129

Ponesimod Versus Teriflunomide in Relapsing Multiple Sclerosis: Efficacy Results from the OPTIMUM Phase 3 Randomised, Double-Blind Superiority Study

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Background and aims: Ponesimod, an orally active, highly selective and reversible modulator of sphingosine 1 phosphate receptor 1 (S1P1), causes sequestration of lymphocytes in lymphoid organs thereby preventing lymphocyte recruitment to sites of inflammation. The OPTIMUM study evaluated efficacy of ponesimod versus teriflunomide in adult patients with relapsing multiple sclerosis (RMS).

Methods: Patients (18-55 years) with RMS (expanded disability status scale scores: 0-5.5) were randomised (1:1) to ponesimod 20mg or teriflunomide 14mg for 108 weeks. Primary endpoint was annualised relapse rate (ARR) (confirmed relapses up-to end-of-study [EOS]); 2ndary endpoints included: change from baseline to Week 108 in the symptoms domain of the fatigue symptom and impact questionnaire-RMS (FSIQ-RMS), combined unique active lesions per year (CUALs) on MRI, time to 12-week and 24-week confirmed disability accumulation (CDA). Brain volume loss and no evidence of disease activity (NEDA-3) status were exploratory endpoints.

Results: Of 1133 patients randomised (ponesimod: n=567, teriflunomide: n=566), 86.4% and 87.5% completed study. The efficacy findings are summarised in Table 1. Ponesimod reduced ARR versus teriflunomide by 30.5% (p=0.0003); supplementary analysis results were robust and consistent with the primary analysis (Figure 1). Compared to teriflunomide, ponesimod reduced the FSIQ-RMS weekly symptom score (mean difference -3.57; p=0.0019) and CUALs (p<0.0001). 12-week and 24-week CDA estimates were not significantly different. Brain volume loss at Week 108 was -0.91% versus -1.25% (0.34% difference, p<0.0001) and NEDA-3 was achieved in 25.0% versus

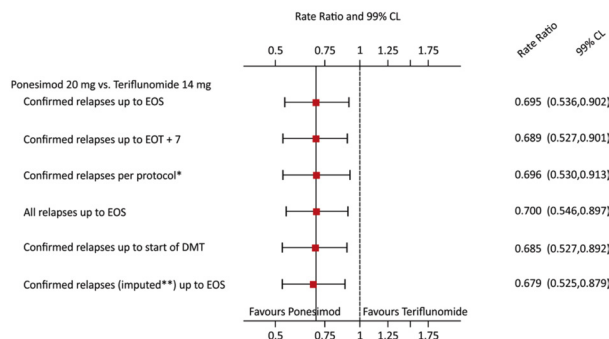
16.4% patients (odds ratio: 1.70, p=0.0004), favouring ponesimod versus teriflunomide.

Table 1: Summary of Efficacy Outcomes

Endpoint	Ponesimod 20 mg N=567	Teriflunomide 14 mg N=566
ARR up to EOS[†]		
Mean estimate	0.202	0.290
(95% CL)	(0.173, 0.235)	(0.254, 0.331)
Treatment effect (rate ratio)	0.695	
(95% CL)	(0.570, 0.848)	
p-value	0.0003	
FSIQ-RMS change from baseline to Week 108[‡]		
LS Mean	-0.01	3.56
(95% CL)	(-1.60, 1.58)	(1.96, 5.16)
LS Mean Difference	-3.57	
(95% CL)	(-5.83, -1.32)	
p-value	0.0019	
CUAL from baseline to Week 108[‡]		
Mean estimate (lesions per year)	1.405	3.164
(95% CL)	(1.215, 1.624)	(2.757, 3.631)
Treatment effect (rate ratio)	0.444	
(95% CL)	(0.364, 0.542)	
p-value	< 0.0001	
Time to first 12-week CDA[‡]		
Hazard ratio	0.83	
95% CL	(0.58, 1.18)	
Log-rank p-value	0.2939	
Time to first 24-week CDA[‡]		
Hazard ratio	0.84	
95% CL	(0.57, 1.24)	
Log-rank p-value	0.3720	

ARR, annualised relapse rate; CDA, confirmed disability accumulation, CL=Confidence limit, CUAL, combined unique active lesions; EOS, end of study; FSIQ-RMS, fatigue symptom and impact questionnaire-relapsing multiple sclerosis; LS= least squares
[†]Negative binomial model is applied with Wald confidence limits and p-value. Offset: log time (years) up to end of study.
[‡]Covariates: EDSS strata (≤3.5, >3.5), DMT in last 2 years prior to randomisation strata (Y, N), number of relapses in year prior study entry (≤1, ≥2), DMT = disease modifying therapy for multiple sclerosis; EDSS = Expanded Disability Status Scale
[§]MMRM = Mixed effects repeated measurements model with unstructured covariance, treatment, visit, treatment by visit interaction, baseline by visit interaction as fixed effects, baseline FSIQ score, EDSS strata (≤3.5, >3.5), DMT in last 2 years prior randomisation strata (Y, N) as covariates. A negative change from baseline indicates an improvement in fatigue symptoms.
[¶]Negative binomial model is applied with Wald confidence intervals and p-value. Offset: Log Time (years) up to last MRI scan.
[‡]Covariates: EDSS strata (≤3.5, >3.5), DMT within last 2 years prior to randomization strata (Y, N), and Gd + T1 lesions at baseline (absent or present).
[§]Stratified by EDSS category and DMT within 2 years, Cox regression with Wald confidence limits

Figure 1: ARR Supplementary Analysis (Forest plot with 99% CL)



ARR, annualised relapse rate; CL, confidence limit; DMT, disease-modifying therapy; EOS, end of study; EOT, end of treatment
^{*}per protocol set, ^{**}Relapses with missing expanded disability status scale (EDSS) score imputed as confirmed relapses
Rate ratio: treatment effect, i.e. ARR of ponesimod 20 mg relative to that of teriflunomide 14 mg

Conclusion: Ponesimod was superior to teriflunomide on ARR, fatigue symptoms, MRI activity, brain atrophy and NEDA-3 status.

Disclosure: Funding was provided by Janssen Research & Development, LLC, and OPTIMUM study was supported by Actelion Pharmaceuticals, Part of Janssen Pharmaceutical Companies, Allschwil, Switzerland.

EPR2130

The effect of clinical and modifiable prepregnancy and delivery parameters on the clinical status of MS patients : Results of a greek cohort study

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Background and aims: The objective of this study was to retrospectively evaluate the effect of pre-pregnancy disability level and administered Disease Modifying Treatment (DMT), exclusive breastfeeding, epidural anaesthesia during child delivery and diagnosis of postpartum depression (PPD) on the natural course of Multiple Sclerosis (MS) in terms of current disability status and present relapse rate (rr).

Methods: 100 Greek female MS patients who became pregnant during the years 2006-2009 were retrospectively followed up in regards to the above mentioned parameters as well as pregnancy and postpartum clinical relapses. All had an established diagnosis of Relapse Remit Multiple Sclerosis (RRMS) with disease duration of 15 years. All patients' present clinical status has been assessed with EDSS scale and rr calculation.

Results: Pre-pregnancy EDSS and DMT administration were the most accurate predictors of current EDSS and present rr respectively with very high accuracy ($p < 0.001$). Pregnancy and postpartum clinical relapses could predict current EDSS with high accuracy and present rr with medium to high accuracy ($p < 0.01$). Exclusive breastfeeding was a predictor of present rr with medium accuracy and of current EDSS with medium to high accuracy ($p < 0.01$). Epidural anaesthesia did not seem to have any predictive value while PPD could predict both current EDSS and present rr with medium and low accuracy respectively ($p < 0.04$).

Conclusion: Pre-pregnancy clinical parameters had the highest predictive capability while delivery modifiable ones ranged from nil to high predictive value which may imply that the immune system eventually returns to its pre-pregnancy levels of activity at a patient specific time span.

Disclosure: Nothing to disclose

EPR2131

Quantifying the relationship between disability progression and quality of life in patients treated for neuromyelitis optica spectrum disorder (NMOSD): Insights from the SAKura studies

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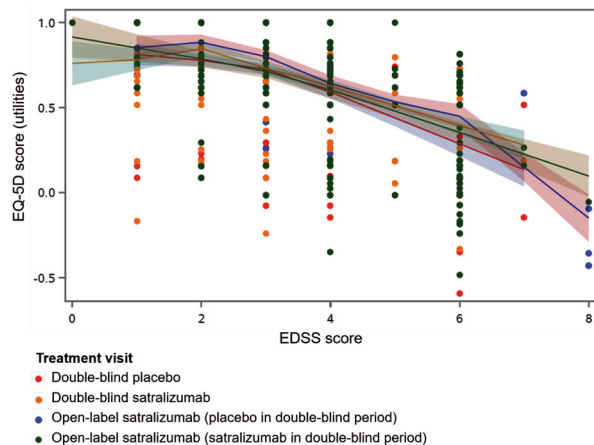
Background and aims: To date, no specific scales have been developed to relate NMOSD-related disability and quality of life (QoL). The Expanded Disability Status Scale (EDSS), developed to quantify disability in multiple sclerosis, has not been validated in NMOSD. The EuroQol 5-dimensions (EQ-5D) scale has been applied in patients with NMOSD, though studies are sparse and of limited validity as, currently, none are based on clinical trial data. We combined EDSS and EQ-5D data from 2 clinical trials to quantify the relationship between disability and QoL in NMOSD patients.

Methods: SAKuraSky (NCT02028884) and SAKuraStar (NCT02073279) were Phase 3, multicentre, randomised, international, double-blind, placebo-controlled, parallel assignment studies of satralizumab, administered in combination with baseline immunosuppressants (SAKuraSky) or as monotherapy (SAKuraStar). Patients completed the EDSS and EQ-5D at baseline and at 24-week intervals thereafter. Inclusion criteria specified a baseline EDSS score ≤ 6.5 . The relationship between disability and QoL was assessed by estimating EQ-5D utilities (UK tariff) for each incremental EDSS category. A repeated-measures linear model was used to regress health utilities on EDSS score-derived health states.

Results: Overall, 180 patients completed at least 1 set of EDSS and EQ-5D questionnaires. The most commonly reported EDSS value was 3 (moderate disability), with mean EQ-5D score decreasing in relation to each incremental increase in EDSS disability (Table, Figure). The relationship between EDSS and EQ-5D score remained consistent across the different treatment groups (Figure).

EDSS category	No. of records per EDSS category (%)	EQ-5D score, mean (SD)
0 (no disability)	4 (0.3)	1.00 (0.00)
1 (minimal signs of disability)	122 (9.2)	0.80 (0.20)
2 (minimal/mild disability)	277 (21.0)	0.83 (0.20)
3 (moderate disability)	396 (30.0)	0.76 (0.20)
4 (significant disability)	284 (21.5)	0.61 (0.25)
5 (severe disability)	40 (3.0)	0.53 (0.24)
6 (requires walking aids)	185 (14.0)	0.37 (0.32)
7 (unable to walk)	7 (0.5)	0.31 (0.27)
8 (restricted to powered wheelchair/bed)	6 (0.5)	-0.24 (0.18)

Table – Distribution of patients and mean EQ-5D score (UK tariff) by EDSS category



Scatter plot of EQ-5D score (UK tariff) by EDSS state

Conclusion: These results, generated from high-quality clinical trial data, demonstrated a strong and consistent relationship between disability and QoL in patients with NMOSD.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.; writing and editorial assistance was provided by ApotheCom, UK.

EPR2132

Effect of interferon beta-1a treatment on serum neurofilament light chain levels in patients with a 1st clinical demyelinating event in the REFLEX trial

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Background and aims: In REFLEX, patients (pts) with a first clinical demyelinating event (FCDE) treated with subcutaneous interferon beta-1a (scIFN beta-1a) 44mg once (qw) or 3 times weekly (tiw) had significantly delayed conversion to multiple sclerosis (MS; McDonald [McD]-2005 criteria). Effects of scIFN beta-1a 44µg qw or tiw vs placebo (PBO) on serum Neurofilament light chain (sNfL) were assessed. Predictive value of NfL for conversion to McD-MS was explored.

Methods: Pts were randomised to scIFN beta-1a tiw (n=171), qw (n=175) or PBO (n=171) over 2yrs; pts converting to clinically definite MS (CDMS) switched to open-label scIFN beta-1a tiw (only data collected to CDMS conversion included). Serum NfL levels analysed at baseline (Month [M]0), M6, M12, M24. Pts with M0 sNfL data ≥1 other time point were included. Treatment effect on sNfL levels was compared using ANCOVA on log-transformed sNfL data, M0 log-sNfL concentration as covariate, with data presented for M6, M12. Percentages of pts converting to McD-MS 2005 by M24 were calculated by Kaplan-Meier curve.

Results: At M0, a median sNfL concentration of 26.1pg/ml defined low/high NfL subgroups. At M6, least square mean (LSM) sNfL concentration was significantly reduced vs PBO with scIFN beta-1a tiw and qw. At M12, only scIFN beta-1a tiw significantly reduced sNfL concentration vs PBO (Figure 1). Proportionally fewer pts with low sNfL converted to McD-MS by M24 (tiw:49.1%[37.9%-60.3%];qw:69.4%[59.0%-79.8%]; PBO:80.2%[71.5%-88.8%]) than high sNfL (tiw:75.2%[65.6%-84.8%];qw:80.6% [72.2%-89.0%]; PBO:91.2%[84.7%-97.6%]).

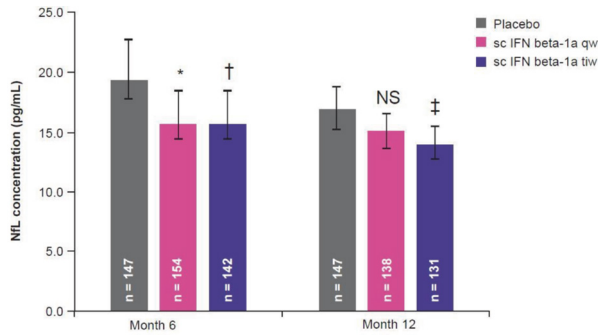


Figure 1: Serum NFL Concentrations (LSM [95% CI]) at Month 6 and 12 by Treatment Group (Statistical significance versus placebo: *P=0.001, †P=0.002, ‡P=0.015, NS non-significant. CI, confidence intervals; IFN, interferon; LSM, least square mean; qw, once weekly; sc, subcutaneous; tiw, 3 times weekly.)

Conclusion: Treatment with scIFN beta-1a tiw or qw reduced sNfL levels in pts with FCDE as early as 6-months post-baseline. High baseline sNfL levels were associated with earlier conversion to McD-MS.

Disclosure: Funded by Merck KGaA, Darmstadt, Germany

EPR2133

Long-term, real-world effectiveness of natalizumab treatment in relapsing-remitting multiple sclerosis (RRMS): data from ≥ 6 years in the TYSABRI® Observational Program (TOP) French and global cohorts

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Background and aims: TOP began >10 years ago and is the largest ongoing real-world study in natalizumab-treated RRMS patients. Country-specific data on relapse and disability outcomes, alongside global data, can provide information on natalizumab's effectiveness in local clinical practice.

Methods: Annualized relapse rate (ARR) and cumulative probability of 24-week confirmed disability worsening (CDW; Expanded Disability Status Scale [EDSS] score increase ≥ 1.5 from baseline of 0.0, ≥ 1.0 from baseline of 1.0-5.5, or ≥ 0.5 from baseline ≥ 6.0) and confirmed disability improvement (CDI; EDSS score decrease ≥ 1.0 from baseline ≥ 2.0) were analysed using data from July 2007 to November 2018 in the TOP French (n=189) and global (n=6295) cohorts. Updated data (as of November 2019) will be presented.

Results: At baseline, median (range) disease duration was 8.2 (0.3-34.9) years in the French cohort and 7.2 (0-43.9) years globally, and median (range) EDSS score was 3.5 (0-7.0) in the French cohort and 3.5 (0-9.5) globally. ARR decreased in the French cohort from 1.96 in the year pre-initiation to 0.19 on natalizumab, consistent with the global decrease from 2.00 to 0.21. ARR also decreased in the French and global cohorts regardless of baseline EDSS score or prior therapy use. At 6 years, cumulative probabilities of CDW and CDI were, respectively, 26.2% and 41.8% in the French cohort and 24.8% and 31.3% globally.

Conclusion: Generally consistent with global TOP results, natalizumab ARR remained low and disability stabilized over ≥ 6 years in the French cohort. These results support natalizumab's long-term effectiveness in real-world settings.

Disclosure: This study is supported by Biogen. Detailed disclosures of each author will be included in the e-poster/oral presentation.

EPR2134

JCV serostatus and viral replication in patients with Multiple Sclerosis treated with Ocrelizumab

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Background and aims: Rituximab has been associated with progressive multifocal leukoencephalopathy (PML) by John Cunningham Polyomavirus (JCPyV), while the long-term effects of ocrelizumab use, recently approved for multiple sclerosis (MS), are essentially unknown. Here we reported our preliminary data of an ongoing project aimed to explore the anti-JCPyV serostatus and the JCPyV replication in MS patients treated with ocrelizumab.

Methods: 30 MS patients (age 41+/-9, 6 primary progressive, 16 naïve to treatments) starting treatment with Ocrelizumab were recruited. Anti-JCPyV index, JCPyV-DNA in urine and plasma samples, IgG and IgM titres and lymphocyte subsets were longitudinally assessed

Results: At baseline 26/30 patients were anti-JCPyV seropositive (>0,4), 3/30 seronegative (<0,2), and 1/30 was indeterminate (>0,20 and <0,4). 8/26 seropositive and 0/3 seronegative patients had detectable JCPyV-DNA (range: $4 \cdot 10^4$ - $5 \cdot 10^7$ copies) in urine; all were negative for plasma JCPyV-DNA. At 3 months (T3) 27/30 were positive for anti-JCPyV antibodies, 3/30 negative. Mean anti-JCPyV index was marginally reduced at T3 (t-test $p=0.058$). Patients were persistently positive for urinary JCPyV DNA at T3. CD4, CD8 and NK counts and IgG titres did not significantly change from baseline to T3; CD19 counts were significantly lowered ($p<0.001$), as well as IgM titre.

Conclusion: Our data indicate that Ocrelizumab is not associated with increased JCPyV replication; we found a discordance between anti-JCPyV titre and urine JCPyV-DNA load at baseline, suggesting a possible overestimation of PML risk. The validity of anti-JCPyV index to monitor PML risk during ocrelizumab treatment needs to be carefully assessed, considering its potential long-term impact on immunoglobulin titres.

Disclosure: Nothing to disclose

EPR2135

Understanding heterogeneity in comparative effectiveness studies of natalizumab and fingolimod in multiple sclerosis: effect of analytical methodology

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Background and aims: Natalizumab and fingolimod present similar indication as 2nd-line treatment in relapsing-remitting multiple sclerosis (MS) but important differences in terms of safety. Comparative effectiveness studies have shown variable results. These studies used different methods to control indication bias and manage censoring in time-to-event analysis. The objective of this study was to evaluate the impact of statistical methods on the results of analysis of comparative effectiveness.

Methods: 3 observational MS registries (MSBase, Danish MS register and French OFSEP registry) were combined. Four outcomes were studied: count of relapses, time to 1st relapse, time to 1st disability worsening and improvement. 2 propensity scores methods were used: matching and weighting allowing for estimating Average Treatment effect for Treated (ATT) and Average Treatment effect for the Entire population (ATE). Analyses were conducted in intention-to-treat and per-protocol frameworks.

Results: Overall 5,148 patients were included. Irrespective of the methods used, conclusions derived from the different analyses were consistent. In this well-powered sample, 95% confidence intervals of the estimates overlapped, even though point estimates differed between analyses done with different methods. Weighting and matching procedures led to consistent results, confirming that both methods performed well. The most pronounced differences were 2ndary to the type of average treatment effect estimated (ATT with matching and ATE or ATT with weighting). Most differences were related to the definition of censoring; intention-to-treat analyses were more conservative than per-protocol analyses.

Conclusion: This applied study elucidates the influence of methodological decisions on the results of comparative effectiveness studies, given these are sufficiently powered.

Disclosure: This work was part of Mathilde Lefort's Ph.D., which is funded through an unconditional donation from Roche SAS, without any link to the scientific contents of the work.

EPR2136

Influence of Tobacco Smoking in Multiple Sclerosis Onset and Progression

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Introduction: Multiple sclerosis (MS) is widely recognized as predominantly associated with environmental factors, among which tobacco smoking is one of the most preponderant.

Aim: To investigate the association between tobacco smoke exposure and MS onset and progression.

Methods: 120 consecutive MS patients were recruited from the outpatient clinic and questioned for past and current smoking status, as well as daily 2nd-hand smoke exposure history. The following clinical variables were also obtained: disease subtype [relapsing-remitting (RRMS) and secondary progressive (SPMS)], EDSS score and age at disease-onset and progression-onset.

Results: Patients were 73.3% female, mean age of disease onset was 32.19 (± 10.30) and mean disease duration 12.27 (± 10.35) years. 87.5% had RRMS and 12.5% SPMS. In regard to smoking status, 22 patients (18.3%) were current-smokers, 57 (47.5%) non-smokers, 27 (22.5%) past-smokers and 14 (11.7%) were 2nd hand-smokers. 32 (26.7%) were smokers at disease onset. Age at disease onset was significantly lower in smokers at onset (29.53 ± 10.04 years vs 34.19 ± 10.10 years, $p=0.031$). Age of smoking initiation ($R^2 0.14$; $p=0.001$) and pack-year load before onset ($R^2 0.32$; $p<0.001$) significantly predicted a younger age at disease onset. Pack-year load after MS onset ($r=0.214$; $p=0.028$) and smoking duration after MS onset ($r=0.387$; $p=0.026$) were also significantly correlated with EDSS. Current smoking status was not associated with EDSS in the RRMS group. In the SPMS group the EDSS was significantly higher in ever-smokers (7.0) and 2nd hand-smokers (6.8) compared to non-smokers (5.5) ($p=0.012$).

Conclusion: In accordance with current literature, our results show a significant effect of smoking, with earlier onset and worse outcome in MS. Thus, there may be a benefit in smoking cessation even after disease onset.

Disclosure: Nothing to disclose

EPR2137

Characterization of MS lesions: Comparison of a new deep learning based solution with academic standard

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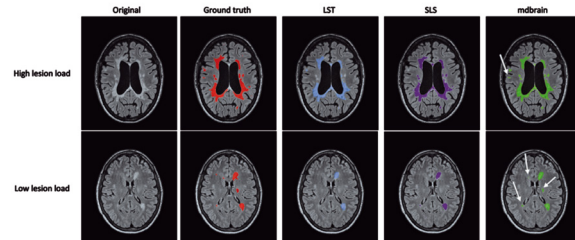
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Background and aims: Comparison of a new Deep Learning (DL) algorithm with SPM-based academic solutions for lesion segmentation in Multiple Sclerosis (MS).

Methods: White matter lesion detection was carried out using three different algorithms: SPM toolboxes (i) LST and (ii) SLS and (iii) the DL-powered software solution mbrain. While (i) and (ii) are already widely used in scientific community, (iii) is a new algorithm using a U-net architecture that fully works in 3D. The model was trained with 77 ground truth segmentation masks using augmentation and was validated on 21 datasets. Algorithms were tested on the LITMS dataset (not part of the training data of) that included patients with confirmed MS (Lesion load: 0.34-52.45mL, according to manual segmentation (3 experts) on 3D-T1w/3D-T2-flair). The performances were validated with the F1 score for the detection and the dice score for the segmentation.

Results: For the detection tests, mbrain showed significantly higher mean F1 score of 0.60 ± 0.08 vs. $0.35 \pm 0.12 / 0.36 \pm 0.12$ for (i)/(ii). Segmentation performance also yielded better mean Dice coefficients of 0.61 ± 0.17 vs. $0.51 \pm 0.20 / 0.51 \pm 0.21$. These results are independent of the lesion load (Table 1). A representative slice of (i)-(iii) is shown in Figure 1.

Figure 1: Representative axial T2-flair slices of two patients from the LITMS dataset. Images of both high and low lesion loads are superimposed with lesion maps of different segmentations, namely: ground truth (red), LST (blue), SLS (violet) and mbrain (green). White arrows indicate lesions detected only by mbrain.



Conclusion: As compared to SPM, mbrain shows better results for both segmentation and detection, independent of the actual lesion load. This is reflected by the improved mean values and a lower standard deviation. Taking into account the shorter evaluation time (~ 10 sec vs. ~ 4 min) and the fully automated evaluation workflow as compared to SPM, our DL algorithm appears to be a valuable tool for daily application in MS diagnostics in clinical practice.

Disclosure: Nothing to disclose

EPR2138

Correlation of lateral ventricles, corpus callosum and thalamus volume changes: A potential new biomarker for multiple sclerosis

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Background and aims: Whole brain atrophy is long studied imaging biomarker in multiple sclerosis (MS) whereas regional morphological changes might contain more specific information and serve as potential early predictors of disease onset and disease progression. This inter dependence of brain regions has been rarely studied. Here, we aim at identifying relationships of regional brain volumes in a group of healthy controls (HC) and compare them with patients with MS (PwMS) with different disability levels.

Methods: MP-RAGE (magnetization-prepared rapid acquisition with gradient echo) images of 2014 PwMS and 102 HC were obtained at 3T (MAGNETOM Skyra Siemens Healthcare, Erlangen, Germany). Morphometry was assessed with the MorphoBox prototype. Partial correlations controlling for age and disease duration were calculated to explore the relationship between regional brain volumes separately for HC and for PwMS, as well as for different physical disability levels (4 groups based on EDSS: 0-1.5; 2.0-3.0; 3.5-4.5 and ≥5.0).

Results: Unexpectedly, corpus callosum and thalamus volumes were positively correlated with lateral ventricles volume in HC. In PwMS the correlation is gradually inverted. The results are summarized in Tables 1-3.

	Healthy individuals	PwMS EDSS 0-1.5	PwMS EDSS 2.0-3.0	PwMS EDSS 3.5-4.5	PwMS EDSS ≥ 5.0
n (% women)	102 (65)	651 (74)	689 (69)	477 (74)	197 (72)
Age	37.1 ± 10.3	38.8 ± 8.7	42.4 ± 9.6	48.0 ± 9.7	49.0 ± 8.9
Disease duration	-	9.7 ± 6.6	11.6 ± 8.1	17.2 ± 9.2	18.9 ± 8.6
Brain volume	1162.3 ± 115.7	1100.3 ± 18.0	1086.1 ± 111.7	1034 ± 9 ± 113.9	1013.6 ± 96.5
Lateral ventricles	17.22 ± 9.5	21.8 ± 11.5	25.6 ± 19.0	30.4 ± 18.1	37.0 ± 23.0
Corpus callosum	5.2 ± 0.9	4.8 ± 0.8	4.8 ± 0.8	4.5 ± 0.8	4.3 ± 0.9
Thalamus	14.3 ± 1.9	13.5 ± 1.5	13.4 ± 1.6	12.8 ± 1.6	12.4 ± 1.4
MUCCA	89.5 ± 7.7	86.0 ± 8.3	84.9 ± 9.2	80.9 ± 10.0	74.2 ± 10.1
TIV	1453.5 ± 132.1	1411.6 ± 120.0	1409.71 ± 128.4	1383.0 ± 131.4	1388.3 ± 121.6

Table 1. Basic characteristics and magnetic resonance volumetric parameters of the enrolled healthy individuals and the PwMS.

Data are displayed as means ± standard deviations; age and disease duration are measured in years; volumetric data are shown in milliliters except area of corpus callosum and MUCCA which are measured in mm². Normalized data are not shown.

EDSS = expanded disability status scale, MUCCA = mean upper cervical cord area, TIV = total intracranial volume.

Table 1

		Healthy individuals	PwMS EDSS 0-1.5	PwMS EDSS 2.0-3.0	PwMS EDSS 3.5-4.5	PwMS EDSS ≥ 5.0
CC / Ventricles	r	0.525	0.050	-0.022	-0.287	-0.387
	p	< 0.001	0.211	0.581	< 0.001	< 0.001
Thalamus / Ventricles	r	0.607	0.110	-0.022	-0.125	-0.294
	p	< 0.001	0.006	0.574	0.008	< 0.001
CC/Thalamus	r	0.526	0.398	0.501	0.480	0.569
	p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
CC / Brain Tissue	r	0.111	0.241	0.296	0.499	0.526
	p	0.277	< 0.001	< 0.001	< 0.001	< 0.001
Ventricles / Brain Tissue	r	-0.220	-0.641	-0.682	-0.732	-0.825
	p	0.029	< 0.001	< 0.001	< 0.001	< 0.001

		Healthy individuals	PwMS EDSS 0-1.5	PwMS EDSS 2.0-3.0	PwMS EDSS 3.5-4.5	PwMS EDSS ≥ 5.0
CC / Ventricles	r	0.529	0.049	-0.015	-0.284	-0.389
	p	< 0.001	0.220	0.695	< 0.001	< 0.001
Thalamus / Ventricles	r	0.620	0.160	0.013	-0.169	-0.274
	p	< 0.001	< 0.001	0.734	< 0.001	< 0.001
CC/Thalamus	r	0.524	0.398	0.497	0.459	0.528
	p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
CC / Brain Tissue	r	0.097	0.241	0.313	0.515	0.531
	p	0.344	< 0.001	< 0.001	< 0.001	< 0.001
Ventricles / Brain Tissue	r	-0.225	-0.595	-0.660	-0.697	-0.818
	p	0.027	< 0.001	< 0.001	< 0.001	< 0.001

Table 2 + 3. Relationships between particular brain structures (normalized on total intracranial volume) in healthy individuals and PwMS. In the first table, zero-order correlations are shown; the second table contains correlations after controlling for age and (in PwMS) also disease duration.

CC = corpus callosum (area); EDSS = expanded disability status scale; p = p-value/significance PwMS = patients with multiple sclerosis; r = Spearman's correlation coefficient.

Table 2 + 3

Conclusion: The correlation between lateral ventricles versus corpus callosum and thalamus, respectively, is strongly positive in HC regardless of age. In PwMS, this relationship becomes weaker and eventually negative in patients with moderate and severe physical disability, whereas the relationship between corpus callosum and thalamus does not change. The results suggest different rates of atrophy of specific structures at different disability levels and might have implications to understand the biology of regional brain atrophy in MS.

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EPR2139

A substantial 'ependymal-in' gradient of thalamic damage in progressive multiple sclerosis

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Background and aims: Cortical gray matter (GM) damage contributes to multiple sclerosis (MS) progression and exhibits a 'surface-in' gradient, associated with meningeal tertiary lymphoid-like structures (TLS). We studied the pathology of thalamus, a subcortical GM structure early involved in MS.

Methods: Thalamic medial nuclei from 41 post-mortem secondary progressive MS (SPMS) cases were evaluated by immunohistochemistry for demyelinating activity. NeuN+ neurons, MHC-class II+ microglia/macrophages, CD3+T and CD20+ B-cells were counted in 10 SPMS cases with TLS, 10 without TLS and 8 controls. Microglial phenotypes and sub-ependymal infiltrates were further characterized and neurofilament light chain (NfL) levels measured in paired CSF.

Results: Active demyelination was observed in 40% of thalamic lesions (TL). Microglia density was increased near sub-ependymal surface (83% in TL vs Ctrl; 66% in normal appearing thalamus, NAT, vs Ctrl) and reduced in the most internal layers (42% in TL; 17% in NAT). Neuron density was decreased, with a gradient from the sub-ependymal surface (42% in TL vs Ctrl; 28% in NAT vs Ctrl) towards inner regions (20% in TL; 9% in NAT). The gradient was higher in cases with TLS. CSF-NfL levels reflected this gradient. Microglia was markedly activated closely to CSF (TMEM119+ cells). Sub-ependymal infiltrates in cases with TLS had higher number of B-cells, clustered with Ig+ plasma cells and CD35+ follicular dendritic cells.

Conclusion: A gradient of microglial activation and neuronal loss characterizes TL and NAT in SPMS. This associates with presence of TLS, providing evidence for intrathecal inflammation as major driver of subcortical GM damage in MS.

Disclosure: Nothing to disclose

EPR2140

Safety of satralizumab based on pooled data from phase 3 studies in patients with neuromyelitis optica spectrum disorder (NMOSD)

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Background and aims: Satralizumab reduced NMOSD relapse risk in 2 phase 3 studies: SAKuraSky (satralizumab in combination with baseline immunosuppressants; NCT02028884), and SAKuraStar (satralizumab monotherapy; NCT02073279). We evaluated the safety of satralizumab vs placebo across both SAKura studies.

Methods: SAKuraStar and SAKuraSky are randomized studies, consisting of a double-blind (DB) period (satralizumab 120mg Q4W vs placebo) followed by an open-label extension period (satralizumab only). The combined DB/extension period was defined as the overall satralizumab treatment (OST) period (cut-off 7 June 2019). Safety was evaluated in the DB and OST periods using adverse event (AE) rates per 100 patient-years.

Results: The pooled DB population included 178 patients (satralizumab, n=104; placebo, n=74). 166 patients received satralizumab in the OST period. Mean/median satralizumab exposures in the OST period were 133.3 and 128.6 weeks, respectively. Rates of AEs and serious AEs were comparable between treatment groups in the DB period (Table). Infection rates were lower with satralizumab vs placebo, with no increased risk of opportunistic infections (Table). AE, serious AE, and infection rates were comparable between the DB and OST periods (Table). 4 patients (3.8%) on satralizumab and 6 (8.1%) on placebo withdrew from the DB period due to an AE. The injection-related reaction (IRR) rate was higher with satralizumab vs placebo (Table); IRRs were mostly mild-to-moderate and did not lead to treatment discontinuation. No deaths or anaphylactic reactions were reported.

Events/100 PY (95% CI)	Double-blind period		OST period
	Satralizumab (n=104)	Placebo (n=74)	Satralizumab (n=166)
AEs	478.49 (448.18, 510.31)	506.51 (463.38, 552.59)	418.79 (399.83, 438.41)
Serious AEs	14.97 (10.02, 21.50)	17.98 (10.66, 28.42)	12.57 (9.47, 16.36)
Infections	113.04 (98.56, 129.04)	154.85 (131.43, 181.24)	112.41 (102.69, 122.79)
Serious infections	4.13 (1.78, 8.14)	6.99 (2.81, 14.41)	3.88 (2.26, 6.22)
Injection-related reactions	17.03 (11.73, 23.92)	8.99 (4.11, 17.07)	12.11 (9.07, 15.84)

AE, adverse event, OST period, overall satralizumab treatment period; PY, patient year

Table – Pooled adverse event rates across the SAKuraSky and SAKuraStar trials

Conclusion: In patients with NMOSD, satralizumab was well tolerated and showed a favourable safety profile. The long-term OST data were consistent with the DB periods.

Disclosure: Funded by Chugai Pharmaceutical Co. A member of the Roche Group; ClinicalTrials.gov, NCT02028884/NCT02073279; writing and editorial assistance was provided by ApotheCom, UK.

EPR2141

Neurofilament light chain levels in patients with inflammatory demyelinating conditions associated with antibodies to myelin oligodendrocyte glycoprotein (MOG-Abs)

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Background and aims: Neurofilament light chain (NfL) is a marker of axonal injury, increased in serum/CSF of patients with several neurological disorders in correlation with clinical and radiological activity.

Objective of our study was to assess NfL concentration in patients with MOG-Ab-associated conditions according to clinical/paraclinical characteristics and to evaluate intraindividual changes over time.

Methods: Sera and available (n=17) CSF samples of 63 consecutive MOG-Ab-positive patients tested using a live cell-based assay were analysed for NfL using SIMOA Nf-light kit (SR-X analyser). 60 follow-up samples of 28 patients were also analysed. Clinical and radiological data at sampling and at last follow-up were collected in each case.

Results: We observed a moderate correlation between serum NfL values and age at sampling, with higher levels detected in older patients (rs=0.41, p<0.001). The correlation between paired serum/CSF values (rs=0.42, p=0.09) and between serum MOG-Ab titer and serum NfL levels (rs=0.15, p=0.11) did not reach statistical significance. CSF only MOG-Ab positive cases had higher CSF NfL levels in comparison with seropositive ones. Interestingly, NfL concentration correlated with disability at sampling (rs=0.43, p=0.001) but did not differentiate monophasic and relapsing cases. When analysing follow-up samples, NfL levels decreased (n=30) or remained stable (n=23) in comparison with 1st measurement in most cases, including those on relapse, in parallel with a decrease of clinical disability in comparison with 1st event.

Conclusion: NfL could be a potential biomarker of neurological disability in MOG-Ab positive patients. Future prospective studies will clarify their role in the clinical practice.

Disclosure: Nothing to disclose

EPR2142

Common Pathways of Disease-Modifying Therapies in Patients With Newly Diagnosed Multiple Sclerosis

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Background and aims: Several disease-modifying therapies (DMTs) have been available for the treatment of multiple sclerosis (MS) in the past decade. This study describes the most common pathways of DMT treatment used by US patients with newly diagnosed MS.

Methods: Newly diagnosed MS adults were identified from January 2007 to October 2017 in the US-based IBM MarketScan Commercial and Medicare databases. Patients had at least 1 year of continuous enrolment prior to their initial MS diagnosis. DMT pathways were assessed for up to 3 lines of therapy (LOTs) during a follow-up period of 2 to 10.5 years.

Results: Of 29,647 patients with at least 2 years of follow-up from MS diagnosis, 14,627 were treated with DMTs. Overall, 49% had 1 DMT LOT during follow-up, 25% had 2 DMT LOTs, and 27% had 3 DMT LOTs. Many DMT pathways were observed, and glatiramer acetate (GA) was the most common with 40% of patients initiating GA: 19.4% had 1 GA cycle only, 4.7% had 2 cycles, and 5.9% had 3 cycles. Intramuscular interferon beta-1a (IFNβ-1a) was the 2nd most common pathway (10.2%) followed by subcutaneous IFNβ-1a (6.3%). Use of other DMTs such as dimethyl fumarate and fingolimod increased from 1st LOT to 2nd LOT, while use of GA, IFNβ-1a, and interferon beta-1b decreased.

Conclusion: GA and IFNβ-1a were the most common DMT pathways among MS patients in this US pharmacy benefits database. Oral therapies were used more commonly as second or 3rd therapies, although they only became available partway through the period of study.

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EPR2143

Human papillomavirus infections in patients suffering from relapsing remitting multiple sclerosis under fingolimod

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Background and aims: Fingolimod (Fg) is an immunosuppressive drug used in the treatment of Relapsing remitting multiple sclerosis (RRMS) available in France since 2012. In 2018, HPV infections have been reported in patients treated with fingolimod. We aim to describe a series of cases of HPV lesions (location, treatment and prognosis) under fingolimod.

Methods: This is a cohort of 14 RRMS patients followed at Pitié-Salpêtrière. Clinical data were collected retrospectively for the MS evolution, and prospectively for clinical characteristics, treatment of HPV lesions and MS therapeutic strategy after HPV diagnosis

Results: We report 14 patients (9 women) in whom HPV lesions were diagnosed under fingolimod with no prior records of HPV disease. At the moment of diagnosis they were aged 35 yo (±6), on fingolimod for 3.17 years (±2.1), with a mean MS evolution of 13.6 years (±6.4). Lesions were genital (85.7%), cutaneous (21.4%) or anal (14.3%). Treatment with fingolimod was discontinued in 4 patients.

Conclusion: HPV infection, transmitted via direct contact and increased in immunocompromised patients, can cause gynecological and ENT cancers. The prevalence of these lesions under fingolimod is underestimated. A systematic dermatological and gynecological follow up are required to screen for precancerous lesions before and during treatment. Anti HPV vaccine might be discussed case by case. Systematic prevention and screening of HPV lesions in RRMS patients under fingolimod are necessary to avoid HPV-associated neoplasia.

Disclosure: Nothing to disclose

EPR2144

Early Retirement and MS on the UK MS Register

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Background and aims: Multiple Sclerosis (MS), a chronic degenerative disease typically diagnosed in a patient's early 30s, it profoundly impacts disability and socio-economic status. In the 'healthy population, the rate of medical retirement is ~3%. We compared this retirement rate with population of the UK MS Register (UKMSR).

Methods: We examined the UKMSR population (aged ≥18, confirmed diagnosis of MS) that completed the demographic questionnaire about employment.

Results: 11,277 people with MS (pwMS) fitted the criteria, 2194 declared themselves as retired (19%). Mean age for retirees was 65.7±8.6 years (mean±standard deviation), compared to 50.1±10.3 years in non-retirees. 70.1% of retirements were due to a medical condition; 448 aged <60; 50% of the retired group declared an EDSS ≥ 6.5, compared to 34% in the overall population. There was a higher proportion of pwMS diagnosed with Secondary Progressive MS (SPMS) in the retired group (15.4%) compared to the overall population (6.0%), and a higher proportion whose current disease type was SPMS (36.6% compared to 18.4%). 78.8% of retirees had previously worked in Managerial, Professional or Administrative roles – higher than the 65.6% of the rest of the portal.

Conclusion: A significant proportion of the UKMSR population retires earlier than the general population. Their disability levels are also higher than the rest of the UKMSR and they have higher rates of progressive MS at diagnosis. Those retirees are in professions that would nominally appear to support them in continuing to work – perhaps with appropriate aids/breaks.

Disclosure: Nothing to disclose

EPR2145

Lifestyle and adherence to the Mediterranean diet within a Southern Italy cohort of Patients with Multiple Sclerosis

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Background and aims: The role of diet on Multiple Sclerosis (MS) has not been comprehensively elucidated. The objectives of the study are to: 1) Describe Lifestyle and dietary behaviours of a cohort of Southern Italy patients with MS; 2) Analyze their adherence to the Mediterranean Diet (MeDi) and its impact on MS.

Methods: We enrolled 435 patients. All participants underwent a clinical examination, updating disease phenotype, Expanded Disability Status Scale (EDSS), Multiple Sclerosis Severity Score (MSSS), ongoing disease-modifying therapy, and comorbidities. We collected biometric parameters and life and dietary habits, following the Med Diet Score (MDS). Higher values of MDS indicate a greater adherence to the MeDi. Face-to-face interviews were conducted. The questionnaire consisted of 29 items.

Results: 81.3% showed relapsing-remitting phenotype. At survey time, 72.8% of respondents were no smokers. 52.9% declared to regularly perform physical activity, 75.8% stated to be interested in nutrition and 45.6% used food supplements.

There was no significant heterogeneity in adherence to the MeDi in relation to socio-demographic and clinico-radiological features. To explore the influence of the MeDi on disease course, a multivariate linear regression analysis was performed to analyze the relationship between MDS and MS clinical measures. Significant inverse correlation between MDS and both MSSS ($\beta=-0.04$, $p=0.015$) and EDSS ($\beta=-0.03$, $p=0.014$), at survey time, were found (table 1).

	Median	IQR	Correlation with MDS	
			R	p
EDSS (baseline)	2.0	1.5 - 3.0	-0.09	0.055 ₁
	Median	IQR	Correlation with MDS	
			B	p
MSSS (at survey time)	2.8	1.3 - 4.9	-0.04	0.015*
EDSS (at survey time)	2.5	1.5 - 4.0	-0.03	0.014*

Table 2. A multivariate linear regression to analyze the relationship between MDS and MS clinical measures. Data were adjusted for sex, age, disease duration, ARR 1 year before baseline, disease phenotype, radiological and therapeutic features.

Table 1. A multivariate linear regression to analyze the relationship between MDS and MS clinical measures. Data were adjusted for sex, age, disease duration, ARR 1 year before baseline, disease phenotype, radiological and therapeutic features.

Conclusion: The dietary behavior influences disease outcomes of long term disability (EDSS, MSSS). Since neurodegeneration is associated to microinflammation the diet influencing low-grade chronic systemic inflammation, may impact on disease progression.

Disclosure: Nothing to disclose

EPR2146

Alemtuzumab-induced thyroid disease: observational data from an Italian cohort of patients

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Background and aims: Patients treated with Alemtuzumab are at the risk of developing secondary autoimmunity, mainly alemtuzumab-induced-thyroid disease (AITD), which occurs in 17-34% of cases and develops after 6 months following the 1st course, with a peak incidence after 3 years. AITD is a dynamic spectrum of diseases. The aim of this work is to describe AITD clinical presentation, evolution and management in a cohort of Italian Alemtuzumab treated-patients.

Methods: Data were collected from 10 Italian MS centers. Globally, 542 patients were treated between 2015-2019. Thyroid function tests (TF) were performed prior to drug administration and every 3 months.

Results: 98 (18.17%) patients developed AITD, mainly GD (48.27%), with a median onset 16 months after the last dose. In particular, 19,29% had AITD in the 1st year after 1st dose, 51.21% within the 1st and 2nd year and 30.5% after 2 years or more. The majority of AITD were quite easily resolved with a conservative approach, however, in a minority of cases, a fluctuating course developed, with a quick shift from hyperthyroidism to hypothyroidism and vice versa, hard to manage with medical therapy.

Conclusion: AITD incidence is expected to increase over time. A further increase in AITD has not yet emerged after two years due to a low proportion of patients with a longer follow-up. Based on our experience and in line with current recommendations, a strict thyroid-function monitoring prior and after alemtuzumab is fundamental, in order to detect and treat AITD promptly and have favorable outcomes.

Disclosure: LM has received compensation for speaking activities, and/or consulting services from Merck, Biogen, Novartis, Roche, Sanofi, and TEVA.

EPR2147

Pre-treatment with Natalizumab Reduces Risk of Alemtuzumab-Associated Secondary B-Cell Autoimmunities

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Background and aims: Alemtuzumab (ALEM) carries a substantial risk for secondary b-cell-mediated autoimmunities (sAI). Hyperrepopulation of immature B-cells following administration is considered the substrate of sAI. Natalizumab (NAT) hampers the transmigration of lymphocytes into the brain but also shifts precursor B-cells, including autoreactive clones, from the bone marrow to the peripheral circulation, potentially making them a substrate for consequent ALEM depletion. We therefore hypothesise, that pre-treatment with NAT could prevent ALEM associated B-cell hyperrepopulation and sAI.

Methods: We included 17 patients with multiple sclerosis switched from NAT to ALEM (NAT-ALEM cohort) and compared cell-surface and intracellular marker from peripheral blood mononuclear cells (PBMCs) measured by FACS to either a control cohort of 16 (natalizumab “naïve”) ALEM patients (nALEM cohort) or to the depletion rates from the CARE-MS-I.

Results: NAT-ALEM patients had significantly increased (naïve) B-cell frequencies at ALEM start (baseline, BL) compared to nALEM controls. After 12 months, CD19+ cells and naïve B-cells did not reach BL levels (-30%, -6% respectively) in the NAT-ALEM group, whereas they fully recovered in the nALEM group (+9%, +32% respectively). Moreover, the recovery rates of immature B-cells at month 12 showed a discrepancy of about 120% (-31% vs. +90% in the CARE-MS-I study population). Most impressively, only 2/17 (11,8%) NAT-ALEM patients developed sAI, in contrast to 50% in the control cohort.

Conclusion: We show that pre-treatment with NAT appears to substantially lower the incidence of ALEM-associated secondary autoimmunities, most likely by making precursor B-cells, including autoreactive clones, accessible to a subsequent CD52 depletion.

Disclosure: Tobias Moser received financial support by the austrian society of neurology (ÖGN).

EPR2148

TH17 Abundance Predicts Disease Reactivation after Natalizumab Withdrawal

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Background and aims: Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system, driven by an imbalance of inflammatory and regulatory immune cell subsets. However, the exact pathogenesis remains to be further elucidated. Here, we aimed to investigate the immunological signature of patients with reactivated disease after natalizumab discontinuation as compared to stable patients in order to define immunological markers for disease reactivation.

Methods: 26 patients switched from natalizumab (NAT) to fingolimod (FTY) were included in this study and divided into 2 groups depending on disease reactivation. We analysed peripheral blood mononuclear cells (PBMCs) by fluorescence- activated cell scanning (FACS) for various cell-surface and intracellular markers at timepoints 0 (baseline, just before FTY start) and months 1, 3, 6 and 12. The mean NAT wash-out phase was 11.4 weeks.

Results: 10 patients (38%) showed radiological or clinical disease activity in the 12 months observational period after switching to FTY. We found significant correlations between disease reactivation and frequency of TH17 cells. Interestingly, the 2 important regulatory subsets of the TH17 pathways, namely CD39+ regulatory T-cells (Tregs) and CD27+ natural killer (NK) cells, were significantly reduced. On the other hand, we found no associations between disease activity and TH1 cells, memory B-cells, as well as with the conventional regulatory subsets.

Conclusion: Active MS is strongly correlated with an imbalance of proinflammatory TH17 cells and their regulatory counterparts. Measuring TH17 pathways appears to be a proper monitoring tool for disease activity. Also, the inhibiting role of CD27+NK cells in MS deserves further attention.

Disclosure: Tobias Moser has received a research grant by the Austrian Society of Neurology (ÖGN).

EPR2149

Pharmacokinetic/pharmacodynamic properties of eculizumab support established efficacy in patients with NMOSD: findings from the phase 3 PREVENT study

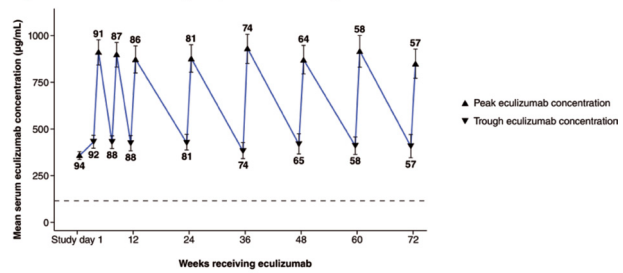
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Background and aims: During PREVENT (NCT01892345), patients with aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder who received eculizumab (n=96) had significantly lower risk of relapse than placebo (n=47). Eculizumab was EMA-approved in August 2019 for this indication.

Methods: The eculizumab group received intravenous 900mg/week for 4 weeks, followed by 1200mg² weeks (maintenance dose). Serum eculizumab concentration was measured by ELISA with lower limit of quantification (LLOQ) 9.38µg/mL. The target for complete complement inhibition was >116µg/mL. Serum free C5 concentration was measured by ELISA with LLOQ 0.027µg/mL; <0.5µg/mL represented complete complement inhibition. Haemolytic activity was measured using percentage chicken red blood cell (%cRBC) haemolysis semi-quantitative assay; <20% represented complete inhibition. Patients with ≥1 time-matched pharmacokinetic and pharmacodynamic measurement were included in the analysis. Trough/peak measurements were recorded. Cerebrospinal fluid (CSF) analysis was available for a subset of patients.

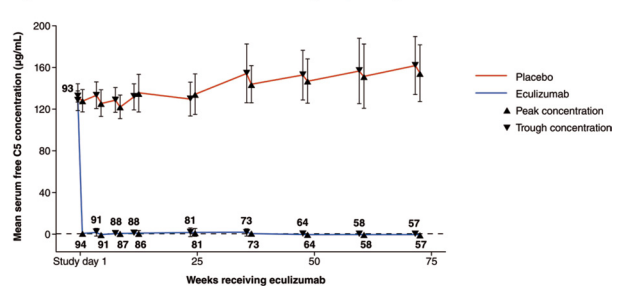
Results: After the 1st dose, mean serum eculizumab concentration was 359µg/mL (Figure 1); 813/841 (96.7%) of subsequent trough samples were >116µg/mL. Mean serum free C5 concentration dropped from 128µg/mL to 1.1µg/mL (Figure 2) and was <0.5µg/mL in 93/94 (98.9%) patients; 832/838 (99.3%) of subsequent trough samples were <0.5µg/mL. Mean haemolytic activity was reduced from 91.3% to 2.26% cRBC haemolysis (Figure 3); 815/834 (97.7%) of subsequent trough samples were <20%. CSF data from eight patients supported serum observations.

Figure 1. Mean serum eculizumab trough and peak concentrations during PREVENT



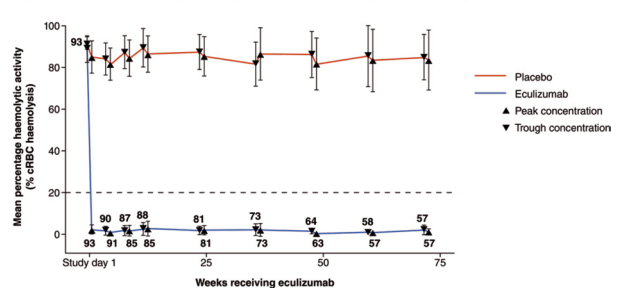
The numbers in bold represent the number of PK samples at each visit. Study day 1 trough value not shown was < LLOQ. Horizontal dotted line indicates target concentration of 116 µg/mL. Error bars represent 95% confidence intervals based on standard error of the mean. Only samples from scheduled visits from patients in the eculizumab group are shown. Eculizumab concentrations below the LLOQ (9.38 µg/mL) from samples after first eculizumab dose were analysed as 0.5 × LLOQ. Two trough (pre-dose) study day 1 samples with > LLOQ concentration were excluded. Of the 96 eculizumab-treated patients, no PK data were available for one patient. PK, pharmacokinetic; LLOQ, lower limit of quantification.

Figure 2. Mean serum free C5 concentrations at eculizumab trough and peak during PREVENT



The numbers in bold represent the number of free C5 samples in the eculizumab group at each visit. Horizontal dotted line indicates 0.5 µg/mL (< 0.5 µg/mL represents complete inhibition). Peak (post-dose) study day 1 mean was > 0.5 µg/mL, owing to one high free C5 value from a patient with a corresponding serum eculizumab sample concentration < LLOQ. Error bars represent 95% confidence intervals based on standard error of the mean. Only samples from scheduled visits are shown. Free C5 concentrations below the LLOQ (0.027 µg/mL) from samples after first eculizumab dose were analysed as 0.5 × LLOQ. Two trough (pre-dose) study day 1 samples with serum eculizumab concentration < LLOQ were excluded. Of the 96 eculizumab-treated patients, no free C5 data were available for one patient. C5, complement component 5; LLOQ, lower limit of quantification.

Figure 3. Mean percentage haemolysis activity (percentage cRBC haemolysis) at eculizumab trough and peak during PREVENT



The numbers in bold represent the number of haemolysis samples in the eculizumab group at each visit. Horizontal dotted line indicates 20% cRBC haemolysis (< 20% represents complete inhibition). Error bars represent 95% confidence intervals based on standard error of the mean. Only samples from scheduled visits are shown. Two trough (pre-dose) study day 1 samples with serum eculizumab concentration > LLOQ were excluded. Of the 96 eculizumab-treated patients, no haemolysis data were available for one patient. cRBC, chicken red blood cell; LLOQ, lower limit of quantification.

Conclusion: Serum eculizumab was maintained at >116µg/mL, resulting in rapid, complete and sustained inhibition of serum free C5 (<0.5µg/mL) and haemolytic activity (<20% cRBC haemolysis) for most samples. Pharmacokinetic/pharmacodynamic data corroborate reduced risk of relapse with eculizumab during PREVENT.

Disclosure: Research funding for this study was provided by Alexion Pharmaceuticals.

Muscle and neuromuscular junction disease 2

EPR2150

Paraneoplastic and non paraneoplastic Lambert-Eaton Myasthenic Syndrome: a retrospective descriptive study

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Background and aims: Clinical and electrophysiological characteristics that allow to distinguish paraneoplastic (PN) Lambert-Eaton myasthenic syndrom (LEMS) from non PN are largely unknown. The aim of this study is to describe the electrophysiological triad of LEMS on different nerve/muscle couples and to compare these characteristics between PN and non PN LEMS.

Methods: We retrospectively analyzed the electrophysiological data (compound muscle action potential (CMAP) amplitude at rest, decrement at 3Hz stimulation, increment after brief exercise) from the 19 LEMS diagnosed at Pitié Salpêtrière from January 2009 to December 2019. We compared characteristics of the 11 PN LEMS with the 7 non PN LEMS (the remaining diagnostic assessments being unavailable).

Results: Median/abductor pollicis brevis (M/APB) and ulnar/abductor digiti quinti (U/ADQ) were the most often altered couples (decrement in 100% resp. 86.4% of cases, increment in 100% resp. 89.3% of cases). The decrement worsened after the 5th stimulation in 63.3% of cases. The CMAP amplitude was most often decreased for PN LEMS (93.2% vs 69.4%). A decrement at 3Hz stimulation was most frequent for PN LEMS (78.1% vs 53.2%), as well as an increment after brief exercise (84.1% vs 59.4%).

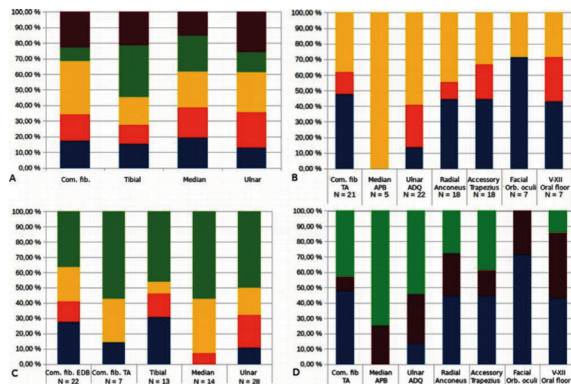


Figure 1. Electrophysiological data according to the nerve/muscle couple for the whole cohort
A: Compound muscle action potential (CMAP) amplitude at rest at diagnosis according to the nerve/muscle couple. Blue: Normal (N); Orange: [0,5N – N]; Yellow: [0,2N – 0,5N]; Green: [0,1N – 0,2N]; Brown: < 0,1N
B and D: Severity (B) and pattern (D) of the decremental response at 3Hz stimulation at diagnosis according to the nerve/muscle couple. Blue: no significant decrement; Orange: decrement of 10 to 20%; Yellow: decrement > 20%; Brown: decrement that does not worsen after the 5th stimulation, in “U”; Green: progressive decrement, that keeps worsening after the 5th stimulation
C: Increment after brief exercise at diagnosis according to the nerve/muscle couple. Blue: no significant increment; Orange: Increment of 60 to 100%; Yellow: Increment of 100 to 200%; Green: Increment > 200%
 Com. fib.: Common fibular; TA: Tibialis anterior; APB: Abductor pollicis brevis; ADQ: Abductor digiti quinti; Orb. oculi: Orbicularis oculi; EDB: Extensor digitorum brevis

Figure 1: Electrophysiological data according to the nerve/muscle couple for the whole cohort

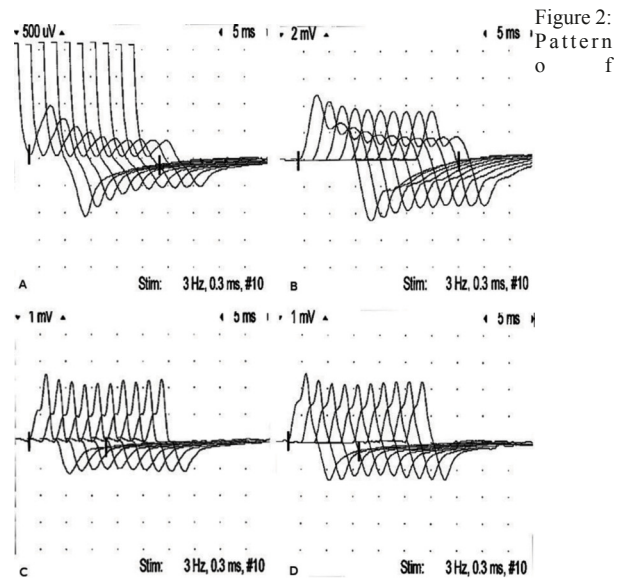


Figure 2. Pattern of decremental response at 3Hz repetitive stimulation
A and B: Progressive decrement, that keeps worsening after the 5th stimulation A: Ulnar/abductor digiti quinti; B: Common fibular/tibialis anterior
C and D: Decrement in “U”, that does not worsen after the 5th stimulation. Ulnar/abductor digiti quinti of other patients

decremental response at 3Hz repetitive stimulation

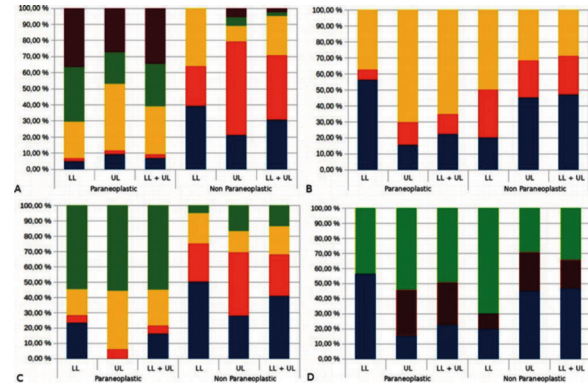


Figure 3. Comparison of electrophysiological data between paraneoplastic and non paraneoplastic Lambert-Eaton Myasthenic Syndrome

A: Compound muscle action potential (CMAP) amplitude at rest at diagnosis according to the limb. Blue: Normal (N); Orange: [0,5N – N]; Yellow: [0,2N – 0,5N]; Green: [0,1N – 0,2N]; Brown: < 0,1N
B and D: Severity (B) and pattern (D) of the decremental response at 3Hz stimulation at diagnosis according to the limb. Blue: no significant decrement; Orange: decrement of 10 to 20%; Yellow: decrement > 20%; Brown: decrement that does not worsen after the 5th stimulation, in “U”; Green: progressive decrement, that keeps worsening after the 5th stimulation
C: Increment after brief exercise at diagnosis according to the limb. Blue: no significant increment; Orange: Increment of 60 to 100%; Yellow: Increment of 100 to 200%; Green: Increment > 200%
 LL: Lower Limb; UL: Upper Limb; Global: LL + UL + Face

Figure 3: Comparison of electrophysiological data between paraneoplastic and non paraneoplastic Lambert-Eaton Myasthenic Syndrome

Conclusion: The M/APB and U/ADQ couples are particularly sensitive for the diagnostic of LEMS. The electrophysiological pattern of PN LEMS seems to be more severe as non PN, for CAMP amplitude as well as decrement and increment. If confirmed in a validation cohort, the severity of the electrophysiological picture could be included in a prediction score of PN LEMS.

Disclosure: Nothing to disclose

EPR2151

Efgartigimod in Myasthenia Gravis: Phase 3 Trial Design

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Introduction: Myasthenia gravis (MG), an autoimmune disease causing debilitating muscle weakness, is mediated by IgG autoantibodies. Neonatal Fc receptor (FcRn) recycles IgG extending its half-life. Efgartigimod, a human IgG1 antibody Fc-fragment engineered for optimal blocking of FcRn, outcompetes endogenous IgG-binding, prevents IgG recycling, reducing IgG and autoantibody levels.

Methods: This 26-week, randomised double-blind, placebo-controlled Phase 3 trial of efgartigimod evaluates efficacy, safety, and quality of life in patients (age >18 years) diagnosed with generalized MG class II, III, and IV on stable concomitant standard of care MG therapy. Inclusion criteria are MG-ADL score of ≥ 5 points (>50% non-ocular). A maximum of 20% of acetylcholine receptor antibody (AChR-Ab) seronegative patients will be allowed in the trial. Following screening, eligible patients receive 4 weekly doses of IV 10mg/kg. Subsequent treatment is tailored according to clinical condition, based on MG-ADL score.

Results: 167 patients enrolled at 51 sites in 15 countries. Efficacy endpoint is the percentage of AChR-Ab seropositive patients whose MG-ADL decreases within the first treatment cycle by at least 2 points from baseline for ≥ 4 consecutive weeks. 2ndary endpoints include additional MG-ADL and QMG assessments.

Conclusion: Efficacy and safety findings will be reported at the conclusion of the trial.

Disclosure: Clinical trial supported by argenx BVBA

EPR2152

Rest or Exercise (RESTOREX) in Myasthenia Gravis: a randomized controlled trial

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Background and aims: In Myasthenia Gravis (MG), the effect of exercise is not well known. In this study the efficacy and safety of exercise in MG in comparison to rest is presented

Methods: In this single-center open-labeled randomized clinical trial the patients were randomized to exercise (30min walk) or rest. The Primary endpoint was 50% change in Myasthenia Gravis Quality of Life (MG-QOL15) at 3 months and 2ndary endpoints were change in Myasthenic Muscle Score (MMS), Myasthenia Gravis Activities of Daily Living (MGADL), grip strength, AChEI and prednisone dose, 6 minute walk test (6MWT), decrement in trapezius muscle and adverse events

Results: 20 patients in each arm, were matched for demographic and clinical parameters. The patients in exercise arm had significantly better MG-QOL15 (P=0.02), increase in number of steps (P=0.03) and the distance covered in 6MWT (P=0.003). The scores of MG-QOL15 (P=0.03), MMS (P=0.048), and distance travelled (P<0.001) also revealed significant group difference. Intragroup comparison revealed that both exercise and rest arm significantly improved with respect to MG-QOL15 in exercise (P=0.001) and rest (P=0.001), MMS in exercise (P=0.001) and rest (P=0.001), reduction in pyridostigmine (P=0.03) and prednisone (P=0.001) dose in exercise, increase in number of steps in exercise (P=0.001) and increase in walking distance in 6MWT in both exercise (P=0.001) and rest arm (P=0.023). There was no adverse event in any group

Conclusion: The study provides class II evidence of improved quality of life in mild to moderate MG by 30 min walk compared to rest

Disclosure: Nothing to disclose

EPR2153

AChR antibody positivity rate in ocular myasthenia gravis: a matter of age?

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Background and aims: Anti-acetylcholine receptor antibodies (AChR Abs) are detected in 85-90% of patients with generalized myasthenia gravis (GMG), with higher positivity rates in late-onset cases. AChR Ab sensitivity is thought to be much lower in ocular MG (OMG), though in a recent study it was as high as 70.9% in association with increasing age of onset.

We hypothesized that, like in GMG, there has been, in the last decades, a shift in OMG age at onset towards a higher prevalence of late-onset cases that may account for increased AChR Ab sensitivity.

Methods: We compared patients with symptom onset before (N=69) and after January 1st, 1998 (N=100). All had purely OMG over a follow-up ≥ 2 years. AChR Ab were tested by radioimmunoassay. Seronegative cases had increased jitter on single fiber-electromyography and/or positive response to neostigmine. Onset age, sex, presence of thymoma, AChR Ab positivity were recorded. The correlation between clinical variables and Ab result was evaluated by multiple logistic regression (MLR) analysis.

Results: Age at onset, male/female ratio and AChR Ab positivity rate were significantly increased in the population with onset in the last 2 decades; thymoma frequency was similar in the 2 series. These data are shown in the table. On MLR analysis the only variable associated with AChR Ab positive result was OMG onset after 50 years-of-age ($p < 0.00001$).

	Onset before 1998 69 patients	Onset since 1998 100 patients	p
Age at onset, years (mean \pm SD)	35.4 \pm 18.69	55.05 \pm 17.68	< 0.00001 [§]
Age at onset \geq 50 years	20/69 (29%)	67/100 (67%)	< 0.0001*
Male/female ratio	39/30 (1.3/1)	76/24 (3.17/1)	0.0115*
Rate of thymoma patients	4/69 (5.8%)	6/100 (6%)	NS*
AChR Ab positivity	36/69 (52%)	73/100 (73%)	0.0086*

[§]Mann-Whitney Test; * Fisher Exact Test; NS = not significant

Table: characteristics of OMG patients

Conclusion: From our results, current AChR Ab sensitivity in OMG may be higher than generally thought. This finding was associated with a rising prevalence of late-onset cases, paralleling epidemiological changes in GMG.

Disclosure: Nothing to disclose

EPR2154

Diagnostic value of NGS in distal myopathies

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Background and aims: Distal myopathies (DM) are a heterogeneous group of muscle diseases caused by mutations in different genes. The new generation sequencing technology (NGS) has improved the diagnosis, although a proportion of patients remain still undiagnosed.

The objective was to evaluate the efficiency of a NGS approach using a self-costumed panel of neuromuscular genes in patients with DM.

Methods: 75 patients who remained undiagnosed of a series of 125 cases with DM on follow up in a Neuromuscular Unit in the Valencia Country were studied. 35 cases were sequence by PANEL1 (40 genes; Ion Torrent technology) during 2016-2017 and 40 cases were sequence by PANEL2 harboring of 272 genes based on Illumina technology from 2017-2019.

Results: A definitive molecular diagnosis was reached in 45% of the investigated cases, being the frequency of genes as follows: 27% ANO5, 18% TTN, 9% DYSF, 9% MYOT, 6% GNE, 6% HSPB1, 6% MYH7 and a single case was detected of each of these genes: HNRPDL, VCP, COL6A2, BICD2, EMD, NEB and TPM2. A probable diagnosis was obtained in 16% cases, with the following yield: ANO5, TTN, TCAP, DYSF, POLG, CAPN3, COL6A1, BAG3, HNRPDL and LDB3. 39% of the cases remained unsolved.

Conclusion: Our results demonstrated the efficacy of NGS in the diagnosis of DM. This approach is also useful to diagnose atypical phenotypes in DM. However, this procedure provides a large amount of unprocessed data that requires experience and sometimes biological analysis in tissues or cells to confirm the pathogenicity of the variants found.

Disclosure: This research has been granted support by: - Carlos III Research Institute projects: PI11/0203 and PI16/00316 - ISABEL GEMIO FOUNDATION FOR THE RESEARCH OF MUSCLE DYSTROPHIES AND OTHER RARE DISEASES: 2018/0200

EPR2155

The prevalence of inherited neuromuscular disorders in Northern Norway

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Background and aims: Epidemiological studies on inherited neuromuscular disorders are important to plan for better health care services. In this study, we aim to investigate the point prevalence of inherited neuromuscular disorders in Northern Norway.

Methods: This study was based on patient registries and electronic patient records, and performed in Northern Norway, with a point prevalence estimated for 10th October 2019

Results: We identified 539 patients, giving a total point prevalence of 110.8/100,000 (95%CI 101.8–120.6). The prevalence of children (<18 years old) and adults (≥18 years old) were 55.7/100,000 (95%CI 42.7–72.6/100,000) and 124.5/100,000 (95%CI 113.9–136.1/100,000), respectively. The prevalence of inherited neuropathies, myopathies and spinal muscular atrophies were 38.6/100,000 (95%CI 33.5–44.2/100,000), 66.6/100,000 (95%CI 59.7–74.3/100,000) and 3.7/100,000 (95%CI 2.3–5.8/100,000), respectively. Disease specific point prevalence was among others Charcot-Marie-Tooth 30.0/100,000 (95%CI 25.5–35.3/100,000), hereditary neuropathy with liability to pressure palsies 8.0/100,000 (95%CI 5.9–11.0/100,000), myotonia congenita 11.7/100,000 (95%CI 9.0–15.2/100,000), myotonic dystrophy type I 13.4/100,000 (95%CI 10.5–17.0/100,000), myotonic dystrophy type 2 6.4/100,000 (95%CI 4.5–9.0/100,000), Duchenne muscular dystrophy 7.3/100,000 (95%CI 4.6–11.5/100,000), Becker muscular dystrophy 1.6/100,000 (95%CI 0.6–4.1/100,000), facio-scapulohumeral muscular dystrophy 3.7/100,000 (95%CI 2.3–5.8/100,000), and limb-girdle muscular dystrophy 12.7/100,000 (95%CI 9.9–16.3/100,000).

Conclusion: The prevalence of inherited neuromuscular disorders in Northern Norway is higher than previously suggested in European studies. The prevalence was especially high for myotonia congenita and limb-girdle muscular dystrophy, but Charcot-Marie-Tooth neuropathy was lower than previously reported in the Norwegian population.

Disclosure: Nothing to disclose

EPR2156

Long-term follow-up in presymptomatic LOPD patients

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Background and aims: Late-onset Pompe disease (LOPD) is characterized by a wide spectrum of clinical presentations ranging from classical forms with manifested muscle weakness and/or respiratory impairment to isolated hyperckemia. A better awareness of the disease and the diffusion of newborn screening programs increased number of patients diagnosed at presymptomatic stage. The identification of these patients raises the consideration how to follow these patients in the view of early detection of disease progression to start therapy.

Methods: Herein we report on 8 patients with presymptomatic Pompe disease followed at our Neuromuscular Unit since the diagnosis was made. Patients were followed every 6-12 months with clinical examination including functional tests, pulmonary function tests and muscle MRI

Results: The patients had a mean age of 29 (range 4-58) years, a median follow-up duration of 10 (range 4-15) years. All patients were diagnosis because of isolated hyperckemia (CK range 400 to 1100IU) and/or myalgia. Muscle biopsy revealed a vacuolar myopathy with glycogen storage in 4 pts whereas was unspecific in 3pts, not performed in 1. Muscle GAA residual activity range from 3.8% to 15%. 2 patients, after respectively 9 and 6 yrs of follow-up, start ERT because of detection of signs of muscle weakness and respiratory impairment. 6pts were stable over the years with only persistent mild hyperckemia but no other signs of progression.

Conclusion: Our data demonstrated that presymptomatic LOPD patients may remain clinically silent for decades but they should be monitored closely for overt signs of the disease to promptly start ERT

Disclosure: Nothing to disclose

EPR2157

Motor Function Change Over Time Among Nusinersen-Treated Participants with Infantile-onset Spinal Muscular Atrophy (SMA) in the ENDEAR-SHINE Study Who Met the Permanent Ventilation (PV) Definition

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Background and aims: Participants with infantile-onset SMA who completed the Phase 3 ENDEAR study (NCT02193074) were eligible to receive nusinersen in the open-label extension study, SHINE (NCT02594124).

Methods: At final analysis of the ENDEAR study, 68% of control and 39% of nusinersen-treated participants had died or received PV (defined as tracheostomy or ≥ 16 hours/day of ventilatory support continuously for >21 days in the absence of an acute reversible event). Participants requiring PV in ENDEAR could continue into SHINE. Post hoc analyses (15 October 2018 SHINE data cut) evaluated motor function change for nusinersen-treated participants in ENDEAR, who continued into SHINE and reached PV in either study.

Results: The median (min, max) time from 1st nusinersen dose to date of PV (in ENDEAR or SHINE) was 90.5 (38, 525) days (n=24). For participants on nusinersen, median (min, max) time was 207 (23, 387) days from date of PV to last assessment in ENDEAR (n=18) and 922 (272, 1300) days to last assessment in SHINE (n=24). The majority of participants who reached PV in ENDEAR-SHINE (n=24) demonstrated improvements in total HINE-2 and CHOP INTEND scores over time following PV. Among participants with ≥ 2 evaluable efficacy assessments following PV (n=21), mean improvements (SD) in HINE-2 and CHOP INTEND scores from 1st available assessment following PV to last study visit were 3.0 (3.4) and 4.1 (7.6), respectively; range of time between assessments was 126–1234 days.

Conclusion: Participants treated with nusinersen who reached PV during ENDEAR-SHINE continued to demonstrate clinical benefit assessed via motor function change over time.

Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Horsham, UK): funding was provided by Biogen.

EPR2158

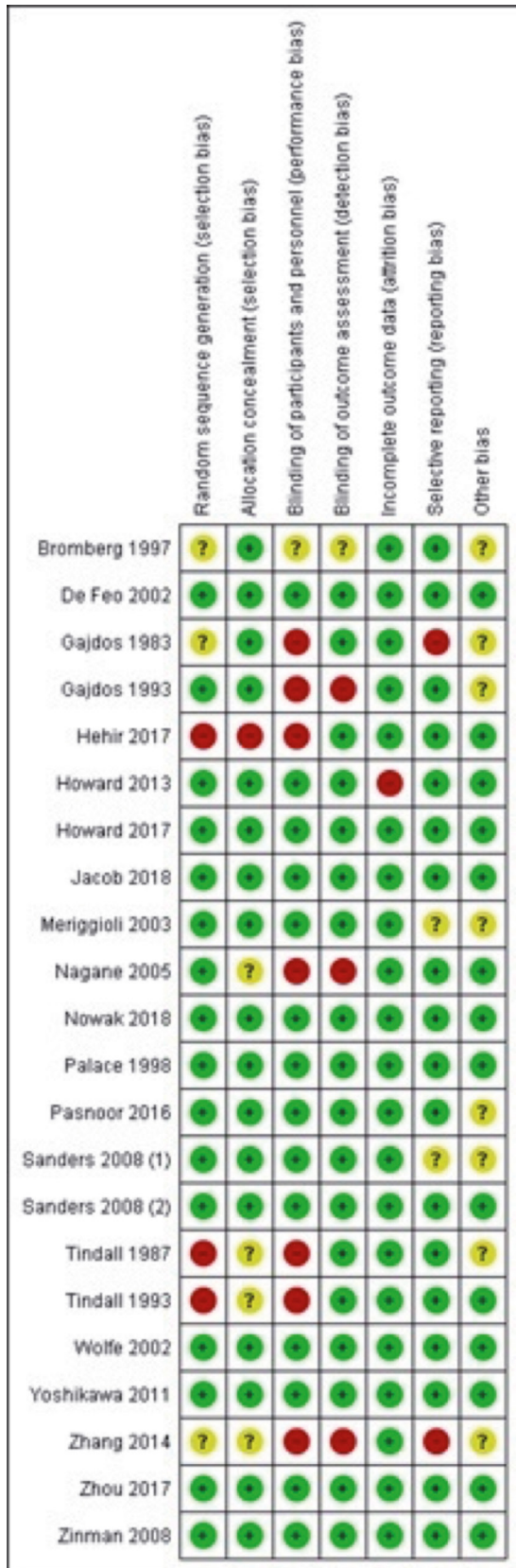
Efficacy and safety of non-steroidal immunosuppressive treatments in Generalized Myasthenia Gravis patients. A systematic review and meta-analysis

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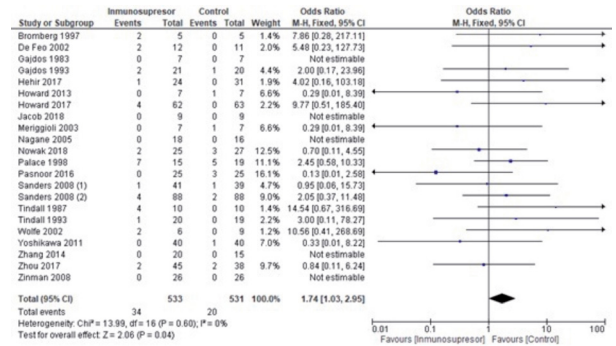
Background and aims: Myasthenia Gravis (MG) treatment consists of the use of acetylcholinesterase inhibitors, corticosteroids and, in cases of insufficient response, immunosuppressive treatments. Our aim is to evaluate the efficacy and safety of immunosuppressive drugs in generalized MG through a systematic review and meta-analysis.

Methods: We performed a systematic review (PUBMED, EMBASE and Clinical trials gov, 2 January to 1 February 2019) to identify all the randomized clinical trials and cohort studies evaluating the effects of adding immunosuppressive drugs to the treatment of patients with generalized MG. Data analysis was performed using Review Manager 5 software and results were summarized as odds ratio (OR), mean difference and 95% confidence intervals (CI). We evaluated: (1) change in the Quantitative Myasthenia Gravis (QMG) score at the end of the study from baseline and (2) number of dropouts due to adverse events (AE).



Risk of bias summary

Results: A total of 323 manuscript were retrieved in the systematic review. We selected 22 articles. Treatment with tacrolimus, cyclosporine, cyclophosphamide, rituximab and eculizumab showed significant effects on the QMG score. There were more dropouts in the experimental groups compared to placebo, with statistically significant differences (OR 1.74, 95%CI 1.03-2.95).



Forest plot of meta-analysis of EA in all the studies, odds ratios, overall odds ratios and 95% CI related to each categorical outcome measure

Conclusion: Tacrolimus, rituximab and eculizumab stand out as the treatments with better efficacy and safety profile in generalized MG resistant to 1st-line treatments, although more studies with greater homogeneity are needed to draw conclusions that lead to algorithms of therapeutic decision.

Disclosure: Nothing to disclose

Neuroepidemiology; Neurotoxicology; Neurotraumatology

EPR2159

Laugh is in the air: a case series of neurological problems due to recreational use of laughing gas.

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Background and aims: In recent years recreational use of laughing gas (nitrous oxide) has grown more popular. Well known adverse effects include polyneuropathy or subacute spinal cord degeneration due to vitamin B12 deficiency. Therefore, the number of patients presenting with these types of neurological problems is increasing.

Methods: Case series describing clinical features and ancillary investigations of patients using laughing gas, presenting at our outpatient clinic and emergency department during 2017-2019.

Results: We found 12 patients with a median age of 21 years, of which eight presented in 2019. Common complaints were paresthesias and lower limb weakness. 7 patients were diagnosed with axonal polyneuropathy using EMG. In 4 patients MR imaging showed T2-hyperintensities of the cervical dorsal columns, indicating subacute spinal cord degeneration. There was no correlation between clinical presentation and the cumulative amount of laughing gas used. All patients received vitamin B12 suppletion and were advised to stop using laughing gas. Whereas most patients fully recovered, some retained minor symptoms. 2 patients experienced problems in activities of daily living and were referred to a rehabilitation physician.

Conclusion: Due to increased recreational use of laughing gas more patients with neurological complaints have been presenting at our hospital, especially those of younger age. This is probably an underestimation, assuming patients with minor complaints might not seek medical help. With vitamin B12 suppletion and complete cessation of laughing gas use, symptoms may fully disappear. In some cases however, complaints may persist.

Disclosure: Nothing to disclose

EPR2160

Myelopathy after nitrous oxide inhalation

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Background and aims: Nitrous oxide (N₂O) is a common medical inhalational anaesthetic but it's also widely used for recreational activities. N₂O irreversibly alters B12 activation, causing posterior myelopathy and sensorimotor polyneuropathy.

Methods: Case report

Results: Case 1

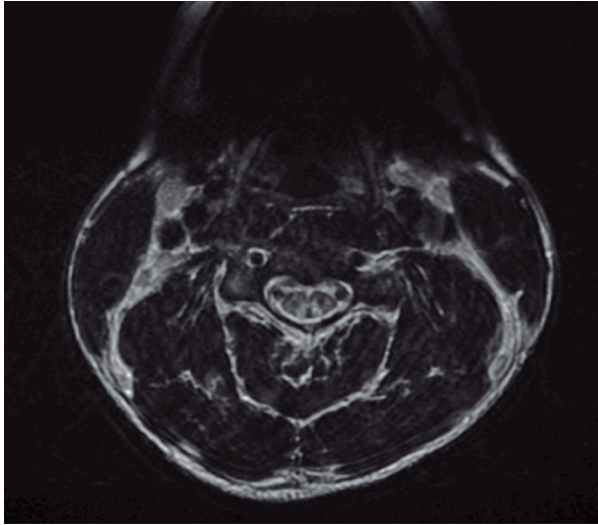
A 30-year-old man, vegetarian, was admitted with paresthesia, progressive motor deficit of the 4 limbs, inability to walk, bladder impairment and fecal incontinence within 6 days after using N₂O for 4 hours. Clinical examination showed a sensory deficit up to T3-T4 level, proprioceptive loss, tetraparesis with distal predominance, anal sphincter hypotonia, Lhermitte's sign. MRI of the spinal cord showed abnormal T2-weighted hyperintensity in the posterior area at C3-C5 levels, without contrast enhancement. B12 was 131pmol/dl. CSF was normal and all infectious and autoimmune investigations were negative. Urines were positive for benzodiazepine. He was treated with high doses of B12 and corticosteroids showing clinical improvement but had permanent sequelae at 12 months.

Case 2

A 28-year-old man started using nitrous oxide, 3-4 capsules/day for 4 days (cannabis withdrawal context). He complained of distal paresthesias of upper limbs, Lhermitte's sign and anxiety. Clinical examination was normal. MRI of the spinal cord showed hyperintensity in T2 in the posterior area of C5-C7. Other tests (including CSF, B12 and homocysteine) were normal. High doses of B12 vitamines rapidly improved the sensory symptoms.



Cervical MRI case 1: abnormal T2 weighted hyperintensity in the posterior aspect of C3-C5



Cervical axial MRI case 1 abnormal T2 hyperintensity in the posterior columns

Conclusion: We present 2 cases of myelopathy after nitrous oxide inhalation that illustrate the clinical variability and the risks related to its consumption.

Disclosure: Nothing to disclose

EPR2161

Short-term outcomes of immediate post-traumatic seizures after lateral fluid percussion brain injury in rats

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Background and aims: Immediate and early seizures are important pathophysiological consequence of tissue damage in traumatic brain injury (TBI). They also represent a significant risk factor for post-traumatic epilepsy (PTE) development. A thorough analysis of acute seizures and their consequences are complicated in clinical studies. Our study aimed to analyze immediate post-traumatic seizures, hemodynamic, breathing and reflexes disturbances after TBI in rats.

Methods: The study was performed on 60 male Wistar rats aged 6 months. Craniotomy localized above right sensorimotor cortical area was performed under isoflurane anesthesia. After complete awakening from anesthesia, TBI was modelled using lateral fluid percussion. During the impact itself and following 5 min, video-recording was carried out. The recordings were analyzed for jumps, running, walking movement, tonic and clonic components of the seizure, tail seizures, apnea periods, ataxic breathing, loss of righting reflex and pain sensation.

Results: Immediate post-traumatic seizures were observed in 100% of animals and were highly heterogeneous, similarly to human ones. Strong correlations between duration of seizure and loss of righting reflex, pain sensation and posture recovery were found. Hemodynamic changes contributed to longer recovery time after seizure. Prolonged immediate seizures, ataxic breathing, loss of reflexes were associated with acute mortality.

Conclusion: We analyzed for the 1st time detailed semiology of immediate post-traumatic seizures in rats. The duration of immediate seizures correlates with loss of reflexes and predicts mortality. The results confirm an importance of acute seizures in the pathogenesis of TBI.

Disclosure: Supported by RFBR, grant №19-015-00258

EPR2162

Association of social relationships with incident cardiovascular events and all-cause mortality

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Background and aims: To examine how different aspects of social relationships are associated with incident cardiovascular events and all-cause mortality.

Methods: In 4139 participants from the population-based Heinz Nixdorf Recall study without previous cardiovascular disease (mean (standard deviation) age 59.1 (7.7) years, 46.7% men), the association of self-reported instrumental, emotional, and financial support and social integration at baseline with incident fatal and non-fatal cardiovascular events and all-cause mortality during 13.4-year-follow-up was assessed in 5 different multivariable Cox proportional hazards regression models: minimally adjusted model (adjusting for age, sex, social integration or social support, respectively); biological model (minimally adjusted + systolic blood pressure, low-density and high-density lipoprotein cholesterol, glycated hemoglobin, body-mass-index, antihypertensive-, lipid-lowering-, and antidiabetic medication); health behavior model (minimally adjusted + alcohol consumption, smoking, physical activity); socio-economic model (minimally adjusted + income, education, employment); depression model (minimally adjusted + depression, antidepressants, anxiolytics).

Results: 339 cardiovascular events and 530 deaths occurred during follow-up. Lack of financial support was associated with an increased cardiovascular event risk (minimally adjusted hazards ratio=1.30 (95% confidence interval=1.01-1.67)). Lack of social integration (social isolation) was associated with increased mortality (minimally adjusted hazards ratio=1.47 (1.09-1.97)). Effect estimates did not decrease to a relevant extent in any regression model.

Conclusion: Perceiving a lack of financial support is associated with a higher cardiovascular event incidence and being socially isolated is associated with increased all-cause mortality. Future studies should investigate how persons with deficient social relationships could benefit from targeted interventions.

Disclosure: Nothing to disclose

EPR2163

Hereditary peripheral neuropathies in Bulgaria: genetic and ethnic features

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Background and aims: Hereditary peripheral neuropathies (HPN) are a heterogeneous group of diseases caused by mutations in more than 80 genes. They are the most common hereditary neurological disease, though their prevalence varies among the different populations. The purpose is to determine the genetic variety between the main ethnic groups in Bulgaria (Bulgarian, Roma and Turk), their distribution in the different administrative districts in the country.

Methods: 3 sources of data were used: 1.patients that were referred to the Expert Centre for Hereditary Neurologic and Metabolic Disorders, 2.field studies and screening programs in more than 2500 towns and villages in the country, 3. National Genetic Laboratory database.

Results: In total 835 patients with genetically confirmed mutations were included. In 542 Bulgarians, living in 25 districts, were found mutations in 12 different genes (PMP22, YARS, MPZ, GJB1, GARS, MFN2, HINT1, HSP22, SH3TC2, NDRG1, GDAP1, BSCL2). In the Roma population (n=262), inhabiting 22 districts, were determined genetic defects in 7 different genes (NDRG1, CTDP1, HK1, HINT1, GJB1, PMP22, MPZ). In 31 Turks, living in 7 districts, were confirmed genetic defects in 5 genes (GJB1, PMP22, MPZ, BSCL2, HINT1). The mutations were inherited in different traits: autosomal dominant HPN were observed in 86.3% of the Bulgarians, autosomal recessive HPN - in 95.4% of Roma patients, and X-linked mutations - in 48.4% of the Turks.

Conclusion: Genetic heterogeneity was found among the population in Bulgaria, as well as all inheritance patterns (autosomal-dominant, autosomal-recessive and X-linked). Specific ethnic distribution of the mutations and inheritance manners were determined.

Disclosure: Nothing to disclose

EPR2164

Electrographic changes and mortality in early period of traumatic brain injury: From humans to animal model

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Background and aims: Nonconvulsive electrographic seizures (ES) and epileptiform activity (EA) in early period of TBI often remain undiagnosed. The aim of the study was (1) to reveal occurrence and short-term outcomes of ES and EA in patients with acute TBI on invasive ECoG recordings and compare its sensitivity with scalp EEG recordings; (2) to determine possible neural substrate of early post-traumatic EA using a TBI model in rats.

Methods: ECoG (mean 37h) were recorded in 11 patients with acute TBI subjected to surgical treatment with a decompressive craniotomy. Abnormalities were obtained in scalp EEG and invasive ECoG recordings. TBI in 36 adult male Sprague-Dawley rats was modeled using lateral fluid percussion. ECoG and local field potentials were recorded in animals during 7 days before and after TBI to reveal early electrographic abnormalities and an involvement of cortico-hippocampal and cortico-thalamic networks.

Results: EA was recorded in 18% of patients using scalp EEG and in 45% using EEG with ECoG; rhythmic periodic patterns were recorded in 64 vs.91% of patients; ES was recorded in 45% vs.55% of patients. Levels of consciousness predicted mortality during hospitalization.

ECoG abnormalities in almost all rats were independently registered in the cortex (spike-wave discharges) and hippocampus (spikes). The duration of loss of reflexes after TBI predicted acute mortality.

Conclusion: Using ECoG in patients subjected to surgical treatment after TBI increase detectability of acute electrographic abnormalities. In rats they involve cortical and hippocampal networks independently. Loss of consciousness predicts mortality both in patients and in experimental animals.

Disclosure: Supported by RFBR, grant №19-015-00258

EPR2165

Premature mortality and causes of death of people with epilepsy in South Korea

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Background and aims: Previous studies have consistently reported premature mortality of people with epilepsy. However, there is no epidemiological study about mortality of people with epilepsy in South Korea.

Methods: Using the National Health Insurance Service database and National Death Registry of Korea, a retrospective cohort study of people with epilepsy was carried out. Epilepsy patients was defined as a current medication history of antiepileptic drugs AND the presence of International Classification of Disease (ICD)-10 codes of G40* (epilepsy), G41* (status epilepticus), F803 (Landau-Kleffner syndrome), and R56 (convulsion). Incident case was defined as epilepsy patients with 2-year disease free period. Specific causes of death were recorded according to ICD-10 codes.

Results: Using incident patient cohort from 2009 to 2017, 20,213 deaths (among total 138,998 incident patients) were recorded. Overall mortality (standardized mortality ratio, SMR) in incident people with epilepsy was 2.36 (95% CI, 2.33-2.40). The SMRs attenuated with increasing age and disease duration. The SMRs were associated with residence, household income, disease burden, history of status epilepticus, and comorbid disease. The common causes of death were cancer (N=4,503, proportional mortality ratio, PMR: 22.4%), Sequelae of cerebral vascular disease (N=2,044, 10.2%), External causes (N=1,441, 7.2%), and Pneumonia (N=1,198, 6.0%). Among external causes, suicide was the most common cause of death (N=525, 2.6%).

Conclusion: In South Korea, people with epilepsy have a higher risk of premature death. Although symptomatic causes of epilepsy were the most common causes of death, there are many preventable deaths such as suicide.

Disclosure: Nothing to disclose

EPR2166

Prognostic assessment of combined NSE and S100 biomarkers on cognitive outcome after Traumatic Brain InjuryD.F. Muresanu¹, D. Slavoaca², S. Strilciuc²*¹Neurosciences, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj, Romania, ²Neurosciences, "RoNeuro" Institute for Neurological Research and Diagnostic, Cluj-Napoca, Romania*

Background and aims: Traumatic Brain Injury (TBI) is considered a possible risk factor for development of late-life dementia. The link between TBI and dementia development is inconclusive throughout the literature. We explored the association between TBI and dementia development cascade, specifically to investigate whether biomarkers Neuron-Specific Enolase (NSE) and S100 calcium-binding protein B associated are predictors for cognitive outcome after TBI.

Methods: We performed 2ndary data analysis on TBI patients from a single-center clinical trial. NSE and S100 were determined at 48 and 72 hours after admission and neurocognitive outcomes were measured at study days 10, 30 and 90. Pooled ensembles were included in multivariate linear regression models to determine the predictive value of NSE, S100 and their combination on a multidimensional ensemble of TBI outcome scales, controlling for severity of the injury, age, and gender.

Results: A total of 142 patients aged 19-79 with a diagnosis of TBI were included in multivariate linear regression models. A strong prediction value of NSE and S100 at 24h was observed for Hospital Anxiety Depression Scale (30, 90 days), Stroop Color-Word Test, Digit Span (30, 90 days) and Processing Speed Index (10, 30, 90 days) and the combined outcome ensemble.

Conclusion: Using several indicators in conjunction to create a composite biomarker for TBI outcome appears to be a more robust approach for prediction of cognitive outcome.

Disclosure: Nothing to disclose

EPR2167

Post-traumatic Transient Neurologic Dysfunction: A Proposal for PathophysiologyC. Oh¹, S.-Y. Lee², S.J. Lee², J.H. Phi³*¹Department of Neurology, Kangwon National University Hospital, Chuncheon, Korea, Republic of, ²Department of Neurology, Kangwon National University School of Medicine, Chuncheon, Korea, Republic of, ³Division of Pediatric Neurosurgery, Seoul National University College of Medicine, Seoul, Korea, Republic of*

Background and aims: Sudden neurological deterioration which cannot be explained by structural change, ischemia or seizure is often observed among patients with traumatic brain injuries. We aimed to provide new insight into the pathophysiology of posttraumatic transient neurologic dysfunction.

Methods: We describe prolonged but fully reversible focal neurologic dysfunction of unknown origin based on the initial evaluation in 16 patients with traumatic brain injury. We performed brain imaging, including diffusion weighted imaging and computed tomography, and electroencephalography (EEG) during the episodes.

Results: The symptoms consisted of dysarthria, hemiparesis, hemiparesthesia of limbs contralateral to the affected side, or aphasia. These symptoms developed between 12 hours and 15 days after trauma and lasted between 12 hours and 16 days. Structural imaging did not show any significant interval change compared with the immediate posttraumatic images. Perfusion imaging showed increased cerebral blood flow in the symptomatic hemisphere. EEG revealed low amplitude arrhythmic slowing in the corresponding hemisphere.

Conclusion: Transient neurologic dysfunction can occur during the acute phase of traumatic brain injury. Although this may last more than usual transient ischemic attack or seizure, it eventually resolves regardless of treatment. Based on our observation, we propose that this is the manifestation of the transient cortical spreading depression occurring injured brain, analogous to migraine aura.

Disclosure: Nothing to disclose

EPR2168

Decision tree machine learning to predict unfavorable outcome in surgically treated patients with chronic subdural hematomas

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Background and aims: The incidence of chronic subdural hematomas (cSDH) is expected to double in the next 20 years. Although often perceived as a “benign” condition, considerable rates of mortality and poor outcome have been reported. We therefore evaluated factors associated with an unfavorable outcome after surgical treatment of cSDH patients using machine-learning.

Methods: Patients treated for cSDH with surgical evacuation between 2006-2018 at a single institution were retrospectively analyzed. Potential demographical, clinical, imaging and laboratory predictors were assessed and a decision-tree predicting unfavorable outcome (GOS 1-3) was developed using the Classification and Regression Tree (CART) algorithm. Out-of-sample model performance was evaluated using repeated cross-validation.

Results: 755 eligible patients were analyzed. Median age was 75 (IQR 68-81) years and 69% were males. Mortality rate was 1.6% and rate of unfavorable outcome was 14.3%. The developed decision-tree to predict unfavorable outcome had 5 splits and included the following 4 clinical variables (in descending order of calculated importance): GCS, comorbidities, Hb, and age. After cross-validation, the following model performance metrics were obtained: a model accuracy of 0.88 (0.85-0.90), sensitivity of 0.35 (0.19-0.51), and specificity of 0.96 (0.94-0.99).

Conclusion: GCS, comorbidities, Hb, and age were identified as the most important clinical predictors for an unfavorable outcome in cSDH patients after surgery. The developed model was simple and still displayed a high accuracy and very high specificity, the sensitivity was however rather low. Our results might help clinicians to better assess the prognosis in patients with cSDH.

Disclosure: Nothing to disclose

EPR2169

Epidemiological trends of medicated adult parkinsonism in Finland

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Background and aims: Parkinson’s disease is becoming more common as populations age, but more data are needed to refine the prediction models. We investigated epidemiological trends of medicated parkinsonism in Finland.

Methods: The annual numbers of new and prevalent reimbursement rights parkinsonism drugs for persons >30 years of age were obtained from the national authority for years 2001-2018. Standardisation was performed using the direct method and the European Standard Population 2013.

Results: Overall crude incidence was 46.7/100,000 (95% CI 46.2-47.3) person-years and it increased from 40.0 (95% CI 37.9-42.2) in 2001 to 48.5 (95% CI 46.3-50.8) in 2018 ($p<0.0001$). Incidence increased both in men ($p<0.0001$) and women ($p=0.016$) during the study period. However, age-standardized annual incidence fluctuated between 42.9 and 53.1 per 100,000 person-years with no trend ($p=0.32$). Crude prevalence increased from 418.9 (95% CI 412.0-426.0) in 2001 to 486.9 (95% CI 479.8-494.1) in 2018 ($p<0.0001$) but age-standardized prevalence decreased from 488.2/100,000 in 2001 to 446.6/100,000 in 2018 ($R=0.89$, $p<0.00001$; figure).

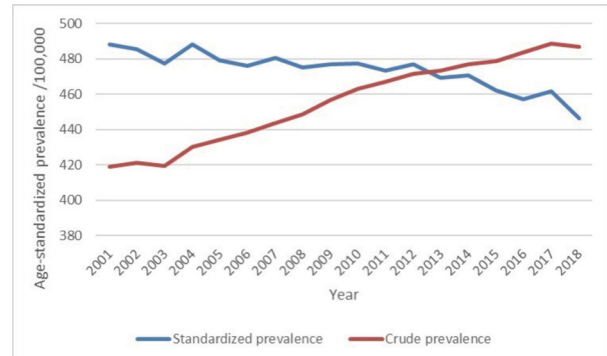


Figure. The annual crude and age-standardized (European Standard Population 2013) prevalence of medicated parkinsonism in people >30 years of age in Finland

Conclusion: Medicated parkinsonism has become more frequent in Finland during the last two decades. However, its age-adjusted prevalence has decreased concurrently.

Disclosure: Jussi Sipilä has received honoraria (Merck, Pfizer, Sanofi), has received a consultancy fee (Rinnekoiti Foundation), has received travel grants and congress sponsorship (Abbvie, Orion Pharma, Merck Serono, Sanquin, Lundbeck, Novartis) and holds shares (Orion Corporation). Valtteri Kaasinen serves as an advisory board member of Abbvie and has received speaker’s honoraria from Orion Pharma, Teva, GE Healthcare, Abbvie and NordicInfu Care AB; travel expenses from NordicInfu Care AB; and research funding from the Finnish Alcohol

Research Foundation, the Päivikki and Sakari Sohlberg Foundation, the International Parkinson and Movement Disorder Society, and Finnish governmental research funding (ERVA).

EPR2170

Predict and Prevent Chronic Traumatic Encephalopathy: Early detection of subtle neuronal dysfunction after Mild CT/MRI Negative Traumatic Brain Injury using Brainstem Auditory Evoked Potentials

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Background and aims: Traumatic brain injuries (TBI) are public health problem of great importance. The conventional imagings CT/MRI are limited in their capacity to assess microstructural or functional damages due to mild TBI (mTBI). There is an increasing urgency to develop new diagnostic modalities for the accurate identification of at-risk patients. The aim of this study is to investigate changes of Brainstem Auditory Evoked Potentials (BAEP) as diagnostic and prognostic neurophysiological markers in mild TBI.

Methods: 75 patients with concussion were included in the study. 1st group (54 patients): BAEPs were conducted in the first month after injury. BAEP follow-up was carried out on the 3rd, 6th month to 16 of them. The 2nd group (21 patients) was not tested immediately after concussion, but on the 3rd, 6th month, 1 year after the trauma (despite the normal results from CT/MRI, complaints of the patients persist and disturb their quality of life).

Results: In the 1st month after the trauma 28 patients had delayed peak latencies, abnormal prolongation of interpeak intervals, interaural differences, low amplitude or absence of main waves. More than one type of abnormalities were found in 17 cases. The abnormalities persist in subsequent BAEP for 25 patients (fig1).

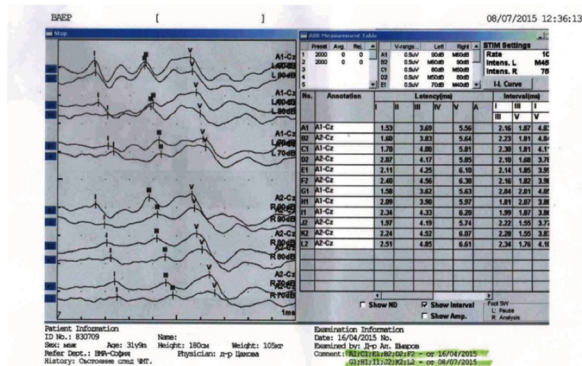


Fig.1. Abnormal BAEP on the 7th day and in 3rd month after the MTBI: delayed peak latency of the main waves I, III, V, abnormal prolongation of interpeak intervals. Some waveforms contain both abnormalities.

Conclusion: BAEP can be applied as a diagnostic method in patients with concussion. Conducting control BAEP has an important role in monitoring the dynamics of pathological process. Persistent BAEP-abnormalities can be used as diagnostic and prognostic neurophysiological markers for the accurate identification of at-risk patients and the initiation of preventative therapy early in the disease course.

Disclosure: Nothing to disclose

Neurogenetics 1

EPR2171

Exome sequencing identifies CHCHD2 variant in a patient with early onset multiple system atrophy and coexisting mitochondrial pathology in muscle

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Background and aims: CHCHD2 associated Parkinsonism is a recently described form of autosomal dominant Parkinson's disease (PARK22), however there is some ambiguity about the exact role of the gene. CHCHD2 variants were mainly reported in late-onset PD cases, but also in 1 patient with late onset multiple system atrophy (MSA), and patients with different forms of dementia. In animal models and human derived fibroblast culture mitochondrial pathology was captured.

Methods: We report a case with an early onset MSA-like phenotype. Brain MRI, electrophysiologic, myopathological studies, and whole exome sequencing was performed for diagnostic purposes.

Results: The patient's symptoms started at age 38 years with progressive orthostatic hypotension. 4 years later proximal muscle weakness and general fatigue developed. Rapidly deteriorating Parkinsonism appeared in the next years, with additional pyramidal signs. Electrophysiologic studies detected mild spontaneous activity plus myogenic lesion, and mild demyelinating neuropathy. Muscle biopsy showed mitochondrial dysfunction with ragged blue and COX negative fibers. EM revealed abnormal, pleioclonal mitochondria. Hot spot mutations of the mitochondrial genome were excluded. The MRI detected cerebellar atrophy. The exome sequencing identified a heterozygous damaging variant in the CHCHD2 gene absent from in-house and population databases. Additional variants of uncertain significance were present in the SETX and SPG11 genes.

Conclusion: This case report expands the phenotypic spectrum of CHCHD2 associated Parkinsonism, with an early onset MSA-like phenotype characterized by severe orthostasis, and additional mild neuromuscular abnormalities. The muscle biopsy, which was not previously available from patients with CHCHD2 variants, provides an in vivo evidence for mitochondrial dysfunction.

Disclosure: The authors of this publication are members of the European Reference Network for Rare Neurological Diseases - Project ID No 739510.

EPR2172

Asymptomatic Adrenoleukodystrophy in Elderly Males

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Background and aims: Adrenoleukodystrophy (ALD) is an X-linked disease caused by ABCD1 mutations and characterized by wide phenotypic spectrum. Virtually all male patients with ALD who reach adulthood develop a varying degree of disease-related symptoms, with typical onset in the 3rd or 4th decade, and compatible with myelopathy.

Methods: We reviewed the clinical and laboratory information of our cohort of 53 adult ALD patients followed in our Institute from Jan 2004 to Dec 2019.

Results: We identified 2 ALD male patients (4%) who were still asymptomatic in the 7th decade. They both were investigated for ABCD1 mutations because relatives of symptomatic patients, but their neurological examination, brain MRI and adrenal function were normal. The 1st patient was a 62-year-old man with the R389C ABCD1 mutation, who developed erectile dysfunction at the age of 70. The 2nd one was a 64-year-old man with the W339G ABCD1 mutation, 1st seen at the age of 56.

Conclusion: Our observation suggests that ALD males may not develop any symptom or sign even late in life, and lends support to previously published case series where exceptional, asymptomatic elderly ALD males are mentioned, but not well documented. It is impossible to predict when these individuals will develop the disease, if ever. However, their existence should be kept in mind for genetic counseling, and may be in agreement with recent results from newborn screening showing ALD is more common than previously described. Finally, these individuals may represent a rare but unique opportunity for the identification of ALD protective factors.

Disclosure: Nothing to disclose

EPR2173

MCI and AD: a predictive model for risk assessment and disease progression

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Background and aims: Cognitive decline is normally associated with aging, although it can sometimes be suggestive of pathological neurodegeneration, Mild Cognitive Impairment (MCI) and ultimately, Alzheimer Disease (AD). This study aimed to identify a set of predictive biomarkers specific for MCI and AD.

Methods: 436 patients (245 MCI and 191 AD) were recruited at the IRCCS Santa Lucia. Genomic DNA was subjected to genotyping analysis by Open Array platform, which consisted of 120 Single Nucleotide Polymorphisms (SNPs). The results were processed by statistical (Information Theory and Logistic Regression) and bioinformatic (GSEA, IPA, String, Phenolyzer) tools for assessing the significant association with the diseases and selecting the SNPs to be tested as predictive/prognostic biomarkers for MCI and AD.

Results: Statistical results identified 11 SNPs and 12 SNPs as candidate predictors for MCI and AD, respectively. The logistic regression performed on these data revealed that 2 SNPs were significantly associated with MCI (Table 1) and 4 SNPs with AD (Table 2). Given these results, 2 accurate models were developed for classifying MCI/AD cases and control subjects (Table 3). Bioinformatic analysis indicated that the associated SNPs participate in several biological pathways implicated in the etiopathogenesis and progression of MCI and AD.

Gene	Informative SNP	p-value	Biological pathways
VSIG4	rs1044165	0.01	<ul style="list-style-type: none"> cell survival adhesion/cellular localization Neuroinflammation Angiogenesis Neurotransmitter-related processes
MAOA	rs2072743	0.13	
miR-4482	rs45596840	0.99	
MAOA	rs1137070	0.38	
PTGS2	rs20417	0.99	
MAOB	rs1799836	0.02	
CLOCK	rs6811520	0.99	
miR-6499-5p	rs3734050	0.07	
CYP24A1	rs2248359	0.99	
CYP24A1	rs2248137	0.99	
miR-6810	rs62182086	0.94	

Table 1. Statistical results showing candidate SNPs predictors and associated SNPs obtained by logistic regression. The cut-off of significant p-value was set a p<0.05. In bold characters are reported the SNPs significantly associated with MCI. In addition, the biological pathways in which the SNPs have been implicated.

Table 2. Statistical results showing candidate SNPs predictors and associated SNPs obtained by logistic regression. The cut-off for significant p-value was set at p<0.05. In bold characters are reported the SNPs significantly associated with AD. In addition, the biological pathways in which the SNPs have been implicated.

Gene	Informative SNP	p-value	Biological pathways
MAOA	rs2072743	0.08	<ul style="list-style-type: none"> Beta-amyloid metabolism Trafficking Neuroinflammation Dopamine-related processes
MAOA	rs1137070	0.67	
VSIG4	rs1044165	1.73*10⁻⁶	
MAOB	rs1799836	0.16	
CLOCK	rs6811520	0.98	
ATF6	rs13401	0.12	
PTGS2	rs20417	0.99	
SEMA6A	rs26595	0.03	
IL6	rs1800795	0.02	
miR-4482	rs45596840	0.99	
IL2RA	rs12722489	0.05	
SLC41A1	rs1772159	0.09	

Table 2. Statistical results showing candidate SNPs predictors and associated SNPs obtained by logistic regression. The cut-off of significant p-value was set a p<0.05. In bold characters are reported the SNPs significantly associated with AD. In addition, the biological pathways in which the SNPs have been implicated.

Disorder	AUC	Sensitivity	Specificity
MCI	0.94	0.74	0.89
AD	0.93	0.64	0.94

Table 3. Accuracy, sensitivity and specificity results of the model created for classifying MCI/AD cases with respect to controls.

Conclusion: This study presents an accurate model for evaluating the risk of MCI and AD considering patient's genetic make-up. Interestingly, bioinformatic analysis highlighted a network of genes that could elucidate overlapping and specific disease mechanisms involved in the progression from MCI to AD and could therefore be exploited for drawing a trajectory of disease.

Disclosure: Nothing to disclose

EPR2174

Autosomal dominant optic neuropathy caused by pathogenic OPA1 mutation in Leber's hereditary optic neuropathy m.3460G>A mutation carriers: one family

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Background and aims: Autosomal dominant optic atrophy (ADOA) caused by OPA1 gene mutations and Leber's hereditary optic neuropathy (LHON) caused by mitochondrial mutations are both common causes of inherited bilateral visual loss, due to selective loss of retinal ganglion cells, with a different clinical course: slowly progressive for OPA1-ADOA vs. acute or subacute onset for LHON.

Methods: Clinical and genetic characterization of 1 family with several affecteds with clinically ADOA, with a pathogenic OPA1 mutation and LHON mutation m.3460G>A of the mitochondrial DNA (mtDNA).

Results: 5 family members (female index, maternal half-brother, daughter, mother and mother's brother) had childhood-onset slowly progressive visual loss and optic atrophy, compatible with ADOA. The pattern of inheritance was autosomal dominant (or maternal). 2 affecteds were reviewed in clinic, the index showed no additional neurological features, the daughter had learning difficulties. ADOA gene panel showed for both pathogenic heterozygote OPA1 mutation c.2708_2711delTTAG, causal of ADOA, and LHON mutation m.3460G>A of the mtDNA, heteroplasmic.

Conclusion: For the LHON mutation carriers in this family, the OPA1 mutation is interpreted as causal for the visual loss, given the ADOA clinical course. LHON mtDNA pathogenic mutations have incomplete penetrance (10% risk of LHON for female mutation carriers, 50% for male carriers). A contribution of the LHON mutation to the clinical phenotype cannot be affirmed in the ADOA-affecteds of this family, but LHON mutation carriership has impact for genetic counselling and would have diagnostic consequences in case of a LHON-like acute or subacute onset of rapidly progressive visual loss in this family.

Disclosure: Nothing to disclose

EPR2175

Clinical variability of variant of ataxia-telangiectasia among Bulgarian patients with mutations in ATM

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Background and aims: Ataxia telangiectasia (AT) is a multisystemic disorder caused by biallelic mutations in the ATM gene, classified in 2 main phenotypes - classic AT, leading to reduced life expectancy and loss of ambulation by the age of 10 years and a milder phenotype, known as variant AT (vAT).

To present the clinical and genetic spectrum of the Bulgarian patients with vAT.

Methods: The study encompassed 28 patients, with genetically verified vAT, from 4 pedigrees. All of them underwent neurological evaluation, neuroophthalmological, neuropsychological assessments, NCS, brain MRI and measurement of serum AFP. Immunological test were performed in 5/28.

Results: The age at onset in our group was 8.3 years \pm 9.3, varying between 14 days and 40 years. The main symptoms are dystonic and choreic hyperkinesias, static and postural tremor, more prominent in the upper limbs and the neck, dystonic disarthria and dysphagia. Mild ataxia of stance and gait was present in 5/28. Dilated conjunctival vessels were observed in 4/28. Cognition was spared. Brain imaging was normal in all affected, except in 1, with cerebellar atrophy. AFP was elevated in all tested individuals. The immunological tests revealed elevated ANA in 5/5 and absolute lymphopenia in 3/5. p.V2716A in ATM gene was

the most common mutation, found in 23 in homozygous state and in the rest 5 in compound heterozygous state.

Conclusion: Clinical features, due to mutations in ATM gene can be very broad. The disease may appear as dystonia, of early onset, without frank cerebellar involvement, but with elevated AFP.

Disclosure: Nothing to disclose

EPR2176

Action tremor as prominent neurological feature in AARS2-related ovarian failure

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Background and aims: Biallelic mutations in the AARS2 gene, coding for mitochondrial alanyl-tRNA synthetase, have been associated with a severe form of infantile cardiomyopathy and, more recently, with ovarioleukodystrophy in women.

Methods: We characterized the clinical and neuroimaging phenotype of 2 sisters presenting with postural tremor and primary amenorrhea. They underwent massive multigene panel sequencing encompassing 280 genes related to ataxia.

Results: The patients, aged 31 and 25 years, presented with postural tremor, which started at the age of 18 (Patient 1) and 11 years (Patient 2). Both sisters had primary ovarian failure due to hypergonadotropic hypogonadism. Neurological examination in Patient 1 revealed downbeat nystagmus, slight tandem walking difficulty, and prominent action hand tremors. Similar features were seen in Patient 2. There was no evidence of neuropsychological impairment in both sisters. Brain MRI revealed small subcortical areas of white matters T2-hyperintensities in Patient 1 only. Targeted re-sequencing revealed that both sisters carried the c.446G>A/p.Cys149Tyr and c.385A>C/p.Thr129Pro missense mutations in compound heterozygosity. Mutations were validated by Sanger sequencing, segregated with the phenotype in the family, and their pathogenicity was confirmed in silico.

Conclusion: This work expands the phenotypic and imaging spectrum of AARS2-associated diseases, to include non-progressive tremor in absence of overt leukoencephalopathy or mental impairment.

Disclosure: Nothing to disclose

EPR2177

Patients with Cerebellar Ataxia, Vestibular Areflexia and Neuronopathy Syndrome (CANVAS) of Polynesian ancestry have a novel conformation of their RFC1 repeat.

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Background and aims: Cerebellar ataxia with neuropathy and bilateral vestibular areflexia syndrome (CANVAS) is a neurodegenerative disease with onset in mid- to late adulthood. The genetic basis was recently shown to be the biallelic expansion of a pentanucleotide (AAGGG)_n repeat in RFC1. Here, we describe CANVAS genetic testing in New Zealand and Cook Island Māori.

Methods: A cohort of 28 patients - 15 European and 13 New Zealand or Cook Island Māori - clinically diagnosed with CANVAS syndrome were screened with flanking PCR testing of the RFC1 pentanucleotide expansion. In the 27 patients who were found to have no PCR product (consistent with homozygous expansion), repeat-primed PCR was performed using both reference and pathological configurations of the pentanucleotide expansion.

Haplotype analysis was performed using Illumina whole genome sequencing from which HpaMap2 makers were extracted and used in Linkdatagen and Merlin programs.

The <https://shiny.wehi.edu.au/rafehi.h/mutation-dating/> program was used to estimate the most recent common ancestors.

Results: In the New Zealand and Cook Island Māori patients there was a novel, possibly population-specific configuration of the pathogenic CANVAS AAGGG repeat embedded in the variant AAAGG repeat. They shared the same core haplotype previously described in European CANVAS patients. There were no apparent phenotypic differences.

Conclusion: Presence of a common disease haplotype among the New Zealand and Cook Island Māori suggests

this novel configuration is a founder effect with the most recent common ancestor at approximately 1430 CE. The finding of the same core haplotype as previously described, supports a single origin of the CANVAS mutation.

Disclosure: Nothing to disclose

EPR2178

Per2 C111G polymorphism influences cognition in Subjective Cognitive Decline and Mild Cognitive Impairment. A 10-year follow-up study.

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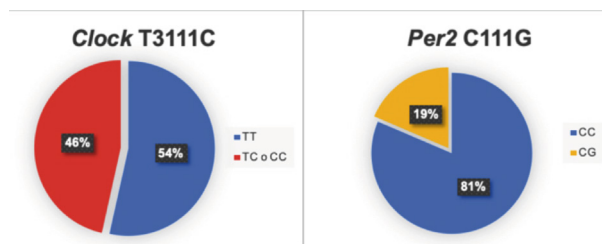
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Background and aims: Clock and Per2 genes have been involved in sleep-wake cycle alterations and neurodegenerative diseases. We aimed to evaluate the effect of Clock T3111C and Per2 C111G polymorphisms on cognitive function and progression to AD in Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI).

Methods: We included 71 subjects (43 SCD, 28 MCI), who underwent Clock and Per2 genotyping at baseline and neuropsychological follow-up at baseline and every 2 years for a mean time of 10 years. We subdivided our sample in subjects who developed AD (SCD-c, MCI-c) and non-converters (SCD-nc, MCI-nc).

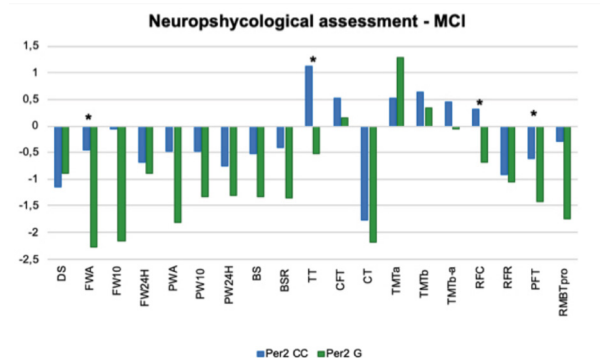
Results: Clock T3111C polymorphism was detected in 46% of cases, Per2 C111G in 19% of cases (Fig.1). Per2 G carriers presented lower premorbid intelligence score ($p=0.045$), lower education ($p=0.009$) and lower frequency of family history of AD ($\chi^2=8.99$, $p=0.01$) than CC carriers (Tab.1). MCI-Per2 G carriers had worse performance in tests assessing for executive function, language and visuo-spatial abilities at baseline (Fig.2). During follow-up, 2 SCD and 14 MCI subjects progressed to AD: Clock T3111C prevalence did not differ between converters and non-converters; both SCD-c subjects presented the Per2 G allele, while none of SCD-Per2 CC carriers converted to AD ($p=0.004$).



Prevalence of Per2 C111G and Clock T3111C polymorphisms

Features	Per2			Clock		
	CC carriers	G carriers	p	T carriers	C carriers	p
Age at baseline (±SD) in years	64.33 ± 9.06	65.22 ± 7.26	0.838	64.45 ± 9.18	64.02 ± 8.68	0.818
Age at onset (±SD) in years	59.95 ± 9.88	62.38 ± 7.96	0.645	60.61 ± 10.61	59.61 ± 8.75	0.782
Follow-up time (±SD) in years	10.68 ± 4.53	12.60 ± 4.68	0.207	11.27 ± 4.59	10.62 ± 4.65	0.678
Sex (females, males)	38, 19	10, 3	0.472	27, 11	22, 11	0.690
Familiarity (%)	61.4%	15.4%	0.01*	42.1%	63.6%	0.07
Education in years(±SD)	10.65 ± 4.61	7 ± 3.05	0.009*	9.92 ± 4.87	10.06 ± 4.21	0.838
TIB (±SD)	110.13 ± 8.23	104.29 ± 10.74	0.045*	110.20 ± 8.20	107.80 ± 9.45	0.424
MMSE (±SD)	28.45 ± 1.66	28.31 ± 1.49	0.591	28.08 ± 1.79	28.82 ± 1.31	0.065
ApoE4 (%)	33.4%	23.07%	0.131	28.9%	36.3%	0.647

Demographic data. Values quoted in the table are mean (±SD) or n (%). p indicates level of significance for comparison between SCD-nc and SCD-c and between MCI-c and MCI-nc (statistical significance at $p<0.05$, in bold characters).



Z-score mean values for neuropsychological tests. DS-Digit Span; FWA-Five Words Acquisition; PWA-Paired Words Acquisition; BS and BSR-Babcock Short Story; TT-Token Test; CFT-Category Fluency Task; CT-Corsi Tapping Test; TMT-Trail Making Test; RFC-Rey-Osterrieth Figure copy; PFT-Phonemic Fluency Test; RBMT-Rivermead Behavioral Memory Test.

Conclusion: Per2 G carriers had lower cognitive reserve proxies, worse scores on non-memory tests, and presented less frequently family history of AD. Nevertheless, conversion to AD was more frequent in SCD-Per2 G carriers. Further studies are needed to assess the role of this polymorphism on the risk of progression to AD.

Disclosure: Nothing to disclose

EPR2179

Association between methylation of SNCA gene and rs3756063 polymorphism in patients with Parkinson's disease in Russian population

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Background and aims: The genetic background of Parkinson's disease (PD) is complex. Monogenic forms represent only 10-15% of PD cases. Epigenetic mechanisms and, specifically, DNA methylation can explain the mystery of "missing heritability". We studied correlation between DNA methylation of SNCA gene and PD-associated single nucleotide polymorphism (SNP) rs3756063 that it is located inside the CpG island of SNCA intron 1 and may influence the methylation process.

Methods: In total, 44 PD patients and 26 healthy controls were studied. DNA methylation was analyzed by performing bisulfate sequencing of intron 1 region of SNCA gene containing 27 CpG sites. In each CpG site, we calculated a percent of methylation: $(C/C+T)*100$. The genotype (rs3756063) was identified by direct sequencing.

Results: We found higher frequency of G allele in PD group compared to controls but the difference did not reach the significance. Multiple comparisons for all 27 CpG sites showed methylation differences between PD patients carrying C and G alleles, with significant hypomethylation for 21 CpG sites in the presence of G allele ($p<0.05$). Comparisons between PD groups with C/C, C/G and G/G genotypes showed significant difference for 18 CpG sites, with the lowest methylation in the presence of G/G genotype ($p<0.05$).

Conclusion: This is the 1st data on the association between rs3756063 and SNCA gene methylation in patients with PD from Russian population. We suggest that the presence of G allele is associated with SNCA hypomethylation and could play a role in the disease pathogenesis.

Disclosure: The study was supported by RSF 17-75-20211.

Neuroimaging 2

EPR2180

MRI as a decision support tool in a large exome sequenced limb-girdle muscular dystrophy cohort

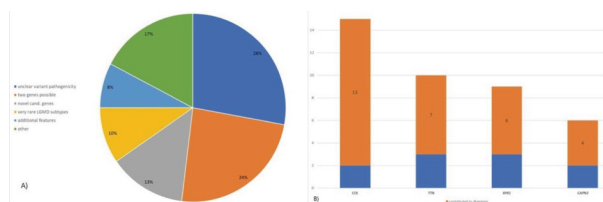
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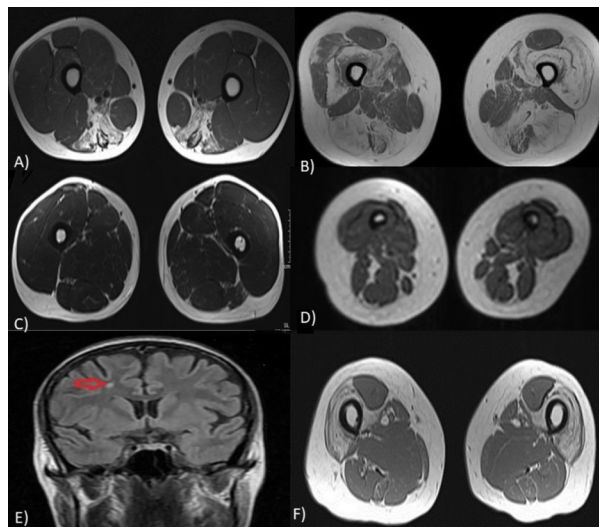
Background and aims: Muscle MRI is increasingly more available tool in diagnostic of neuromuscular disorders. Many of limb girdle muscular dystrophies (LGMDs), a heterogenous disease group associated with more than 30 genes, have muscle involvement pattern specific for a disease subtype. Here we investigate the utility of muscle MRI in assessing pathogenicity of whole exome sequencing (WES) variants in a large cohort of LGMD individuals.

Methods: In the MYO-SEQ project analysis of exome sequencing data was performed for 1891 individuals with LGMD. As part of this project we gathered 105 muscle MRIs, one muscle CT (in this case muscle MRI was not possible due to severe dyspnoea), 2 brain MRIs and 1 heart MRI. Imaging was performed in the participating centers and send to Newcastle for a second opinion.

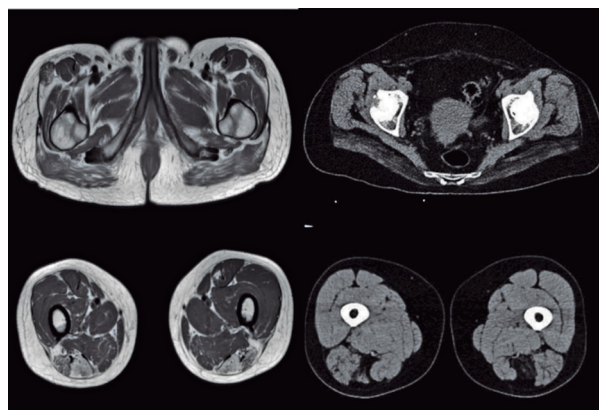
Results: We requested MRIs for the following reasons: difficulties in assessment of pathogenicity of genetic variant (29 cases), possible pathogenic variants in 2 genes (25), novel candidate genes suspected (14), vary rare disease subtypes (10), individuals with additional phenotypic features (8) and other reasons (18). Muscle MRI was helpful in confirming/excluding variants in COL (suggestive/all considered variants in this gene 13/15) TTN (7/10) RYR1 (6/9) and CAPN3 (4/6). Overall, MRI was helpful in establishing diagnosis of 48 cases (45%). We performed theoretical studies on the whole MYO-SEQ cohort (n=1891) and, assuming 100% sensitivity and specificity, muscle MRI could contribute to diagnosis of msx. 34% of cases.



A) Reasons for requesting MRI in exome sequenced LGMD individuals
 B) In orange: number of cases when MRI contributed to final diagnosis divided by variants in chosen genes



A) 1 pathogenic variant in CAPN3 and 2nd with conflicting pathogenicity (final dgn. LGMD R1) B) Hmz variant in DYSF not present in ClinVar (final dgn. LGMD R2) C) Rare, bioinformatically damaging variant in COL6 likely excluded D) COL6 variant excluded; gene list extended (dgn. PURA syndrome) E) Brain MRI in LGMD R23 F) hmc mut. in BVES



2 patients with likely pathogenic variants in a novel candidate gene (never before associated with neuromuscular diseases) and similar phenotype. Involvement of gluteus maximus, semitendinosus and semimembranosus muscle in muscle MRI (Pt 1) and muscle CT (Pt 2)

Conclusion: Muscle MRI is a powerful diagnostic tool in diagnosis of LGMD and in assessing variants generated with WES.

Disclosure: The MYO-SEQ project was funded by Sanofi Genzyme, Ultragenyx, LGMD2I Research Fund, Samantha J Brazzo Foundation, LGMD2D Foundation and Kurt+Peter Foundation, Muscular Dystrophy UK, and Coalition to Cure Calpain 3. Analysis was provided by the Broad Institute of MIT and Harvard Center for Mendelian Genomics (Broad CMG) and was funded by the National Human Genome Research Institute, the National Eye Institute, and the National Heart, Lung and Blood Institute grant UM1 HG008900 and in part by National Human Genome Research Institute grant R01 HG009141

EPR2181

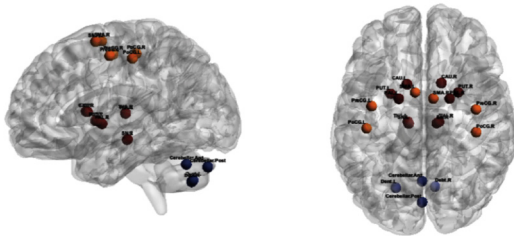
Functional Connectivity measured by the Global Efficiency of the Motor Network is decreased in Parkinson's disease in comparison to Healthy Controls

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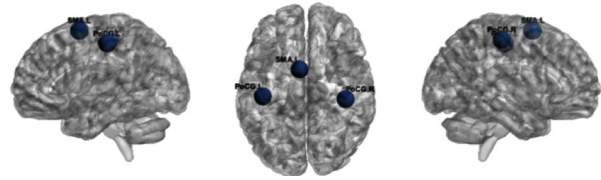
Background and aims: Functional MRI is a helpful tool to study network connectivity in healthy subjects and disease. We hypothesized that motor network connectivity would be impaired in Parkinson's disease (PD) in comparison to Healthy Controls (HC), and also that both subforms of PD (Tremulant and Akinetic-Rigid) would show patterns different from each other. This study aimed to evaluate functional connectivity of areas related to tremor on the motor network of all groups.

Methods: 85 subjects (54PD, 31HC) were enrolled in this study and were submitted to structural and functional MRI. BOLD sensitive images were acquired and pre-processed using the CONN software. Important hubs of the motor network related to tremor were chosen as Regions-of-interest (ROIs). Statistical analysis was set to conservative parameters.

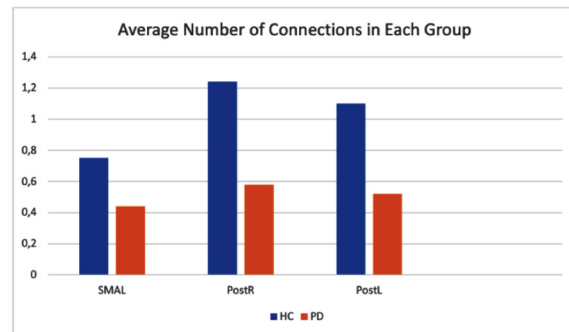


Regions of Interest (ROIs), bilaterally: In orange, cortical ROIs (Pre-central gyrus, Post-central gyrus, Supplementary Motor Area); in red, subcortical ROIs (caudate, putamen, pallidum, thalamus); in blue, cerebellar ROIs (cerebellar anterior network, cerebellar posterior network and dentate nucleus).

Results: Pairwise analysis showed no significant difference amongst groups. Network analysis demonstrated reduced global efficiency (GE) of the motor circuit of PD in comparison to HC (0.0231 versus 0.0297, p-value=0.042). Areas that most contributed for reduction were left supplementary motor area (SMAL) and bilateral post central gyrus (PostCG). No difference was found between the subgroups of PD.



Results of Global Efficiency of the motor network in the PD group versus HC group. Blue areas are Postcentral gyrus right and left and left and right SMA.



Graphic representation of the average number of connections in each group. On the x axis, the ROIs that were responsible for the difference in GE between the two groups. On the y axis, the average number of connections in each group.

Conclusion: Functional connectivity measured by the GE of the motor network is diminished in PD in comparison to HC, due to decreased connectivity of SMAL and bilateral PostCG. There is a global impairment of the motor network in PD, and it does not affect just the basal ganglia, but also areas associated with movement modulation, such as the SMA and PostCG. These could possibly be new targets for therapies such as transcranial magnetic stimulation and for posterior neuroimaging studies.

Disclosure: This project received a grant by FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo*) and was supported by IIEP (Instituto Israelita de Ensino e Pesquisa) of the Hospital Albert Einstein**. * Foundation for Research Support of São Paulo State ** Israeli Institute of Teaching and Research of Hospital Albert Einstein

EPR2182

Diagnosis of Idiopathic Parkinson's Disease: Automated Assessment of the Substantia Nigra on Susceptibility Map-weighted Imaging Using Convolutional Neural Networks

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Background and aims: It has been reported that degeneration in the substantia nigra (SN) in idiopathic Parkinson's disease (IPD) can be determined by visually assessing susceptibility-weighted imaging (SWI). Our study aims to implement and evaluate a convolutional neural networks (CNN)-based method for assessing the SN on susceptibility map-weighted imaging (SMWI).

Methods: In this retrospective study, we enrolled 296 patients with dopamine transporter (DAT) imaging-proved IPD and 183 subjects with normal DAT activity from our institute. All subjects underwent both 3-echo time GRE imaging for SMWI. We developed a CNN-based algorithm for determining abnormality in the SN on SMWI. DAT imaging served as a reference standard. Diagnostic performance was tested per SN and per participant by using the receiver operating characteristic (ROC) curve analysis. The results from the CNN-based algorithm in the internal dataset were compared with the interpretations from two reviewers.

Results: The mean value of the 5 areas under the ROC curve (AUC) produced by 5-fold cross-validation was 0.992 (standard deviation, 0.0006) from our dataset by the CNN-based algorithm. The diagnostic sensitivity and specificity for nigral degeneration by the reviewers were 96.05% and 96.67% (per SN) and 99.12% and 93.33% (per participant), respectively from our dataset, and 100% and 100% (per SN) and 100% and 100% (per participant), respectively from the dataset for external validation. These results did not show significant difference.

Conclusion: Our CNN-based algorithm shows high diagnostic performance for detecting nigral degeneration in IPD, which is comparable with that by visual interpretation.

Disclosure: Nothing to disclose

EPR2183

Patterns of Cerebellar Atrophy and Resting State Functional Connectivity Changes in Relapsing-Remitting MS Patients Starting Fingolimod and Natalizumab: A 2-Year Study

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Background and aims: Fingolimod and natalizumab are effective treatments for relapsing-remitting multiple sclerosis (RRMS). We compared their effects on cerebellar atrophy and resting state (RS) functional connectivity (FC) in RRMS after two years of treatment.

Methods: RRMS patients starting fingolimod (n=23) or natalizumab (n=27) underwent 3T MRI scans at month 0 (M0), 6 (M6), 12 (M12) and 24 (M24). 15 healthy controls (HC) were also acquired at M0 and M24. Baseline and longitudinal changes of cerebellar volume (SUIT, SPM12 a Jacobian integration method) and RS FC (seed-based analysis from bilateral CrusI/CrusII) were estimated.

Results: At M0, no cerebellar volumetric difference was found, while patients' groups showed a reduced intra-cerebellar, inter-cerebellar and thalamo-cerebellar RS FC vs HC. Fingolimod-patients experienced significant cerebellar atrophy compared to natalizumab-patients at M6 vs M0 (-1.28% vs -0.06%), M24 vs M6 (-1.38% vs +0.01%) and M24 vs M0 (-0.93% vs -0.10%) and compared to HC (-0.29%) at M24 vs M0 (p<0.001). While RS FC was longitudinally stable in HC, patients' groups showed a reduced cerebellar RS FC with fronto-parietal regions and an increased cerebellar RS FC with bilateral cerebellar regions and deep grey matter. In natalizumab-patients, longitudinal RS FC changes were linear and independent from atrophy. In fingolimod-patients, cerebellar RS FC mainly decreased at M6, while after M6 it mainly increased and was associated with lower cerebellar atrophy progression.

Conclusion: Natalizumab is superior to fingolimod in limiting cerebellar atrophy progression. Both drugs promote cerebellar networks reorganization. Increased RS FC may compensate cerebellar structural damage accumulation.

Disclosure: Nothing to disclose

EPR2184

Brain perfusion changes in Alzheimer's disease networks and their association with pathophysiological features in amnesic mild cognitive impairment patients.

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Background and aims: Previous studies found brain perfusion changes in amnesic mild cognitive impairment (aMCI) patients in cortical regions included in the default mode network (DMN) (posterior cingulate cortex and precuneus) and the limbic network (LIN) (hippocampus). However, no study investigated the perfusion within the DMN and LIN and its relationship with Alzheimer's disease (AD) features.

Methods: We collected the apolipoprotein E (APOE) status, cerebrospinal fluid (CSF) beta-amyloid 42, phosphorylated tau and total tau levels, 3T MRI features (hippocampal volumes and cortical thickness from T1-weighted, white matter hyperintensities on FLAIR), and associative learning and memory functioning on the paired associate learning (PAL) task in 14 aMCI (age, years: 72.8±7.2; Mini-Mental State Examination: 26.1±1.8), recruited in the PharmaCog study. Cerebral Blood Flow (CBF) was extracted from the DMN, LIN, somatomotor (SMN), and visual (VIS) networks using arterial spin labelling (ASL) and were correlated with CSF measures, MRI features, PAL performance (number of errors), and APOE status.

Results: Perfusion was reduced in the DMN (Mann-Whitney, U=8, p=0.043) and LIN (U=3, p=0.005) in APOE ε4 carriers (N=8) compared to non-carriers (N=6). Moreover, LIN perfusion was associated with CSF beta-amyloid 42 level (rho=0.818, p=0.001), and associative learning and memory impairment (rho=-0.621, p=0.024). No association was detected with MRI markers and vascular burden, nor between perfusion in SMN and VIS and the investigated features.

Conclusion: Our results confirm an association between CBF reduction in AD networks and AD pathophysiological features in aMCI, supporting an involvement of brain perfusion in upstream AD processes.

Disclosure: Nothing to disclose

EPR2185

White Matter Abnormalities in Obstructive Sleep Apnea are reversible after CPAP-treatment

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Background and aims: Recent evidences demonstrated the role of white matter (WM) lesions in the pathogenesis of Obstructive Sleep Apnea (OSA), a clinical entity characterized by repetitive collapse of the upper airway during sleep. However, the involvement of silent WM lesions as well as the brain morphologic modifications after treatment still remains unknown. This study aimed to investigate the microstructural integrity of normal appearing white matter (NAWM) in OSA patients before and after CPAP-treatment, using a neuroimaging approach.

Methods: Magnetic resonance imaging data were acquired from a total of 17 never-treated OSA patients. Diffusion tensor imaging (DTI) and Tract-based spatial statistics (TBSS) were performed to assess microstructural NAWM changes. In order to assess the therapy efficacy, OSA patients underwent MRI evaluations at 2 time-points, baseline and after 3 months of CPAP treatment.

Results: CPAP treatment significantly increased fractional anisotropy in NAWM of brainstem, in the corpus callosum and in bilateral internal capsule of patients with OSA at follow-up compared to baseline ($p < 0.05$ TFCE-corrected). Moreover, patients with OSA also showed increases of axial diffusivity in the major tracts of the right hemisphere ($p < 0.05$ TFCE-corrected) after CPAP treatment compared to baseline.

Conclusion: This study improves the knowledge on the therapy efficacy with CPAP in OSA patients, as our results demonstrate that DTI metrics of NAWM in major tracts such as the corpus callosum and the internal capsule were significantly increased after CPAP treatment. This could represent a potential beneficial effect of therapy with CPAP.

Disclosure: Nothing to disclose

EPR2186

Plaque perfusion and elastography in carotid vulnerable plaque detection

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Background and aims: Vulnerable plaque diagnostics is still a challenge. The aims of the study were to correlate density plaque perfusion with plaque elastography and symptoms of stenosis.

Methods: Patients with carotid stenoses $\geq 50\%$ were included to the study. Duplex sonography of carotid plaque with B-mode, color mode, Doppler mode, plaque perfusion without contrast agent and plaque elastography examinations were performed in all patients. Plaque perfusion was evaluated visually in 5-point scale. Correlation between plaque perfusion and elastography results, symptoms in corresponding carotid territory and plaque progression were statistically evaluated.

Results: Totally 78 patients (39 males; age 67.7 ± 9.0 years) with 97 carotid stenoses $\geq 50\%$ (21 symptomatic, 13 asymptomatic progressive and 63 asymptomatic stable stenoses) were included to the study. No, minimal, low, moderate and major plaque perfusion were detected in 8, 20, 33, 25 and 11 plaques, resp. Weak correlation between plaque perfusion and plaque elastography was detected ($r = 0.37$, $r < 0.01$). Plaque with no/minimal perfusion were less frequently heterogenous (28.6% vs. 68.9%), ulcerated (0% vs. 20.7%), and symptomatic (14.3% vs. 40.6%), had lower elasticity (55.0 vs. 86.4) and were detected less frequently in patients with diabetes mellitus (14.3% vs. 36.2%).

Conclusion: Symptomatic carotid stenoses have higher density of plaque perfusion compared with asymptomatic stenoses.

Disclosure: Supported by the Ministry of Health of the Czech Republic grant No. 17-31016A.

EPR2187

Neural correlates of (non-)behavioural signs of consciousness – what can we learn from resting state neuroimaging?

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Background and aims: Unresponsive patients at the bedside may present covert consciousness. This retrospective cross-sectional study aimed to determine brain regions needed to demonstrate behavioural signs of consciousness.

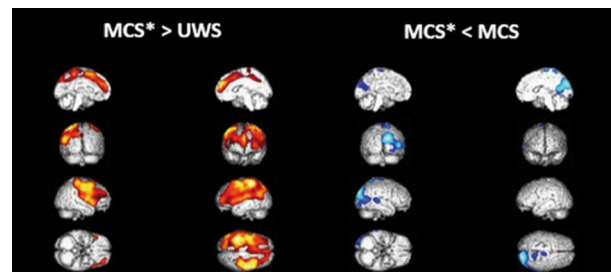
Methods: We looked at the 18fluorodesoxyglucose Positron Emission Tomography (FDG-PET-scan) of 96 patients with disorders of consciousness (see table 1). All patients were assessed 5 times with the Coma Recovery Scale-Revised. The diagnosis of MCS* was based on the FDG-PET relative preservation of global brain metabolism as assessed by 3 experts. We compared brain metabolism of patients in MCS* to UWS and MCS and performed seed-based connectivity analyses. MRI and EEG data were also analysed. Prognosis was collected using the Glasgow Outcome Scale Extended.

Results: Out of the 35 behavioural UWS, 22 presented a partial preservation of brain metabolism (i.e., patients in MCS*), specifically in the fronto-parietal networks (Fig 1 – left). Patients in MCS* had more hypometabolism in the right posterior regions (Fig 1 – right). We found a higher correlation between the right superior temporal gyrus (seed) and motor cortices, somato-sensory associative areas, prefrontal area, and the thalami in MCS compared to MCS*(Fig 2), as well as a higher connectivity (EEG) in the theta band in the left hemisphere. Finally, MCS* patients had a 50% chance to recover signs of consciousness (MCS) at follow-up, while no patient in UWS improved.

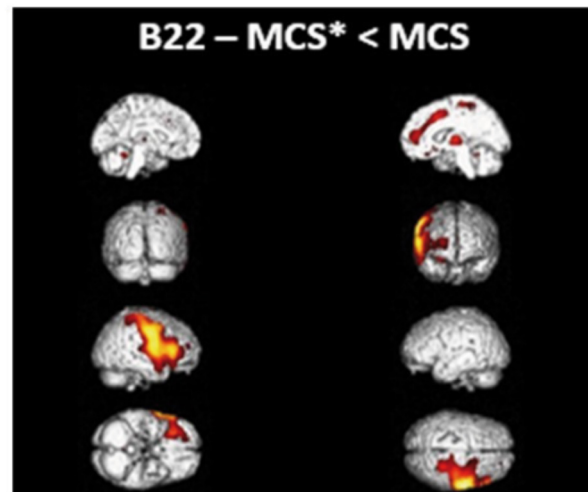
Conclusion: Many patients clinically unresponsive may present covert consciousness. The integrity of the connectivity between the superior temporal gyrus and sensori-motor regions, prefrontal cortex and thalami is crucial to clinically demonstrate signs of consciousness.

	UWS (n=13)		MCS* (n=22)		MCS (n=59)	
Gender	7 men (57%)		11 men (50%)		32 men (54%)	
Aetiology(%TBI)	0 TBI (0%), 9 anoxia, 1 stroke, 3 mixed		10 TBI (43%), 6 anoxia, 3 stroke, 2 mixed, 1 meningitis		33 TBI (57%), 11 anoxia, 10 stroke, 4 mixed, 1 meningitis	
Age – mean±SD min-max	52±14 – 30-74 years old		40±14 – 21-73 years old		40±14 – 18-78 years old	
TSO – mean±SD min-max	551±517 – 1715 days	36-	354±244 – 2009 days	28-	760±606 – 4786 days	32-
CRS-R total score – median±IQR min-max	6±1 – 2-6		5±2 – 4-8		12±3 – 4-21	
% preserved – mean±SD min-max	27.07±7.27 – 9.13- 36.96%		46.11±6.84 – 36.56±75.40%		55.69±11.29 – 30.76- 83.27%	

Table1: Clinical characteristics of DOC patients included in the PET-scan analyses.



MCS* compared to UWS presented higher brain metabolism in the frontoparietal network, mesiofrontal area, anterior and posterior cingulate cortices, and the precuneus (left – red). Compared to MCS, they presented lower brain metabolism in the precuneus, the right supplementary motor area, superior temporal gyrus and visual cortex (right – blue).



Brain regions showing higher connectivity with B22 (right superior temporal gyrus) in MCS as compared to MCS* (in red), namely the premotor and supplementary motor cortices, the somatosensory associative areas, the dorsolateral prefrontal cortex, the inferior frontal gyrus and the thalami.

Disclosure: Nothing to disclose

EPR2188

Neuroanatomic Correlates of Angioedema in stroke patients with thrombolysis

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Background and aims: **Background:** Oral angioedema (OA) is a rare, but life-threatening complication in ischemic stroke patients receiving intravenous thrombolysis with recombinant tissue plasminogen activator. This study intended to determine associations between thrombolysis-related OA and ischemic stroke lesion-sites using a voxel-wise lesion analysis.

Methods: Prospective registry data were used to identify ischemic stroke patients with thrombolysis-related OA between 2002 and 2018. Ischemic stroke patients with thrombolysis-treatment but without OA admitted in the years 2011 and 2012 comprised the control group. Ischemic lesions were manually outlined on magnetic resonance imaging (1.5 or 3T) or computed tomography scans, and transformed into stereotaxic space. We determined the lesion overlap and compared the absence or presence of OA voxel-wise between patients with and without lesions in a given voxel using the Liebermeister test. Stroke severity was rated using the National Institute of Health Stroke Scale (NIHSS) score and blood-pressure, heart rate, blood glucose levels, and body temperature were determined on admission.

Results: 15 ischemic stroke patients with thrombolysis-related OA were identified. The voxel-wise analysis yielded associations between OA and ischemic lesions in the insulo-opercular region with a right-hemispheric dominance. Mean blood-pressure was significantly lower in patients with oral angioedema than in controls. Age, NIHSS-scores, infarct volumes, heart rate, and blood glucose levels did not differ between patients with and without OA.

Conclusion: The voxel-wise analysis linked thrombolysis-related OA to right insulo-opercular lesions. The lower blood-pressure in patients with thrombolysis-related OA may reflect bradykinin-effects causing vasodilatation and increasing vascular permeability.

Disclosure: Nothing to disclose

EPR2189

The use of muscle MRI in the diagnosis of neuromuscular diseases

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Background and aims: Inherited neuromuscular disorders (NMD) are a heterogeneous group of disorders characterized by progressive muscle weakness, different pattern of muscle involvement, age of onset. Thanks to next generation sequencing the numbers of genes responsible for NMD is growing. In recent years muscle MRI has contributed to the diagnosis by evaluating the selective pattern of muscle involvement.

Methods: We retrospectively reviewed the muscle MRI of 533 individuals (age 5-93 years) performed at the John Walton Muscular Dystrophy Research Centre in Newcastle. All patients underwent a muscle MRI, using T1 weighted and STIR axial sequences of the lower limbs. We reviewed the clinical notes and genetic results and correlated to the muscle MRI.

Results: In 83.5% the muscle MRI was performed to direct genetic testing, in 9% to support genetic results, in 5% for academic reasons in already diagnosed patients and in the remaining 2.5% data was missing. The muscle MRI was helpful in directing genetic testing in 48 (11%) cases. Overall, 363/533 (68%) remain genetically undiagnosed whilst 170/533 (32%) had a genetically confirmed diagnosis. The most frequent diagnosis were LGMD 36%, congenital myopathies 22%, FSHD 5%, myofibrillar myopathies 4%, other distal myopathies 14% and others 19%.

Conclusion: Muscle MRI appears to be a useful diagnostic tool to achieve a diagnosis in neuromuscular conditions. Some cases remain still undiagnosed and there is still to learn about selective pattern of muscle involvement in these rare conditions.

Disclosure: Nothing to disclose

EPR2190

Evaluation of the Usefulness of SMwI nigrosome 1 MRI for Differentiating Subclinical Parkinson's disease in Idiopathic REM Sleep Behavior Disorder

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Background and aims: Many patients with assumed idiopathic REM sleepbehavior disorder (iRBD) develop Parkinson's disease (PD), multiple system atrophy (MSA) or diffuse Lewy body dementia (DLB), iRBD is not an independent degenerative disease. RBD is an important prodromal symptom of PD with anosmia and constipation. The present study was performed to probe the susceptibility map-weighted imaging (SMwI) nigrosome1 MRI as neuroimaging biomarker to identify prodromal PD in subjects with iRBD.

Methods: This local ethics committee-approved prospective study enrolled 21 patients with iRBD and 20 healthy subjects who underwent both SMwI at 3T and 18F-FP-CIT PET. The demographic and clinical characteristics of the two group were compared by Mann-Whitney U test. The concordance rate was tested using Cohen's kappa.

Results: Nigrosome1 was intact in 11 patients with iRBD and lost in 9. This shows that 48% of iRBD patients are in subclinical PD. SMwI and 18F-FP-CIT PET results exhibited similar diagnostic performance and had excellent agreement ($k=0.809$ per participant). The disease duration of RBD was significantly different between iRBD with or without nigrosome1 loss. iRBD with nigrosome1 loss was approximately twice longer disease duration compared to iRBD without nigrosome1 loss.

Conclusion: SMwI nigrosome1 MRI is useful to detect early in the preclinical stage of PD in patients with iRBD.

Disclosure: Nothing to disclose

Neuroimmunology 2

EPR2191

Anti-CD20 therapy suppresses cortical pathology in a new rat model of cortical demyelination

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Background and aims: Cortical demyelination is a prominent feature of the multiple sclerosis (MS) brain in the progressive stage and is believed to be a substrate for diffuse cognitive impairment. We recently developed a rat model (Ücal et al., 2017) which reassembles most of the cellular features of brain pathology in progressive MS. B-cell depleting anti-CD20 therapy is effective in the relapsing remitting course of MS as well as in the early progressive stage. The aim of this study was to increase our understanding for the mode of action of B-cells on cortical lesions in our new rat model and whether anti-CD20 therapy can prevent the formation of cortical demyelination.

Methods: Anti-CD20 therapy was administered by intravenous injection into the tail base vein after (Group 1) or before (Group 2) myelin oligodendrocyte glycoprotein (MOG) immunization. Rats were sacrificed at peak disease and brain tissues were analysed in histology with respect to extent of cortical demyelination, microglial activation, neuronal cell loss and astrocytic reactivity.

Results: Histological analyses revealed that the anti-CD20 therapy averted the cortical pathology with significant reductions in demyelination, microglial activation, neuronal loss and astrocyte activation compared with the animals that were treated with an isotype control antibody. Anti-CD20 therapies applied before or after MOG immunization were equally efficacious.

Conclusion: Our results show a favourable impact of the anti-CD20 therapy on preservation of the investigated cortical structures. These findings pave the way for further research on the mode of action of B-cells and might help to improve therapeutic strategies for progressive MS patients.

Disclosure: Nothing to disclose

EPR2192

Safety of autologous hematopoietic stem cell transplantation in multiple sclerosis patients (aHSCT-in-MS): the Zurich experience

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Background and aims: Autologous hematopoietic stem cell transplantation (aHSCT) is used for the treatment of highly-active relapsing-remitting or progressive multiple sclerosis (MS) since 1995. Based on strong data regarding efficacy and improved safety of aHSCT in MS, the Swiss Federal Office of Public Health (FOPH) granted approval in June 2018 with the requirement that patients participate in a prospective registry study at our institution (“aHSCT-in-MS”).

Methods: We used cyclophosphamide and filgrastim to mobilize hematopoietic stem cells and BEAM-ATG regimen for conditioning high-dose chemotherapy.

Results: Until now, 22 MS patients (11 females, 11 males) received aHSCT. Patients had a mean age of 41.3±7.7 years, mean disease duration of 8.6±4.9 years and a mean expanded disease status scale (EDSS) score of 5.0±1.2. 7/22 patients had relapsing-remitting MS, 8/22 secondary-progressive MS and 7/22 primary-progressive MS. All patients had either clinical activity (i.e. relapses, 5/22 of patients), radiological activity (7/22) and/or clinical progression (14/22) before aHSCT, despite conventional highly effective immunomodulatory therapy. The majority of patients developed infectious adverse events (AE), i.e. mucositis and/or enteritis (20/22), upper airway (4/22) and urinary (4/22) infection, reactivation of CMV (2/22), HSV (3/22), VZV (1/22) and BKV (2/22). Other AEs included Uhthoff’s phenomenon (7/22), hypotension (3/22), epistaxis and cholecystolithiasis (each 1/22). Severe AEs included 2 additional, symptomatic CMV reactivations, each 1 hemorrhagic cystitis, gastroenteritis with ileus, laryngitis, cervical abscess, pulmonary embolism, gastrointestinal bleeding, manic episode.

Conclusion: Overall, safety of aHSCT-in-MS is acceptable. However, aHSCT-in-MS requires vigilant monitoring (especially regarding infectious diseases) and optimized antimicrobial prophylactic care.

Disclosure: Nothing to disclose

EPR2193

The microbiome of the nasal cavity in multiple sclerosis: another source of autoimmune response?

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Background and aims: Intestinal microbiome plays a significant role in the pathogenesis of autoimmune diseases, including MS. Significant also seems to be the influence of the microflora of the nasal sinuses, since the nasal cavity has direct bony channels with the cranial cavity. The role in the antigen presentation of the pharyngeal lymphoid ring is also high. Aim was to evaluate the composition of sinuses and nasal microbiome.

Methods: 28 MS patients (78% females), relapsing-remitting, remission (all 1st line injectable drugs) and 15 healthy subjects (hospital staff). Exclusion: 1) signs of acute upper way respiratory infection, 2) chronic sinusitis or nasopharyngitis, 3) taking medications that affect microbiome (local or system antibiotics) for last 3 months, 4) severe comorbidity. EDSS, course of disease, standard nasoscopic procedure for taking biological samples, culture inoculation with an assessment after 5 days, evaluation of antimicrobial resistance. Statistical analysis – Chi-square, ANOVA.

Results: 93% of patients and only 36% of control have deviant microbiome. Normal microflora was presented by *Staphylococcus epidermidis* (7.1% vs 92.7%, $p < 0.001$). The only pathological bacteria in healthy control was *Staphylococcus aureus* (35.7%). Abnormal patient microbiome consists of *Staphylococcus aureus* (60.7%), *Enterobacter* (21.4%), *Escherichia coli* (21.4%) and *Candida* (57.1%). The quantitative representation of conditionally pathogenic strains significantly increases with the duration of the disease ($p = 0.02$), as well as a EDSS score ($p = 0.03$). The composition of microflora does not depend on gender, age and type of drug, and detected even with clinically isolates syndrome.

Conclusion: Nasal microbiom of patients with MS significantly deviate normal and may play role in course of disease.

Disclosure: Nothing to disclose

EPR2194

No change in risk of infection among NMOSD and refractory gMG patients treated with eculizumab: findings from two phase 3 studies and their extensions

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Background and aims: PREVENT (NCT01892345) and REGAIN (NCT01997229) were phase 3, randomized, double-blind studies comparing efficacy and safety of eculizumab and placebo in patients with aquaporin-4 antibody-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD) and refractory acetylcholine-receptor antibody-positive (AChR+) generalized myasthenia gravis (gMG), respectively. We report infection rates in patients treated with eculizumab with or without concomitant immunosuppressant therapy (IST) in PREVENT, REGAIN and respective open-label extensions (NCT02003144 [interim data] and NCT02301624).

Methods: Patients were vaccinated against *Neisseria meningitidis* and randomized to eculizumab (maintenance dose, 1200mg/2 weeks) or placebo, with stable-dose concomitant ISTs permitted. Pooled infection rates were analysed post hoc for subgroups determined by number of baseline ISTs (0, 1, 2 or ≥ 3).

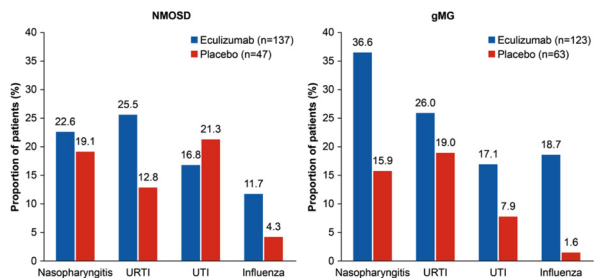
Results: The numbers of patients exposed to eculizumab/placebo were 137/47 (NMOSD; 276.6/51.5 patient-years) and 123/63 (gMG; 304.4/31.1 patient-years). There were no differences in infection or serious infection rates with extent of IST use (Table) nor an increase in infection risk with long-term eculizumab therapy (data will be presented); although, patient numbers were small in some subgroups. Similar infection types were observed in patients receiving eculizumab for each indication (total $n = 260$): most commonly nasopharyngitis ($n = 76$), upper respiratory tract infections ($n = 67$), urinary tract infections ($n = 44$) and influenza ($n = 39$) (Figure). There was one case of meningococcal meningitis (encapsulated) in a patient with gMG receiving eculizumab (2 IST subgroup); this resolved with antibiotic treatment and eculizumab was reinstated.

Table 1. Infection and serious infection rates by baseline IST use

	Infection rates/100 PY (N)				Serious infection rates*/100 PY (N)			
	NMOSD		gMG		NMOSD		gMG	
	Eculizumab	Placebo	Eculizumab	Placebo	Eculizumab	Placebo	Eculizumab	Placebo
No ISTs	192.1 (35)	192.2 (13)	238.2 (2)	305.6 (2)	1.4 (35)	8.0 (13)	0.0 (2)	0.0 (2)
1 IST	183.6 (55)	154.1 (22)	230.6 (41)	253.1 (18)	13.9 (55)	7.0 (22)	16.3 (41)	34.5 (18)
2 ISTs	195.1 (47)	266.7 (12)	171.7 (78)	192.5 (41)	15.1 (47)	47.6 (12)	13.4 (78)	24.1 (41)
≥3 ISTs*	-	-	98.0 (2)	100.1 (2)	-	-	14.0 (2)	0.0 (2)

Infection rates shown per 100 PY to standardize for differences in treatment exposure.
 *A serious adverse event (experience) or reaction was defined as any untoward medical occurrence that, at any dose: results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; or is an important medical event.
 †No patients with NMOSD were receiving ≥3 ISTs at baseline.
 gMG, generalized myasthenia gravis; IST, immunosuppressant therapy; N, total number of patients in category; NMOSD, neuromyelitis optica spectrum disorder; PY, patient-years.

Figure 1. Most common infections in patients with NMOSD (PREVENT + extension) and gMG (REGAIN + extension)



Some patients provided data for both the eculizumab group and the placebo group if they were receiving placebo in REGAIN/PREVENT and then eculizumab in the extension study.
 gMG, generalized myasthenia gravis; NMOSD, neuromyelitis optica spectrum disorder; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Conclusion: In these complement-mediated neurological conditions, overall risk and types of infections were similar in the eculizumab and placebo groups, regardless of concomitant IST.

Disclosure: Research funding for this study was provided by Alexion Pharmaceuticals.

EPR2195

Detection of novel CNS-specific antibodies using human induced pluripotent stem cells-derived astrocytes and neurons: a pilot study on autoimmune-mediated neurological syndromes

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Background and aims: The last decade has seen a thrilling rise in the discovery of CNS-reactive autoantibodies involved in neurological disorders. The identification of such autoantibodies has led to profound changes in therapeutic approaches. Nevertheless, about 10% of the patients developing autoimmune limbic encephalitis remain seronegative for all currently known CNS antigens. Here, we developed a cell-based assay (CBA) to screen for the presence of novel CNS-specific antibodies in sera and cerebrospinal fluid (CSF) using CNS cells derived from human-induced pluripotent stem cells (hiPSC).

Methods: Human iPSC-derived astrocytes and neurons were incubated with paired serum/CSF of 109 patients suffering from inflammatory neurological diseases (IND) and 19 patients with non-IND (NIND). IgG bound to CNS cells were detected using a combination of fluorescently-labelled antibodies. IgG-associated fluorescence intensity (FI) measure was automated using a fluorescence plate reader. Serum or CSF were defined as positive using a ROUT test with a FDR at 2% on quantified FI. Each CBA well was also observed by fluorescence microscopy. To cross-validate the presence of CNS-reactive antibodies, IgG reactivity was analyzed by flow cytometry using hiPSC-derived astrocytes and neurons exposed to the serum/CSF.

Results: Using our CBA, 19 patients (18 IND, 1 NIND) appeared positive on hiPSC-derived astrocytes/neurons including 5 patients previously diagnosed with auto-reactive antibodies and 14 with not-yet reported auto-reactive antibodies, results confirmed by fluorescence microscopy and flow cytometry.

Conclusion: Our hiPSC-based CBA may allow discovering new CNS-reactive antibodies. Such a potent tool opens new perspectives in establishing early diagnosis and optimizing treatments of antibody-mediated diseases of the CNS.

Disclosure: This work was supported by the Swiss National Science Foundation (320030_179531 to RDP) and the Fondation pour la médecine de Laboratoire F4LABMED (to AM). CP has received travel grants or participated to advisory boards for Merck, Biogen IDEC, Roche, Novartis, Genzyme and Celgene. RDP served on the scientific advisory board for Merck, Celgene, and Sanofi; received travel funding and/or speaker honoraria from Celgene and Roche. All other authors have nothing to declare.

EPR2196

Anti-CASPR2 clinical phenotypes correlate with HLA and immunological features

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Background and aims: Antibodies against contactin-associated protein-like 2 (CASPR2-Ab) are associated with acquired neuromyotonia (NMT), limbic encephalitis (LE) and Morvan syndrome (MoS), but recent studies suggest a wider and overlapping spectrum. Herein, we investigated the distribution of symptoms in CASPR2-Ab patients.

Methods: A cluster analysis of neurological symptoms was performed in a retrospective cohort of 56 CASPR2-Ab patients. In parallel, we studied immunological features and HLA.

Results: Cluster analysis distinguished those with predominant limbic symptoms (n=29/56) from those with peripheral nerve hyperexcitability (PNH; n=27/56). In the limbic-prominent group, limbic features were either isolated (LE/-; 18/56, 32.1%) or combined with extra-limbic symptoms (LE/+; 11/56, 19.6%). Those with PNH had either mild PNH isolated or co-occurring with limbic symptoms (PNH/-; 11/56, 19.6%); or severe PNH accompanied by extra-limbic involvement (PNH/+; 16/56, 28.6%), resembling historical MoS descriptions. LE/- and LE/+ patients shared immunological and genetic characteristics, justifying considering them as a single entity (LE). HLA-DRB1*11:01 was carried more frequently by LE (94.0%) compared to PNH/- (40.0%, p=0.048) and PNH/+ (0.0%, p=0.003) patients. CASPR2-Ab positivity in CSF was more frequent in LE (93.1%) than in PNH/- (57.1%, p=0.04) and PNH/+ (0.0%, p=3.4x10⁻⁸) patients. CASPR2-Ab serum values were higher in LE (median 1:40960, range 1:10240-1:81920) than in PNH/- (1:160, 1:20-1:40960; p=0.002) and PNH/+ (1:3840, 1:40-1:20480; p=1.5x10⁻⁵) patients. Only PNH/+ patients had malignant thymoma (87.5%, p=4.1x10⁻¹⁰), serum LGI1-Ab (66.7%, p=2x10⁻⁶), and myasthenia gravis (50.0%, p=3.4x10⁻⁵).

Conclusion: Clinical, immunological, and genetic characteristics of CASPR2-Ab patients support the existence of 3 major disorders (LE, NMT, and MoS), suggesting distinct etiopathogeneses.

Disclosure: This study is supported by research grants from ANR (ANR-14-CE15-0001-MECANO) and FRM (Fondation pour la recherche médicale) DQ20170336751. This work has been developed within the BETPSY project,

which is supported by a public grant overseen by the French National Research Agency (ANR), as part of the second “Investissements d’Avenir” program (reference ANR-18-RHUS-0012). SM-C is supported by a research grant from Fundación Alfonso Martín Escudero (Spain).

EPR2197

Secondary autoimmune diseases and side effects in patients with Multiple Sclerosis treated with autologous hematopoietic stem cell transplantation.

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Background: Autologous hematopoietic stem cell transplantation (aHSCT), an immune reconstitution therapy (IRT), has been largely investigated as effective therapeutic approach for aggressive Multiple Sclerosis (MS). IRTs for MS have shown potential side effects, like 2ndary autoimmune diseases (SAD). Few post-aHSCT data regarding both clinical and subclinical autoimmunity with isolated laboratoristic support are known.

Aims: To describe the occurrence of both clinical and subclinical SADs in a cohort of MS patients treated with intense immunosuppression followed by aHSCT.

Methods: We evaluated 15 patients (14 relapsing-remitting MS, 1 active progressive MS) treated in our Center with aHSCT from 2016 to 2019. All patients underwent the same conditioning protocol (carmustine-cytarabine-etoposide-melphalan -BEAM- plus anti-thymocyte-globulin -ATG-), besides 1 that received high-dosage cyclophosphamide. We collected clinical-radiological data together with blood samples for SADs and lymphocitary immunophenotype at baseline and after every year.

Results: We obtained preliminary data from 5 patients. Medium follow-up was 2 years (range 1-3). No clinical SADs were evidenced. 4 patients showed laboratoristic SADs: 1 anti-smooth-muscle antibody without hepatic anomalies and 1 anti-nuclear antibody (1:320), both after 1 year and with no anomalies at immunophenotype, and 1 high titer β 2-glycoprotein-I IgM (136ru/mL) after 2 years associated with a persistent increase in B-cell percentage at immunophenotype (30-50% of lymphocyte). Ultimately, this patient showed a clinical-radiological relapse causing the start of ocrelizumab; β 2-glycoprotein-I IgM were negative at subsequent controls.

Conclusion: Isolated subclinical positivity with no clinical significance can occur in MS after aHSCT; longer follow-up is needed to better understand the significance of SADs.

Disclosure: Dr. E. Sbragia, Dr. G. Boffa, Dr. E. Capello, Dr. A.M. Raiola, Dr. R. Varaldo and Dr. F. Gualandi have nothing to disclose. Dr. G.L. Mancardi received support

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EPR2198

FEAM: A Novel Modulator for Neuroinflammation

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Background and aims: Neural inflammation is regulated by coagulation proteins including activated protein C (aPC) and its endothelial protein c receptor (EPCR) which together activate protease activated receptor 1 (PAR1) inducing anti-inflammatory effects. We have synthesized a novel molecule based on the binding site of FVII/aPC to EPCR (FEAM) and studied its effectiveness in the treatment of neuroinflammation.

Methods: An in-vitro model for neuroinflammation was induced by LPS applied to N9 microglia cells. In-vivo neuroinflammation was induced by LPS systemic injection to ICR mice and behavior was assessed by the stair-case test. Thrombin and aPC activity from cells and brains were measured by enzymatic fluorescence assays. Proliferation was measured by XTT activity assay. Coagulation factors and inflammation markers levels were evaluated by western blot and real-time PCR.

Results: FEAM prevented the LPS induced increased proliferation rate (1 vs 1.5 arbitrary units (aU), $p < 0.001$) and PAR1 expression in N9 (1.7 vs. 1.2, $p < 0.001$). FEAM also prevented the decreased aPC activity induced by LPS (0.46 vs 0.62 aU, $p < 0.003$) and prevented the elevation of coagulation factors (FX and thrombin) and inflammatory markers (TNF α). In the whole animal model FEAM prevented the LPS induced elevated brain thrombin activity and other coagulation and inflammation factors. FEAM treatment induced improvement in general health indices such as weight, learning and memory and mobility.

Conclusion: In conclusion, FEAM modulation of the FVII-aPC-EPCR pathway may shift the thrombin/PAR1 pathway toward aPC-EPCR mediated protective downstream effects.

Disclosure: ESS JC and NM have a provisional patent "Novel Molecules for the Treatment of Inflammation". FEAM is included in this patent application. This project was supported by the Israel Innovation Authority.

EPR2199

Screening for encephalitis-causing autoantibodies in serum and CSF of first-episode psychosis patients and controls

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Background and aims: Recently, encephalitides caused by autoantibodies directed against neuronal surface proteins have been identified. Psychiatric symptoms dominate early stages of the disease progression, especially in patients with N-methyl-D-Aspartate receptor (NMDA-R) autoantibody encephalitis. Thus, a compelling hypothesis is that a subgroup of psychiatric patients might suffer from autoimmune encephalitides with atypical presentations. Previous studies addressing this hypothesis have reached divergent conclusions, possibly due to serum-only testing and/or testing of psychiatric cohorts years after disease onset.

The aim of this study is to address the hypothesis by autoantibody screening of serum and CSF from patients with first-episode psychosis and healthy controls.

Methods: Serum and CSF were collected from 77 patients presenting with first-episode psychosis, of which around half were naïve to antipsychotic drugs, and 53 control subjects. Reactivity against neuronal specific autoantigens was tested on live HEK293 cells that were transiently induced to express the dopamine receptor 2 (D2R), leucine rich glioma inactivated 1 (LGI1), Gamma Aminobutyric acid Receptors A (GABAA-R), GABAB-R, the glycine receptor, NMDA-R or Contactin associated protein 2 (CASPR2).

Results: All participants were negative in the CSF for NMDA-R autoantibodies. Furthermore, all were seronegative for antibodies to D2R, LGI1, GABAA-R, GABAB-R and the glycine receptor. 1 participant was seropositive for CASPR2 autoantibodies and 1 for glycine receptor autoantibodies, but both were autoantibody-negative in CSF.

Conclusion: No participants fulfilled diagnostic criteria for any autoimmune encephalitis. This study does not support the hypothesis that a subgroup of patients who present with psychosis have an underlying autoimmune encephalitis.

Disclosure: Jakob Theorell's work was funded by the Swedish Wenner-Gren Foundations. No other specific funding was allocated to this project.

EPR2200

Spectrum and treatment of central nervous system complications of immune checkpoint inhibitors

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Background and aims: To describe the spectrum, treatment and outcome of central nervous system complications associated with immune checkpoint inhibitors (CNS-ICI).

Methods: Five-years retrospective nationwide study.

Results: We identified 19 patients with immune-related CNS-ICI. The patients were receiving nivolumab (n=8), pembrolizumab (n=6), a combination of ipilimumab-nivolumab (n=3), ipilimumab-durvalumab (n=1), or atezolizumab (n=1). Underlying malignancies included non-small-cell lung cancer (n=8), melanoma (n=3), bladder (n=2), kidney (n=2), pleural mesothelioma (n=1), small-cell lung cancer (n=1), liposarcoma (n=1), and Hodgkin's lymphoma (n=1). 6 of the patients developed CNS-ICI complications while having known brain metastases. Neurological phenotypes were limbic encephalitis (n=8), meningo-encephalitis (n=4), cerebellitis (n=4), and atypical syndromes (n=3; steroid-responsive isolated confusion in 2 and polyradiculoneuritis associated with subacute parkinsonism in 1). Associated autoantibodies included onconeural (Ma2 [n=7], Hu [n=1]), astrocytic cytoplasmic (GFAP [n=2]), and neuronal surface (CASPR2 [n=1]) specificities. ICIs were withheld and corticosteroid treatment was given in all cases. Additionally, 5 patients received intravenous immunoglobulin, 2 rituximab, 1 plasmapheresis, and 1 infliximab. Overall, 6 patients died (4 of them belonging to the limbic encephalitis group, all harboring Ma2 antibodies, 1 with GFAP-associated meningoencephalitis, 1 atypical seronegative). Re-administration of ICI after CNS complications was attempted in 3 patients (none of whom with limbic encephalitis), without further relapses.

Conclusion: 4 major clinical phenotypes characterize CNS complications of ICIs, each with a distinct immunological background, disease course, and response to treatment. CNS-ICI can develop in patients with known brain metastases. Intriguingly, underlying cancers, antibody prevalence and outcome appear different to those of patients with ICI-induced peripheral neurological manifestations.

Disclosure: This study is supported by research grants from ANR (ANR-14-CE15-0001-MECANO), and FRM (Fondation pour la recherche médicale) DQ20170336751. This work has been developed within the BETPSY project, which is supported by a public grant overseen by the French National Research Agency (ANR), as part of the second "Investissements d'Avenir" program (reference ANR-18-RHUS-0012).

Neuro-oncology 1

EPR2201

Diffuse leptomeningeal glioneuronal tumors: a case-series of three adult patients

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Background and aims: Diffuse leptomeningeal glioneuronal tumor (DLGNT) represents a rare entity, firstly described in 2016 WHO updated classification. Molecular hallmarks are 1p loss and a frequent MAPK pathway activation. Adult cases are exceptional.

Methods: We retrospectively reviewed 3 adult cases with histologically proven DLGNT treated in our department between 2015 and 2019.

Results: It was 1 female and 2 males, aged 29, 32 and 56 years. Initial symptoms were lumbosciatalgia, intracranial hypertension, neurocognitive impairment and Parinaud syndrome. Delay before diagnosis varied from 6 months to 8 years. At diagnosis, all patients presented with diffuse infiltration of meninges with parenchymal localizations in 2 cases. 1 of them presented a cerebral vasculitis-like aspect. Lumbar puncture was inconclusive and diagnosis confirmed after open arachnoid/intraventricular biopsy. DLGNT molecular criteria were fulfilled in 2 patients whereas the 3rd was only histological due to lack of sample. Treatment was heterogeneous including chemo and radiotherapy with different efficacy. Noteworthy is the clinical and partial radiologic response to Carboplatin used in 2 cases. 2 patients died after 24 and 40 months (1 is still alive at 96 months).

Conclusion: As the DLGNT is a rare and heterogeneous entity, diagnosis is difficult especially in adults. In most cases, meningeal biopsy with extensive molecular biology is required for diagnosis and treatment.

Disclosure: Nothing to disclose

EPR2202

Multiparametric assessment of factors influencing 2 HG accumulation in diffuse brain gliomas

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Background and aims: 2HG can be detected non-invasively in IDH-mutant gliomas by in vivo MRS. We investigated factors affecting 2HG accumulation and explored the prognostic value in IDH mutant gliomas and 2HG variations on treatment.

Methods: We prospectively scanned by MEGA-PRESS 70 glioma patients (24 before surgery and 46 IDH mutant operated glioma). CRLB cut-off was 50%. We followed up 9 IDH mutant patients during radiotherapy and chemotherapy. We analyzed radiological parameters and genetic profile. 2HG concentrations in plasma, urine, and surgical samples were measured by GC-MS.

Results: We detected 2HG with a sensitivity of 95% in untreated patients, and of 69% in pre-treated patient. PPV was 100% in both groups. 2HG was lower in pre-treated IDH mutant gliomas (1.1 versus 2.3mM, P=0.02) and decreased during radiotherapy and chemotherapy before any radiological change. 2HG was correlated with tumor volume (P=0.02), choline (r=0.58 P<0.0001), cellular density (r=-0.40 P=0.01), “expansive” presentation, mutant reads, urine 2HG (r=0.80, P=0.003) and inversely correlated with Myo (r=-0.29 P=0.03) and cystic areas (P=0.04). 2HG was higher in IDH2 mutant (4.7 versus 2.4mM, P=0.02) and lower in non R132H IDH1 mutant (1.12mM P=0.004). 2HG detection was associated with longer survival (HR 0.09; 95%CI 0.018-0.52).

Conclusion: Tumor volume, cellular density, previous radio- and chemotherapy and genetic features determine 2HG detection in IDH mutant gliomas. 2HG detection is associated with better outcome and can be reliably monitored during anti-cancer treatments.

Disclosure: Nothing to disclose

EPR2203

Isolated CNS involvement revealing histiocytosis with emperipolesis and BRAF mutation

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Background and aims: Histiocytoses are rare inflammatory myeloid hemopathies with exceptional isolated CNS involvement is exceptional. This case report aims to contribute to our understanding of this entity.

Methods: Retrospective chart review of clinical data, magnetic resonance imaging, biology and histopathological findings of a patient who presented with an atypical neurohistiocytosis with isolated CNS involvement.

Results: 48-year-old man with a history of pleural tuberculosis who presented in July 2019 with paresthesias of the left hemiface. The physical examination revealed a left 5th cranial nerve involvement. Brain MRI showed 3 FLAIR hyperintensities with homogeneous enhancement in the left temporal, occipital and cerebellar peduncle (Figure 1). Brain MRI with perfusion and spectroscopy sequences showed an increased Choline/NAA ratio without hyperperfusion (Figure 2). Blood tests and lumbar puncture were normal. Body CT-Scan and PET-CT did not evidence any systemic lesion. Several hypotheses were discussed: infectious (e.g. tuberculosis), inflammatory (neurosarcoidosis, Behcet's disease) and tumoral (lymphoma). A stereotaxic brain biopsy was rapidly performed. Histological analysis showed parenchymal infiltration with foamy histiocytes. Immunostaining revealed CD68+, CD163+, PS100+, and CD1a- tumor cells and tumor sequencing detected a BRAF(V600E) mutation, overall consistent with Erdheim Chester disease (ECD), BRAF-mutant. However, emperipolesis lesions (Figure 3) - suggestive of Destombes-Rosai-Dorfman disease (RDD) - were also present, suggesting a possible mixed form, never reported to our knowledge.

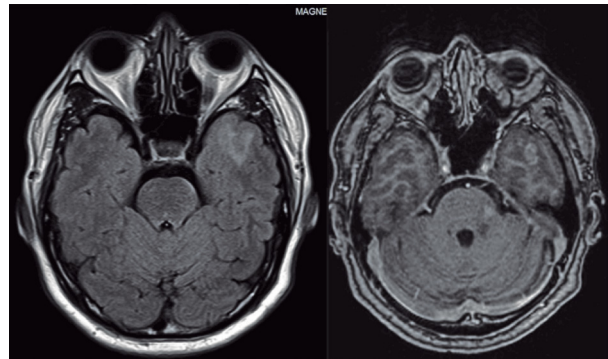


Figure 1

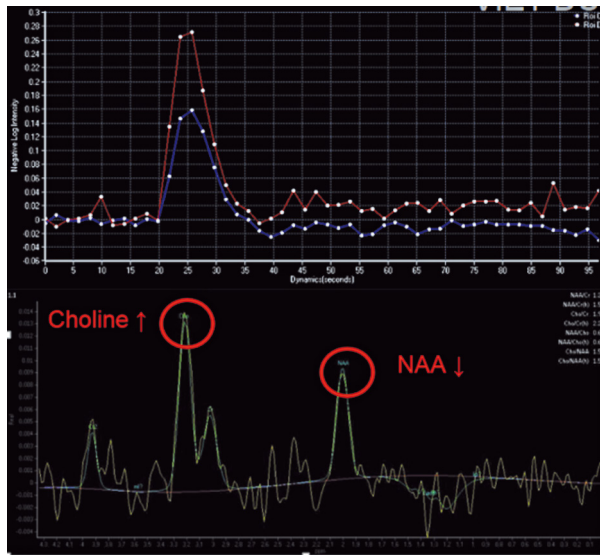


Figure 2

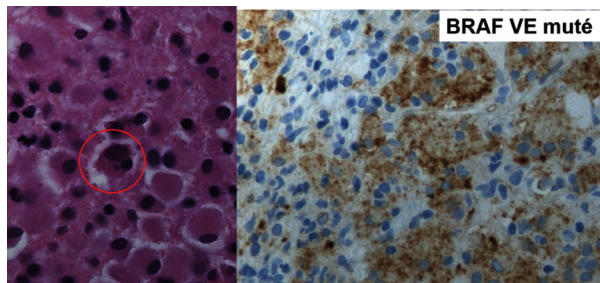


Figure 3

Conclusion: This report expands the spectrum of neurohistiocytosis and raises the question of mixed forms characterized by the presence of both emperipolesis and BRAF mutation.

Disclosure: Nothing to disclose

EPR2204

Initial temozolomide for high-risk low-grade gliomas in a phase II AINO (Italian Association for Neuro-Oncology) study: a post-hoc analysis of the efficacy within molecular subgroups of WHO 2016

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Background and aims: Regarding the optimal treatment strategy for high risk WHO grade II gliomas after incomplete surgery the efficacy of adjuvant chemotherapy to delay radiotherapy and the risk of cognitive defects is still debated.

Methods: A re-evaluation, according to new molecular subgroups of WHO 2016, of long term results of up-front temozolomide for a cohort of high risk grade II gliomas included in a phase II multicenter study (60 patients) has been performed. The primary endpoint was response according to RANO criteria, while secondary endpoints were seizure response, PFS and OS.

Results: Response rate was significantly higher among oligodendrogliomas IDH-mutant and 1p/19q codeleted (76%) than among diffuse astrocytomas either mutant (55%) or wild-type (36%). A reduction of seizure frequency >50% was observed in 87% of patients and a seizure freedom in 72% with a significant association of seizures reduction >50% with the presence of an IDH mutation. Median PFS, PFS at 5 and 10 years, median OS and OS at 5 and 10 years were significantly longer in oligodendrogliomas IDH-mutant and 1p/19q codeleted. In a median follow-up of 9.3 years 67% of patients with oligodendroglioma IDH mutant and 1p/19q codeleted did not recur and 59% did not receive radiotherapy at recurrence with a median follow-up of 8.2 years.

Conclusion: The use of temozolomide as initial treatment is an useful option for oligodendrogliomas IDH-mutant and 1p/19q codeleted, when incompletely resected or progressive after surgery alone, or with intractable seizures. Radiotherapy and/or reoperation and/or second-line chemotherapy, at recurrence, could be useful.

Disclosure: Nothing to disclose

EPR2205

Undiagnosed Lymphomatosis Cerebri progression to space-occupying lesion.

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Background and aims: Lymphomatosis cerebri (LC) is a rare variant of Primary Central Nervous System Lymphoma (PCNSL) in which neuroimaging shows diffuse instead of nodular white-matter distribution.

Methods: A 72-years-old male with medical history of IV right cranial nerve microvascular paresis and bladder carcinoma in remission presented subacute dementia and focal seizures. CT and MRI showed a cortical and white-matter diffuse bifrontal lesion with little, irregular contrast enhancement. CSF analysis ruled out infections. Steroids and antiepileptics were empirically started due to suspicion of gliomatosis cerebri with oedem. Steroids were prescribed for 10 days with posterior tapered schedule. The biopsy 9 days after was inconclusive. Body PET-CT showed no alterations. The patient recovered his previous cognitive level and remained without seizures on lacosamide. 1 year later the patient presented subacute right cerebellar syndrome and forgetfulness.

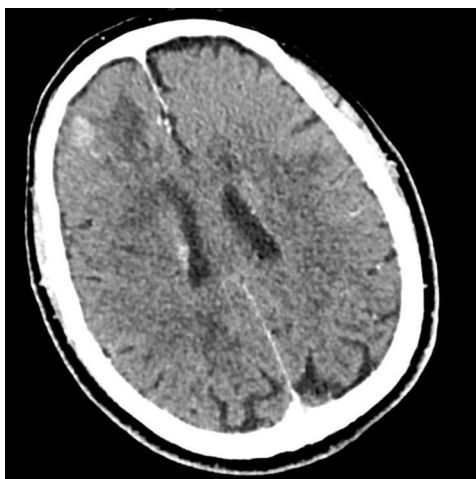


Figure 1: Cranial CT with contrast at admission (before steroid initiation). Bilateral leukopathy especially prominent on right frontal lobe with cortical thickening and associated mild, patchy contrast enhancement.

Results: A new MRI disclosed a homogenous enhancing right cerebellous mass and progression of leukopathy. The cerebellar mass was biopsied. Immunohistochemistry was positive for Diffuse Large B-cell Lymphoma (DLBCL). The patient is currently under induction treatment with high-dose methotrexate and steroids with neurological improvement.

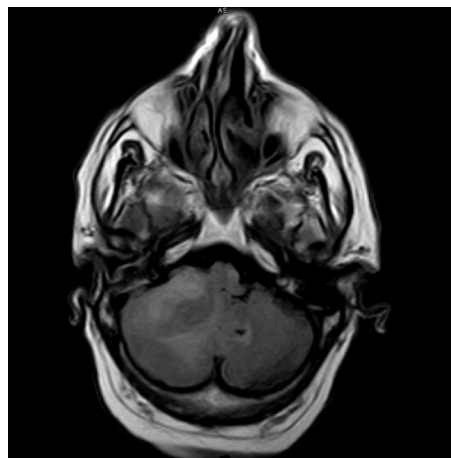


Figure 2: MRI T1-weighted with Gadolinium enhancement. A new onset cerebellar space occupying lesion with homogeneous contrast enhancement and mass-effect compatible with cerebellar lymphoma.

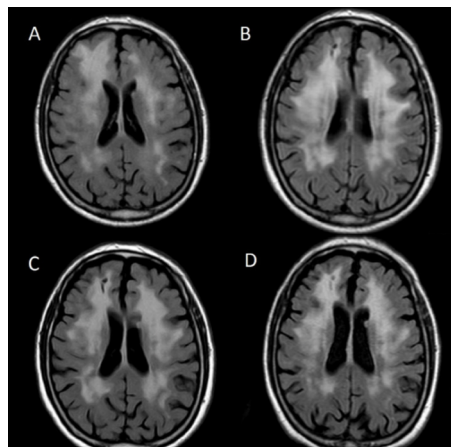


Figure 3: White matter involvement evolution in FLAIR sequences. A-Nov 2018. Asymmetrical leukopathy with marked right frontal lobe involvement. B-Feb 2019. After 50 days of steroid treatment showing decrease in right frontal lobe involvement and a more symmetrical white matter distribution. C and D: Jun 2019 and Dec 2019, respectively.

Conclusion: Leukopathy-like lesions have been described as “sentinel lesions” for PCNSL. Polyclonal B-cell proliferations evolving into monoclonal tumours have been hypothesized. Conversely, an early response to steroid treatment may have obscured initial tests results. The early and transient clinical and radiological response to steroids is consistent with a LC debut of a PCNSL. We highlight the importance of LC in the differential diagnosis of leukopathy and steroid-induced changes in this pathology.

Disclosure: Nothing to disclose

EPR2206

Clinical and Molecular Prognostic Factors for Long-Term vs Short-term Survival of Patients with Glioblastomas

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Background and aims: This study aims to clarify the clinical and molecular characteristics associated with long- or short-term survival in glioblastoma, which remain until now largely unknown.

Methods: We analyzed clinical and molecular characteristics of 74 long-term survivors (>5 years, LTS) and 376 short-term survivors (<1 year, STS) from the Parisian tumor database.

Results: Age at diagnosis ($p < 10^{-11}$), KPS (Karnofsky Performance Score) at diagnosis ($p < 10^{-7}$) and type of surgery (biopsy vs resection, $p < 10^{-9}$) differed according to the long or short survival. The IDH (Isocitrate DeHydrogenase) mutation rate was higher in LTS than STS (29% vs 8.3%, $p < 0.0004$), as well as the promoter methylation of the MGMT gene (O6-methylguanine-DNA methyltransferase) (88% vs 46%, $p < 0.004$), the gain of chromosome 19p (42% vs 22%, $p < 0.03$), and of 19q (32% vs 17%, $p < 0.05$). After adjustment for age at diagnosis, complete loss of chromosome 10 ($p < 0.004$), loss of 10q or 10p ($p < 0.02$ and 0.03) were additionally significantly more frequent in LTS. In the subgroup with IDH wild-type (IDHwt), complete loss of 10 ($p < 0.006$), loss of 10q and 10p ($p < 0.02$ and 0.03), promoter methylation of MGMT ($p < 0.02$) and mutation of P53, ($p < 0.05$) were significantly more frequent in LTS after adjustment for age.

Conclusion: Younger age and better KPS at diagnosis are associated with LTS vs STS, as well as resection vs biopsy. MGMT promoter methylation, loss of chromosome 10 and gain of 19p or 19q might be prognostic for longer survival, as well as P53 mutation for IDHwt patients.

Disclosure: Nothing to disclose

EPR2207

Long-term follow-up of schwannoma growth behavior in adult neurofibromatosis type 2 and schwannomatosis patients using whole-body MRI

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Background and aims: Neurofibromatosis type 2 (NF2) and schwannomatosis (SWN) are related genetic tumor predisposition syndromes caused by distinct gene mutations on chromosome 22, and are characterized by the presence of cranial, peripheral, and/or spinal nerve schwannomas. The long-term growth behavior of schwannomas is unknown but knowledge thereof would help guide patient surveillance and selection for treatment. Whole-body MRI (WBMRI) can detect whole-body schwannoma burden.

Methods: 12 NF2 and 10 SWN patients who underwent WBMRI between 2007-2010 underwent repeat WBMRI between 2018-2019. Schwannomas were segmented on short tau inversion recovery (STIR) sequences. Tumor volume was calculated using a 3-dimensional tumor quantification software (3DQ1). Tumor growth and shrinkage were defined as a volume change $\geq 20\%$ over the entire study period.

Results: Median time between scans was 10 years. 103 schwannomas were analysed (Table 1). 50% of tumors grew by a median 88.3% (NF2-associated) and 100.4% (SWN-associated); all growing NF2-associated schwannomas grew in the setting of exposure to systemic therapy. Excluding resected tumors, 19.4% of tumors shrank by a median 48.5% (NF2-associated) and 37.4% (SWN-associated). All shrinking NF2-associated tumors had been treated with systemic therapy whereas none of the shrinking SWN-associated tumors had been. 19 new tumors developed in 8 patients.

	NF2-associated schwannomas	SWN-associated schwannomas
Number of tumors analysed	46	57
Median % change in tumor volume	+9.4%	+6.1%
Number of growing tumors (%)	23 (50.0%)	29 (50.1%)
• Median growth (%)	• +88.3%	• +100.4%
• Number of tumors treated with systemic therapy (%)	• 23 (100%)	• 1 (3.4%)
Number of shrinking tumors (%)	10 (21.7%)	10 (17.5%)
• Median shrinkage (%)	• -48.5%	• -37.4%
• Number of tumors treated with systemic therapy (%)	• 10 (100%)	• 0 (0%)
Number of new tumors (%)	7 (15.2%)	12 (21.1%)

Table 1. Comparison of schwannoma growth behavior in NF2 and schwannomatosis patients

Conclusion: Half of NF2- and SWN-associated schwannomas grow significantly over a decade. In NF2 patients, growth occurs despite systemic treatment whereas, in SWN patients, schwannomas may shrink spontaneously without treatment. These findings suggest a more aggressive tumor phenotype in NF2 patients. Patient enrollment and correlation of MRI findings with functional outcomes and hormone exposure history are ongoing.

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EPR2208

Clinical and imaging characterization of Dysembryoplastic Neuroepithelial Tumours: an experience of a tertiary hospital in Portugal

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Background and aims: Dysembryoplastic neuroepithelial tumours (DNET) are benign, slow-growing tumours usually presenting with intractable seizure, due to its mainly cortical topography and associated with a good prognosis following tumour resection. We aim to characterize the clinical and imaging features of a case series from a tertiary hospital in Portugal.

Methods: A retrospective study of DNET diagnosed at the laboratory of neuropathology between 2000 and 2019. Clinical and imaging data were collected from the clinical files. Histological samples were reviewed by 2 neuropathologists.

Results: 23 patients with DNET were included, 13 males, with a mean age of 24.61 years [4 to 55]. In some patients clinical data is missing. Tumour localization was mostly in the temporal lobe (52.2%), and 1 patient presented an intraventricular DNET. 19 of 21 patients (95%) presented with epilepsy, 63% of these being refractory to medication. 1 patient presented with headaches and for 1 was an incidental finding on image. 1 patient had associated cortical dysplasia. There were no tumour recurrences. Almost (14 out of 16) all of the epileptic patients were seizure-free and in 5 patients antiepileptic drugs were stopped.

Conclusion: Our study is in accordance with the literature regarding clinical presentation, location and post-surgical outcome. Indeed, patients had no tumour recurrences and most became seizure-free, some of them with antiepileptic drugs suspension.

Disclosure: Nothing to disclose

EPR2209

CXCL13 and CXCL9 as diagnostic and therapy monitoring markers in central nervous system lymphoma

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Background and aims: CNS lymphoma (CNSL) is an aggressive brain tumour with poor prognosis when untreated. Standard diagnostics like MRI and cerebrospinal fluid (CSF) analysis are often not sensitive/specific enough so that invasive biopsy must be performed to confirm diagnosis. This illustrates the need for less invasive biomarkers with high diagnostic yield, particularly in the CSF.

Methods: In this prospective monocentric study, we explored the potential of CXCL13 and CXCL9 as diagnostic, therapeutic and prognostic biomarkers for CNSL. For that purpose, CSF and serum samples were collected from patients presenting with brain lesion(s), in whom diagnostic lumbar puncture was performed during clinical routine. Samples were obtained from patients at different disease stages (first admission, remission, relapse, progress). CXCL13 and CXCL9 concentrations were determined by commercially available ELISA kits.

Results: CSF CXCL13 and CXCL9 levels were significantly increased in patients with CNSL compared to those with lesions of other origin. A cut-off value of 80pg/ml for CXCL13 shows high sensitivity (90.7%) and specificity (90.1%) for the diagnosis of CNSL. CXCL9 at a cut-off value of 84pg/ml is less sensitive (61.5%) and specific (87.1%). The combined elevation of both proteins reached a specificity of 98% at the expense of a low sensitivity (58,5%). Both cytokines correlate with clinical course and therapeutic response; their concentrations decrease upon remission and increase again during CNSL relapse.

Conclusion: Our results suggest CSF CXCL13 and CXCL9 as promising biomarkers for diagnosis and therapy monitoring in CNSL. However, our findings need further validation in independent cohorts.

Disclosure: Nothing to disclose

Neurorehabilitation

EPR2210

French survey about pain perception and management in patients with locked-in syndrome: Preliminary results.

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Background and aims: Patients with locked-in syndrome (LIS) may suffer from chronic pain, which can significantly affect their daily life and well-being. In this survey, we aim to investigate the presence of potential pain and how it is managed in patients with LIS.

Methods: An online survey was completed by patients with LIS through the Association du Locked-In Syndrome (ALIS) and the Centre du Cerveau2 networks. It was divided in 2 sections: a 1st part collecting respondents' socio-demographic information (gender, age, etiology), and a 2nd part collecting data on pain perception and management (type and frequency of pain, daily pain impact, tested treatments).

Results: Among the 58 respondents (20 females, mean age 49±13 yo, 35 strokes), 26 experienced pain in their daily life (45%; median pain intensity: 6.5/10; 54% with leg pain) and 22 of them had punctual pain (85%, presents at certain times of the day). Out of these 26 patients, 19 (73%) received pain treatment (61% pharmacological, 11.5% non-pharmacological such as osteopathy and acupuncture) and judged the treatment efficacy as being moderate (median treatment efficiency: 5 – range 0-10). However, 15/26 (58%) patients are willing to try other non-pharmacological treatments such as hypnosis or meditation. Furthermore, they declared that pain influences their sleep quality (42%), emotions (85%) and attention (58%).

Conclusion: Almost half of the LIS patients experience pain that affect their quality of life, sleep and cognition. Current pharmacological and non-pharmacological treatments are perceived as moderately efficient and more than half of the patients would like to try new non-pharmacological treatments.

Disclosure: This study was supported by the University and University Hospital of Liège, the Belgian National Funds for Scientific Research (F.R.S-FNRS), the European Union's Horizon 2020 Framework Program for Research and Innovation under the Specific Grant Agreement No. 785907 (HBP SGA2), Luminous project (EU-H2020-fetopen-ga686764), the James McDonnell Foundation, the Public Utility Foundation 'Université Européenne du Travail', the "Fondazione Europea di Ricerca Biomedica", AstraZeneca Foundation, "Plan National Cancer" of Belgium (grant number 138), Benoit Foundation (Bruxelles), A.T. is a post-doctoral fellow, and S.L. is research director at the F.R.S-FNRS.

EPR2211

Patients with disorders of consciousness may experience pain during physiotherapy.

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Background and aims: Neuro-orthopaedics disorders are common in patients with disorders of consciousness (DOC) and can lead to potential pain during PT (physiotherapy). These patients' inability to communicate makes pain management difficult for clinicians. In this randomized double-blind placebo-controlled study, we investigated the presence of signs of nociception during PT and following an analgesic treatment.

Methods: During baseline, the NCS-R (Nociception Coma Scale-Revised) was used to assess pain: at rest; following a tactile (TS) and a nociceptive stimulation (NS); and during PT. Patients with signs of potential pain during PT were assessed during a placebo and analgesic treatment conditions on 2 consecutive days in a randomized order. We used Kruskal-Wallis and Wilcoxon tests (post hoc analysis) to investigate difference in NCS-R scores between each condition.

Results: 15 out of 19 patients presented signs of potential pain during PT (78.9%), and only 5 of them already had an analgesic treatment before the study (5/15; 33.3%). Patients showed higher NCS-R scores during PT as compared to the three others conditions, suggesting that passive mobilizations are potentially painful for DOC patients. Out of the 19 patients enrolled, 10 were included in the placebo-controlled trial (time-window too short for treatment administration). We did not find an effect of analgesic treatment on the NCS-R score for any condition.

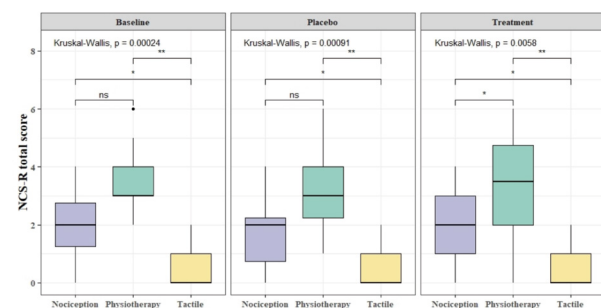


Figure 1: Change in the NCS-R total scores (tactile or nociceptive stimuli or PT), at baseline, after placebo and after treatment administration (n=10, Wilcoxon matched pairs signed rank tests as post hoc analysis, **=p<0.01, *=p<0.05)

Conclusion: This study highlights that PT may be painful for DOC patients and appropriate assessment and treatment before and during mobilizations should become a priority in clinical setting. Future studies should focus on development of sensitive assessment tools and analgesic dosage.

Disclosure: This study was supported by the University and University Hospital of Liège, the Belgian National Funds for Scientific Research (F.R.S-FNRS), the Marie Skłodowska-Curie Actions (H2020-MSCA-IF-2016-ADOC-752686), the European Union's Horizon 2020 Framework Program for Research and Innovation under the Specific Grant Agreement No. 785907 (HBP SGA2), Luminous project (EU-H2020-fetopen-ga686764), the James McDonnell Foundation, the Public Utility Foundation 'Université Européenne du Travail', the "Fondazione Europea di Ricerca Biomedica". A.T. and C.C. is a post-doctoral fellow, and S.L. is research director at the F.R.S-FNRS.

EPR2212

The effect of hypoxic-hypercapnic training on the regression of neurological deficit after a stroke (pilot study).

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Background and aims: In our previous studies, hypoxic-hypercapnic respiratory training (GGRT) have shown efficacy in the rehabilitation of patients after ischemic stroke (IS) in the acute period.

Methods: We continued a pilot, blind, randomized, placebo-controlled study in which 40 patients participated in the acute period of mild to moderate IS. All patients were randomized to exposure group (GE) and placebo group (GP). Patients were evaluated clinically before and after the course of GGRT, or placebo exposure according to the NIHSS, Barthel, Rankin, Rivermead scales, and the Stange test was also used. The average number of training was 7.4±2.1, the time of each training was 20 minutes.

Results: Positive dynamics is noted in all groups on all used scales (p<0.05). During early rehabilitation with GGRT, a decrease in the neurological deficit estimated by NIHSS and an increase in mobility estimated by Reavermead were found: NIHSS GE 4.1±1.2 → 1.2±0.9 (p<0.01), NIHSS GP 4.2±1.7 → 2.5±2 (p<0.01), Rivermead GE 8.1±2.5 → 14.1±1.8 (p<0.01), Rivermead GP 7.4±2.5 → 12.3±1.8 (p<0.01). The degree of restoration of neurological functions in GE is significantly higher than GP (p = 0.036). A similar dynamics is also noted in the assessment by the index of mobility of GE and GP (p=0.027).

Conclusion: GGRT can be an effective and safe way to rehabilitate patients after IS.

Disclosure: Nothing to disclose

EPR2213

Withdrawn

EPR2214

Imaging Correlates of Hand Motor Performance in Multiple Sclerosis: Focus on Structural and Functional Motor Networks

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Background and aims: Hand-motor impairment has a strong impact on daily-life activities in multiple sclerosis (MS) patients and MRI-metrics may contribute to better understand the substrates of these clinical deficits. We applied source-based morphometry, mean diffusivity indices and seed-based analysis, in a large cohort of MS patients to assess the association between altered MRI findings and measures of manual dexterity as well as global disability.

Methods: From 134 HC and 366 right-handed MS patients, brain 3D T1-weighted, diffusion tensor and functional (at rest) MRI scans were acquired and used to perform multivariate analyses between MRI measures of manual dexterity [9 Hole Peg Test (9HPT) and Finger Tapping (FT) test] and Expanded Disability Status Scale (EDSS).

Results: Compared with HC, MS patients showed significant atrophy in motor relevant GM networks, alteration of WM tract integrity, and abnormal resting state (RS) functional connectivity (FC) ($p < 0.001$). The multivariate analysis retained age, lower normalized brain volume (NBV), cerebellar GM network atrophy, and reduced right corticospinal tract fractional anisotropy (FA) as best predictors of EDSS score ($R^2 = 0.40$). Worse right and left 9HPT performance ($R^2 = 0.49$ for both) was predicted by progressive MS phenotype (PMS), age, male-gender, reduced NBV, higher T1 lesion load, reduced cerebellar peduncle FA, and increased left inferior frontal gyrus RS FC. FT performance predictors (right- $R^2 = 0.40$; left- $R^2 = 0.41$) were PMS, age, female-gender, sensorimotor and cerebellar network atrophy and reduced RS FC in sensorimotor regions.

Conclusion: GM tissue loss, WM-tract and RS FC abnormalities in motor-related regions contributed to explain hand-motor dysfunction in patients with MS.

Disclosure: Nothing to disclose

EPR2215

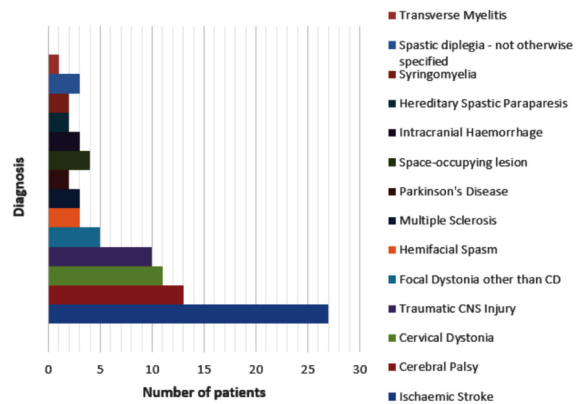
Botulinum Toxin Clinic for Neurology Patients in the Maltese Islands: Analysis of Therapeutic Use and Outcome Measures

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Background and aims: The aim of this retrospective audit was to assess the number of patients making use of the service, the nature of the disorders being treated and further demographic data relating to number of visits, Botulinum toxin dose and time of follow-up. Modes of measurement and documentation of clinical outcomes were also assessed.

Methods: Medical records as well as an online patient register were used to gather the above data. The patients' expectations and objective treatment goals were recorded when information was available from the medical records. Input by other members of the multidisciplinary team such as physiotherapists and occupational therapists was also recorded.

Results: 86 patients have attended the Botulinum Toxin (BoNT) Clinic since its set-up in 2013. Mean patient age was 51 years. The majority of patients were referred following an ischaemic cerebrovascular event (Graph 1). Duration of treatment was influenced by the underlying diagnosis (Table 1). Documentation of clear treatment goals and patient's expectations was low (30%). 70% of cases documented symptomatic improvement, however objective assessment scales were not routinely used. Physiotherapists followed up 76% of patients.



Graph 1. Diagnoses of patients treated at the Botulinum Toxin Clinic

Diagnosis	Number of patients	Botulinum toxin Dose	Average years on Treatment	Average No. of Visits	Average Interval between visits
Ischaemic Stroke	24	50-200U	1.4	4	4 months
Cerebral Palsy	11	50-150U	3	9	5 months
Cervical Dystonia	13	50-100U	5.4	14	4-5 months
Focal Dystonia other than CD	5	50-100U	< 1	2	0-3 months
Traumatic brain / spinal injury	10	100-200U	2.5	6 - 7	3-4 months
Arteriovenous malformation	1	100U	< 1	2	4 months
Intracranial Haemorrhage	3	100U	1	4	4 months
Multiple Sclerosis	3	100U	5	11	4 months
Parkinson's Disease	2	100U	< 1	2	3 months
Hemifacial Spasm	2	50U	3	3	4 months
Spastic Diplegia - not otherwise specified	3	100U	1.5	4	3-4 months
Hereditary Spastic Paraparesis	2	100-200U	3	8	4 months
Syringomyelia	2	100U	3	9	4 months

Table 1. Treatment data for different patient groups

Conclusion: Patients with a vast array of neurological conditions benefit from treatment with BoNT. In patients requiring treatment for a prolonged period, the use of clear outcome measures can help to guide treatment goals and set realistic expectations. Use of objective rating scales has now been implemented following this audit. The recent addition of physiotherapists to the BoNT clinic team has been instrumental in providing valuable input and liaison with other rehabilitation professionals.

Disclosure: Nothing to disclose

EPR2216

Overall clinical complexity of patients in prolonged Vegetative and in Minimally Conscious State: a multi-center observational study.

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Background and aims: Patients in Vegetative State (VS) and in Minimally Conscious State (MCS) show a high burden of medical complications [Estraneo et al., 2018] and care needs [Whyte et al., 2013]. The present observational multi-center study aimed at comparing overall clinical complexity (OCC), including both medical complications (e.g., respiratory failure; heterotopic ossifications, HO; parasympathetic hyperactivity, PSH) and care needs (e.g., management of artificial ways for eating and breathing), in the two diagnostic groups.

Methods: Demographic, anamnestic and clinical data from 264 patients (VS=141; MCS=123; see Table 1) were collected within 1 week after admission to 23 Italian intensive neurorehabilitation units. Medical complications developed in the 1st 3 months of rehabilitation stay were also recorded. Beyond comparing the 2 diagnostic groups, we also compared OCC in patients with vascular, anoxic and traumatic etiology.

	Available Data	DoC	VS	MCS	Anoxic	Vascular	TBI
N		264	141	123	56	125	83
Meanage (SD), (years)	264	57,8 (17,7)	59,6 (16,9)	55,7 (18,3)	54,7 (16,9)	64,7 (13,3)	49,5 (19,8)*
Sex M:F (n)	264	185/79	100/41	85/38	42/14	74/51	69/14*
Etiology	264						
Anoxic		56	42	14*			
Vascular		125	57	68			
TBI		83	42	41			

Note: DoC= Disorder of Consciousness; VS = vegetative state; MCS= minimally conscious state; TBI = traumatic brain injury. *significant group-difference at p<0.05 (Fisher's exact Test, Chi-square Test or ANOVA as appropriate)

Results: Patients in VS showed significantly higher occurrence of percutaneous endoscopic gastrostomy, tracheotomy tube, pressure sores and oxygen therapy than patients in MCS. Moreover, patients in VS developed genito-urinary and respiratory complications, PSH and HO more frequently than patients in MCS. Compared with other etiological groups, post-anoxic patients had lower level of consciousness, higher functional disability and higher presence of gastrostomy, whereas traumatic patients had higher occurrence of craniectomy, HO and need for continuous clinical monitoring, and vascular patients showed more comorbidities before brain injury.

Conclusion: Both VS and MCS show very severe OCC in rehabilitation settings. Frequency of several conditions depends on clinical diagnosis and etiology. These findings could help in guiding clinical management and planning treatment.

Disclosure: Nothing to disclose

EPR2217

Brain-Computer interface (BCI) triggered functional electrical stimulation (FES) and avatar for motor rehabilitation of the lower limbs of chronic stroke patients, a group study.

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Background and aims: Brain-Computer Interfaces (BCIs) show important rehabilitation effect for patients after stroke. Previous studies have shown improvement, also for patients that are in chronic stage and/or have severe hemiparesis and are particularly challenging for conventional rehabilitation techniques.

Methods: For this pilot study 5 stroke patients in chronic phase with hemiparesis in the lower extremity were recruited. All of them participated in 25 BCI sessions about 3 times a week. BCI system was based on the motor imagery of the paretic foot and healthy hand with Functional Electrical Stimulation (FES) and Avatar feedback. Assessments were conducted to assess the changes in motor improvement before, after and during the rehabilitation training.

Results: Our primary measures used for the assessment were 10-meters walk test (10MWT) and Timed "Up and Go" Test (TUG). The results show an improvement in the 10MWT of 8.54 seconds (25.5%) for all 5 patients in self-selected velocity. TUG improvement was 7.3 seconds (16% faster). 1 patient was not able to perform this test the results before the rehabilitation training due to the impermanent and difficulties in mobility, but was finally able to perform this test after the BCI sessions.

Conclusion: These outcomes show the feasibility of this BCI approach for chronic stroke patients, and further support the growing consensus that these types of tools might develop into a new paradigm for rehabilitation tool for stroke patients. However, the results are from only five chronic stroke patients, a broader randomized controlled study involving more patients is already ongoing.

Disclosure: This research is financed by g.tec medical engineering GmbH, which is selling this BCI system.

EPR2218

Effect Of High Frequency Repetitive Transcranial Magnetic Stimulation Of The Contralesional Dorsal Premotor Cortex On Recovery From Post-stroke Severe Motor Impairment

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Background and aims: The traditional inhibition of contralesional M1 (cM1) using low frequency rTMS fails to improve post-stroke severe motor impairment. While previous data suggested that cM1 exerts transcallosal inhibition on ipsilesional M1, there is recent evidence that contralesional PMd (cPMd) has compensatory roles in severely impaired patients.

Objectives: To study whether facilitating cPMd with high frequency rTMS, instead of conventionally suppressing cM1, can improve post-stroke severely impaired upper extremity or not.

Methods: Forty right-handed, first ever stroke patients (3 months post-event) with severe stroke symptoms, severe motor deficit, and radiologically evident massive infarctions at baseline were randomly assigned to two equal groups, to receive ten consecutive sessions of either high frequency rTMS on cPMd; or sham rTMS. MRC scores and UE-FMA were assessed pre- and post-intervention.

Results: One way ANCOVA revealed significant improvements in grand means of MRC in the active group in relation to the sham group ($F=56.093$, $P<0.0005$, $\eta^2=0.603$), mainly proximal MRC ($F=85.551$, $P<0.0005$, Partial $\eta^2=0.698$), whereas no significant improvement in the mean distal MRC ($F=6.380$, $P=0.016$, $\eta^2=0.147$). Similarly, UE-FMA totals were markedly improved in the active group in relation to the sham group ($F=130.331$, $P<0.0005$, $\eta^2=0.779$), mainly proximal UE-FMA ($F=169.915$, $P<0.0005$, $\eta^2=0.821$). Stepwise regression showed that lower baseline MRC of the affected UE is an independent predictor of better response to the novel rTMS approach.

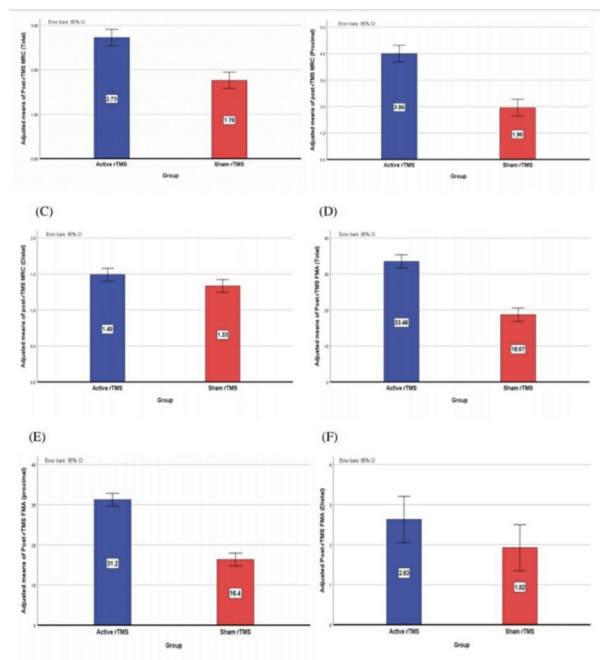


Figure 1. Comparison of adjusted mean of post-rTMS means of (A) mean distal MRC; (B) mean proximal MRC; (C) grand mean MRC; (D) distal UE-FMA; (E) proximal UE-FMA; (F) total UE-FMA of the affected side

Conclusion: Applying high frequency rTMS to cPMd improves motor functions of the disabled UE, mainly proximal, in more severely impaired stroke patients.

Disclosure: Nothing to disclose

EPR2219

Biofeedback therapy using the Anika gloves in the rehabilitation.

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Background and aims: Biofeedback therapy using the Anika computer glove in the rehabilitation of patients with impaired motor function after a stroke. To study the effectiveness of biofeedback therapy using the Anika gloves.

Methods: During the study, rehabilitation measures were carried out in 41 patients aged 45-70 years with ischemic stroke and functional disorders. In the 1st group of 13 (31%) patients underwent traditional rehabilitation (physiotherapy, kinesiomasage, ergotherapy). Traditional rehabilitation and the anika gloves recovery method were used in 28 (68%) patients of the second group.

Results: In both groups, 3 rehabilitation courses were carried out over 3 months. The duration of each rehabilitation course is 10 days. As a result, in the 1st group, the activity of the hands increased by 30-40% due to a decrease of muscle tone in the hands and muscle strength increased from 1-2 points to 2-3 points. In the 2nd group, the activity of the hands increased by 45-60% due to a decrease of muscle tone and muscle strength increased from 1-2 points to 3-4 points ($P \leq 0.09$). There was an increase in the activation of movements in the fingers of the hands.

Conclusion: 1) Rehabilitation measures have shown that the use of Anika computer gloves method with the traditional rehabilitation method increases the effectiveness of treatment and in a short time has a positive effect on fine movements of the fingers.

2) In the comprehensive rehabilitation of patients with stroke, it is recommended to use the Anika computer gloves in order to restore fine motor skills of the hand.

Disclosure: Nothing to disclose.

EPR2220

RTMS increases BDNF levels in patients with posttraumatic chronic disorders of consciousness

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Background and aims: Brain-derived neurotrophic factor (BDNF) is known to be related to the regulation of neuroplasticity underlying cognitive functions recovery. In our research, we concentrated on its role in disorders of consciousness (DOC).

Methods: We included 26 chronic DOC patients, male/female 16/10, age 32±13 years. Etiology was traumatic/non-traumatic in 10/16 patients, respectively. Mean time after accident was 19±17 months. 14 patients were in vegetative state/unresponsive wakefulness syndrome (VS/UWS), mean Coma Recovery Scale-revised (CRS-r) score was 6±0.3; 12 patients were in minimally consciousness state (MCS), mean CRS-r score was 13±4.

We detected BDNF levels in serum and cerebrospinal fluid (CSF) by ELISE before and after 10 sessions of high-frequency repetitive transcranial magnetic stimulation (rTMS) over the left angular gyrus.

Results: We did not find any difference between BDNF levels in serum and CSF in VS/UWS and MCS patients, as well as any changes in its concentration before and after rTMS course in the whole group and in VS/UWS-MCS subgroups. However, we found higher CSF BDNF level in posttraumatic DOC patients (Table 1) and an increase of its concentration after rTMS course, unlike non-traumatic patients (Table 2). We also observed mild clinical improvement after rTMS in patients of both traumatic and non-traumatic etiology (Legostaeva et al., 2019).

Conclusion: BDNF levels in CSF were higher in posttraumatic DOC patients and increased after rTMS course application. This may contribute to the known more favourable outcome of DOC after traumatic brain injury. Yet, our finding requires further investigations.

Disclosure: The study is supported by Russian Science Foundation grant No 16-15-00274

Table 1. Baseline BDNF levels in DOC patients (n=26), pg/ml.

	VS/UWS	MCS	p (Mann-Witney U test)	Posttraumatic	Non-traumatic	p (Mann-Witney U test)
Serum	800 [510; 1010]	770 [675; 915]	1	750 [645; 875]	820 [560; 980]	0.897
CSF	13,8 [10,7; 31,4] *10 ³	20,5 [11,5; 27,2] *10 ³	0.494	28,4 [20,5; 38,3] *10 ³	13,3 [10,7; 19,9] *10 ³	0.036

Table 1

Table 2. Change of BDNF levels after rTMS course (n=21), pg/ml.

	Serum			CSF		
	Before rTMS	After rTMS	p (Wilcoxon signed-rank test)	Before rTMS	After rTMS	p (Wilcoxon signed-rank test)
Whole group	800 [660; 960]	800 [600; 1300]	0.862	14 [10.8; 26] *10 ³	15,6 [8.8; 22,4] *10 ³	0.258
VS/UWS	900 [560; 1070]	760 [510; 850]	0.463	13,6 [10,3; 27,2] *10 ³	15,6 [6,5; 21,5] *10 ³	0.235
MCS	770 [685; 875]	950 [735; 1330]	0.169	18 [11,2; 25,6] *10 ³	16,4 [13,5; 27,8] *10 ³	0.444
Posttraumatic	750 [655; 825]	800 [545; 1380]	0.575	30,2 [17,8; 44,6] *10 ³	38 [22,1; 50,5] *10 ³	0.017
Non-traumatic	900 [680; 1040]	800 [700; 1000]	0.906	11,6 [10,4; 17] *10 ³	13 [6; 15,6] *10 ³	0.814

Table 2

Peripheral nerve disorders 1

EPR2221

Spectrum of IgM-related neuropathies in a large French monocentric cohort

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Background and aims: A sizable number of patients with a peripheral neuropathy have an IgM monoclonal gammopathy (IgM-MG) detected. The aim of this work was to study the spectrum of IgM-related neuropathies (IgM-NP) in a large monocentric cohort of patients with IgM-MG.

Methods: In this retrospective study we reviewed the neurological, neurophysiological, hematological findings and prognosis of patients with an IgM-MG detected by immunofixation between January 2010 and September 2015 in our center (Henri Mondor hospital, Créteil, France). Data were collected from the departments involved in the patients' care and from the centralized database Orbis.

Results: Among 604 patients with IgM-MG, 83 patients (14%) had an IgM-NP (59 males, mean age 67 y.o) including 41 patients with a dysimmune peripheral neuropathy (including 38 Anti-MAG neuropathies), 5 light chains deposits neuropathies (4 AL amyloidosis), 3 cryoglobulinemic neuropathies and 4 patients with neurolymphomatosis. Also, 30 patients suffered from asyndromic neuropathy including 23 with axonal neuropathy. Ataxia, tremor and upper limbs extension were statistically more frequent in dysimmune neuropathies. In AL amyloidosis, neuropathy occurred earlier with consistent small fibers alterations and often with a large fiber neuropathy during its course. Neurolymphomatosis occurred long after the IgM-MG diagnosis, with a good response to hematological treatment. Lastly, asyndromic neuropathies worsened for 1/3rd of the patients with a neuropathic response to hematological treatment in half of the patients treated.

Conclusion: This study emphasized the heterogeneity of the IgM-NP from the initial findings to the prognosis and gave insights on their therapeutic responses.

Disclosure: Nothing to disclose

EPR2222

Quality of life in hereditary neuropathy with liability to pressure palsies is as impaired as in Charcot-Marie-Tooth disease type 1A

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Background and aims: To date only one study assessed quality of life (QoL) in patients with hereditary neuropathy with liability to pressure palsies (HNPP). We aimed to fill in the gap by investigating QoL in cohort of patients with HNPP compared to Charcot-Marie-Tooth type 1A (CMT1A), as well as to analyze sociodemographic and clinical features associated with QoL in HNPP.

Methods: 18 genetically confirmed HNPP patients were age- and gender-matched with 18 CMT1A patients. SF-36 questionnaire was used to assess QoL. Medical Research Council (MRC) Sum Score, CMT Neuropathy Score (CMTNS), Overall Neuropathy Limitation Scale score (ONLS), Falls Efficacy Score (FES), Visual Analogue Pain Scale, Beck Depression Inventory (BDI) and Krupp's Fatigue Severity Scale (FSS) were also used in our study.

Results: Although HNPP patients were less clinically impaired, no difference was observed in these 2 cohorts regarding any of the SF-36 scores. Worse QoL in HNPP patients was associated with lower education ($p<0.01$), physical occupation ($p<0.05$), higher number of clinically affected nerves during disease course ($p<0.01$), worse MRC-SS score ($p<0.01$), worse ONLS scores ($p<0.01$), and with more pain ($p<0.01$), depression ($p<0.01$), and fatigue ($p<0.01$). Worse pain at the moment of testing appeared as a significant independent predictor of worse QoL in HNPP patients ($\beta=-0.93$, $p<0.001$).

Conclusion: QoL was similarly impaired in patients with HNPP and patients with CMT1A. We identified different factors that are associated with QoL in HNPP, and many of these are amenable to treatment which is of special interest in these still incurable diseases.

Disclosure: This study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (grant #175083).

EPR2223

Analysis of responsiveness of two different ability outcome measures in Guillain-Barré syndrome

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Background and aims: Guillain-Barré syndrome disability scale (GDS) is the most commonly used ability measure in Guillain-Barré syndrome (GBS). Recently I-RODS has been developed as a new ability and participation scale to be used in inflammatory neuropathies, including GBS. GDS and I-RODS has not been compared in GBS patients so far. The objective of this study was to compare responsiveness of I-RODS and GDS in GBS patients during a six-month follow-up period.

Methods: GDS and I-RODS were administered in 72 patients from 7 tertiary health care centers from 3 countries. Using these measures patients were tested as follow: on day 14, day 28, month 3 and 6 months from symptom onset. Response was defined as an improvement for one point on GDS and improvement on I-RODS as defined by Draak et al (2014).

Results: Between day 14 and 28 there was an improvement in 28% patients as measured with GDS and only in 10% patients as measured with I-RODS. At month 3 compared to day 14 we noticed improvement in GDS score in 90% of GBS patients and in I-RODS score in 65%. At month 6 improvement was noticed in 94% of patients measured by GDS and 78% according to I-RODS.

Conclusion: Our findings support the use of GDS in an acute phase of GBS when gaining ability to walk is of outstanding importance for patients. On the other hand, it seems that I-RODS has its role during a longer follow-up period since being better by GDS does not necessarily mean doing well.

Disclosure: Nothing to disclose

EPR2224

Ibrutinib, an oral inhibitor of Bruton's tyrosine kinase, is active in anti-MAG antibody polyneuropathy.

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Background and aims: Anti-myelin-associated glycoprotein (MAG) antibody neuropathy is a chronic sensorimotor demyelinating polyneuropathy, associated with IgM monoclonal gammopathy either of undetermined significance (MGUS) or Waldenström's Macroglobulinemia (WM). MYD88L265P is the most common mutation in WM and IgM-MGUS. Ibrutinib, an oral inhibitor of Bruton's tyrosine kinase, has been shown to be effective in WM, especially with MYD88L265P mutation and CXCR4 wild-type. We report on 3 anti-MAG neuropathy patients successfully treated with ibrutinib.

Methods: All 3 patients underwent bone marrow biopsy showing WM, with MYD88L265P mutated and CXCR4S338X wild-type, and were started on ibrutinib 420mg/die. Patients were assessed at baseline, at 3-6 months, and at 12 months in 2 patients with longer follow-up, using INCAT (Inflammatory Neuropathy Cause and Treatment) Disability Score, INCAT Sensory Sum Score (ISS) and Medical Research Council (MRC) sum score. The Modified International Cooperative Ataxia Rating Scale (mICARS) was performed in 2 patients, while it was not used in the patient with Parkinson's disease as major comorbidity. Responders were considered the patients improving by at least one point in 2 clinical scales.

Results: All the patients reported an early and subjective benefit, consistent with objective improvement especially of the sensory symptoms as shown by clinical scales. IgM levels and the monoclonal component steadily decreased. Therapy was well tolerated, and none developed atrial fibrillation. All the patients are still receiving treatment

Conclusion: These preliminary data point to a possible efficacy of ibrutinib in anti-MAG antibody neuropathy, which is the most common disabling paraproteinemic neuropathy.

Disclosure: Nothing to disclose

EPR2225

Video head impulse test findings in patients with chronic inflammatory demyelinating polyradiculoneuropathy

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is treatable, autoimmune peripheral neuropathy. This study analyses the vestibulo-ocular reflex (VOR) as measured by the video-head impulse test (v-HIT).

Methods: 10 patients (age 54.7±21.8, 5F/5M) with CIDP, mean disease duration of 4.2 years, mean MRC Sum Score of 51.9±5.5, mean Inflammatory Neuropathy Cause and Treatment (INCAT) disability score 2.4±0.8 were recruited from an Outpatient Neurology Clinic. 3-dimensional v-HIT was performed. VOR-gain, refixation saccade prevalence and 1st saccade amplitude, onset and duration were examined and compared against age-matched healthy controls.

Results: 6 of 10 patients reported severe imbalance resulting in recurrent falls in 4 patients, 1 patient reported past history of vertigo/dizziness. Horizontal, anterior and posterior canal (HC, AC, PC) VOR-gains for CIDP were 1.0±0.1, 0.90±0.2, 0.78±0.2 and for controls were 0.95±0.1, 0.91±0.1, and 0.82±0.1. VOR-gain was reduced (mean±2SD) in 55 patients. Refixation saccade prevalence for HC, AC, PC were 52%, 23%, 59% in CIDP and 60%, 24% and 54% in controls. 1stsaccade onset latency was longer for HC and PC in CIDP group (p<0.05). Reduced VOR-gain was associated with history of recurrent falls (p<0.05).

Conclusion: Reduction in the VOR-gain is common, and refixation saccades tend to occur later in patients with CIDP. Our findings indicate that gait imbalance in CIDP may be also linked to vestibular impairment. Complementary otolith function testing is necessary to better characterise pattern of vestibular impairment in patients with CIDP.

Disclosure: Nothing to disclose

EPR2226

Interim Analysis of a Post-authorisation Safety Study on the Long-Term Safety of Hyaluronidase-Facilitated Subcutaneous Immunoglobulin 10% in Patients with Primary Immunodeficiency Diseases in Europe

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Background and aims: Recombinant human hyaluronidase (rHuPH20)-facilitated subcutaneous immunoglobulin (fSCIG) 10% is a novel therapy that utilises rHuPH20 to catalyse the hydrolysis of hyaluronan in the extracellular matrix. The resultant increase in subcutaneous tissue permeability enables administering fSCIG at rates, volumes and frequencies similar to intravenous immunoglobulin. We report fSCIG safety data from the interim analysis of an ongoing observational study in patients with primary immunodeficiency diseases (PID).

Methods: This prospective, non-interventional, open-label, uncontrolled, multicentre study, initiated July 2014 in Europe, includes patients aged ≥18 years with PID currently receiving fSCIG (EUPAS5812).

Results: This safety analysis includes 103 of 111 enrolled patients who received ≥1 dose of fSCIG as of 10 January 2019; the mean (SD) fSCIG exposure duration was 2.26 (1.19) years. Incidence of treatment-emergent non-serious (non-infectious) adverse events/treatment-emergent serious adverse events was 2.37/0.24 events per person-year; 553/57 events were observed in 83/28 patients. No neutralising antibodies to rHuPH20 were detected. The median immunoglobulin dose administered was 80.9 (range: 1.3–275.5) mg/kg body weight/week. The proportion of fSCIG administered at home was 91.2% in the first, 93.2% in the second, 93.2% in the third, and 85.2% in the fourth year.

Conclusion: This interim analysis of prospectively collected fSCIG data suggests fSCIG is well tolerated in a real-world population. The volume advantage of fSCIG makes it an attractive candidate in PID. This advantage becomes even more important in diseases requiring higher doses of immunoglobulin, such as chronic inflammatory

demyelinating polyradiculoneuropathy (CIDP). A phase 3 trial of fSCIG in CIDP is ongoing (NCT02549170).

Disclosure: This work was funded by Shire US Inc, a Takeda company.

EPR2227

Clinical heterogeneity of hereditary ATTR amyloidosis related to V30M mutation (hATTRm): experience of a Portuguese reference amyloidosis centre

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Background and aims: Cardiomyopathy has been considered rare in Portuguese hATTRV30M patients, contributing to diagnostic delay. We aim to perform a phenotypical description of hATTRV30M mutation symptomatic patients followed at a specialized tertiary centre in Portugal.

Methods: Retrospective cross-sectional study of symptomatic hATTR patients followed in the last 5 years. Demographic and clinical variables were obtained from hospital clinical registries. Patients were classified as early-onset (<50 years old) or late-onset (\geq 50 years old) according to beginning of 1st symptoms. Cardiomyopathy was defined as septal thickness >13mm and/or DPD Scan=3.

Results: 231 patients were included (female gender 48%) with a mean symptoms' age of onset of 41.9 years old (SD \pm 13.9). From those, 58 (n=25.4%) were classified as late onset patients. Neuropathic phenotype was present in 71 patients (30.7%), mixed phenotype in 150 (64.9%) and cardiac phenotype in 5 patients (2.2%). Neuropathy was present in 166 (92.5%) early onset patients and in 57 (96.6%) late onset patients. Cardiac autonomic manifestations were present in 114 (66.3%) early onset and in 32 (55.2%) late onset patients (p=0.102). Cardiomyopathy was seen in 31 (52.5%) late onset patients and in only 6.9% (n=12) of the early onset group (p<0.001).

Conclusion: hATTRV30 amyloidosis have a phenotype difference regarding the age of onset. Cardiomyopathy can be present in V30M population, more often in the late onset group, demystifying the idea that in this population there is only an early onset neuropathic or mixed phenotype.

Disclosure: Nothing to disclose

EPR2228

Objective markers for onset of transthyretin familial amyloid polyneuropathy in asymptomatic ser77tyr mutation carriers

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Background and aims: Transthyretin familial amyloid polyneuropathy (TTR-FAP) in Israel is commonly due to Ser77Tyr mutation in the TTR gene, identified among Jewish Yemenite descents. Disease onset due to this mutation is usually after the age of 50, with unknown penetrance and fatal within a few years. Early treatment delays disease progression, therefore timely diagnosis of disease-onset is imperative for effective management. Congo-red staining of amyloid deposits is the most objective evidence for active disease, effectively tested in skin punch biopsy, which also enables small fiber neuropathy (SFN) diagnosis by quantifying the intra-epidermal nerve fiber density (IENFD). However, while low IENFD may mark the pre-symptomatic phase of TTR-FAP, it is non-specific, occurring in SFN due to a variety of etiologies.

Methods: We assessed for objective disease hallmarks in asymptomatic TTR Ser77Tyr mutation carriers that have active disease per Congo-red staining.

Results: 11 carriers were identified, which were asymptomatic or had non-specific intermittent neuropathic symptoms with normal IENFD. 2 asymptomatic carriers showed amyloid in skin, accompanied by low IENFD and showed a median neuropathy at the wrist. An additional asymptomatic carrier with a median neuropathy at the wrist attributed to recurrent carpal tunnel syndrome during pregnancies had no amyloid deposits and normal IENFD. 8 carriers showed no median neuropathy at the wrist, 2 had low IENFD but no amyloid and in 3, a skin biopsy was not obtained due to young age.

Conclusion: Electrophysiological evidence for a median neuropathy at the wrist accompanied by skin denervation in asymptomatic mutation carriers suggests active TTR-FAP.

Disclosure: Honorarium for lectures by Pfizer.

EPR2229

Management of Thrombocytopenia in Patients With Hereditary Transthyretin Amyloidosis Treated With Inotersen: Clinical Trial and Postmarketing Surveillance Experience

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Background and aims: Hereditary transthyretin amyloidosis (hATTR) is a rare, progressive, fatal disease causing debilitating autonomic and sensorimotor neuropathy. Efficacy and safety of inotersen, an antisense oligonucleotide inhibitor of transthyretin protein production, were evaluated in a randomized, placebo-controlled pivotal study (NEURO-TTR) and its open-label extension (OLE). During the NEURO-TTR trial, weekly monitoring of platelet counts was implemented after 3 (3%) cases of grade 4 thrombocytopenia (platelet count <25×10³/μL) were reported. This analysis assesses outcomes of enhanced monitoring for thrombocytopenia in patients receiving inotersen in the clinical trial and real-world setting.

Methods: Patients with hATTR received inotersen through NEURO-TTR, OLE, a US expanded access program (EAP), a French compassionate use program (ATU), and an investigator-sponsored trial (IST; includes patients with wild-type ATTR). Data from these 5 studies plus ~3 patient-years of postmarketing exposure were evaluated from 6 July 2018 to 5 January 2019. Data from the US Risk Evaluation and Mitigation Strategy (REMS) were evaluated from 8 October 2018 to 6 August 2019.

Results: As of 5 January 2019, 267 unique patients received inotersen: NEURO-TTR N=112, OLE N=135, EAP N=66, ATU N=2, and IST N=36. Since the implementation of enhanced monitoring in clinical trials, noninterventional studies, and the ongoing REMS program, no cases of grade 4 thrombocytopenia or serious bleeding with severe thrombocytopenia have been reported to date.

Conclusion: With enhanced safety monitoring, events of grade 4 thrombocytopenia or serious bleeding with severe

thrombocytopenia have been successfully mitigated across all current clinical studies and treatment programs.

Disclosure: This study was sponsored by Akcea Therapeutics and Ionis Pharmaceuticals, Inc.; medical writing support was provided by ApotheCom and funded by Akcea Therapeutics.

EPR2230

Argentinean Study in Transthyretin Familial Amyloid Polyneuropathy. "An old illness that we need to think"

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Background and aims: Transthyretin familiar amyloid polyneuropathy (TTR-FAP) has an elevated prevalence in Portugal, Sweden, Japan and Brazil with an aggressive course and high morbi-mortality without an effective treatment. Our objective is to report the identified Argentinean cases.

Methods: Retrospective, multicentric and clinical-epidemiological study.

Results: We identified 94 patients, 45 females. Mean age 35 years old (range 12-78). 98% were born in Argentina, the rest in Bolivia and Perú. The majority of them lived in Buenos Aires (90.21%) and in provinces as Chaco (7.60%), Formosa (1.08%) and Entre Rios (1.08%). Val 30 met was the most common mutation (89.36%) followed by Ala97ser (6.38%), Tyr114cys (2.12%), Ile93val (1.06%) and Ala36pro (1.06%). The ancestors came from Portugal, Spain, Italy, France and Taiwan. The latency between the onset of symptoms and diagnosis was 1 to 10 years. The delay was justified by alternative diagnosis as CIDP (4), ALS (2), lumbar spinal stenosis (2), diabetic neuropathy (2), syringomyelia (2), vitamin b12 deficiency (1), psychogenic (6). 63 patients were symptomatic, 42 had an early onset with a small fibre neuropathy at the presentation, some of them with dysautonomic manifestations as digestive (40), genitourinary (28) and cardiac (22). Renal involvement, ocular and central nervous systems were referred in 10 patients. 35 patients were in the 1st stage of FAP disease scale, 13 in stage 2 and 9 in the 3rd. Some of them were treated with liver transplant and others received tafamidis and inotersen. Died 13 patients.

Conclusion: TTR-FAP is still an underdiagnosed illness in Argentina.

Disclosure: Nothing to disclose

EPR2231

Sensory neuropathies at a single tertiary center: A case series and application of Camdessanché diagnostic criteria

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Background and aims: Sensory neuropathies (SN) are a rare subtype of peripheral neuropathy resulting from dorsal root ganglion degeneration. The etiological diagnosis is divided into autoimmune, paraneoplastic, infectious, toxic, hereditary and in a percentage of cases remains idiopathic. Camdessanché et al established a set of criteria to differentiate SN from other sensory neuropathies.

Methods: Description of patients diagnosed with SN at Hospital Egas Moniz between 2006 and 2019 and retrospective application of the Camdessanché criteria.

Results: We present 23 patients (11 men), aged between 37 and 93 years. The average age of onset was 61.2 years. The phenotype was typically progressive (50.0%), with hyposthesia (90.5%), ataxia (54.5%), and 4-limb involvement (69.6%). Objectively, 56.5% had a pansenitive deficit, 60.9% appendicular ataxia and 72.7% Romberg sign. Aetiologically, 10 patients (43.5%) have a defined etiology (Sjögren, Chemotherapy-induced, HIV, CANVAS Syndrome, Mitochondrial Cytopathy, Vitamin Deficiency) and in the remaining (56.5%) no etiology was identified. The average follow-up was 6.4 years. Applying the Camdessanché criteria, 17 met criteria for possible SN (mean score 9.6) and 4 for probable SN (history of exposure to cisplatin and Sjögren). It was also possible to fit 16 patients into A-D patterns (agreeing with that described by the same author).

Conclusion: Our series differed from other series reported by the higher percentage of idiopathic cases and the absence of paraneoplastic cases. We testified that Camdessanché criteria can be easily applied and have a good sensitivity as previously reported. SN are a rare disorder with a challenging etiological diagnosis.

Disclosure: Nothing to disclose

Sleep disorders 2

EPR2232

Startle Reflex modulation in patients with REM Sleep Behavior Disorder

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Background and aims: RBD may be isolated (iRBD) or associated with Parkinson's disease (PDRBD). RBD derives from an imbalance in different areas of the brainstem, including those involved in the startle reflex. Our aim is to assess the Startle Reflex in patients with iRBD and PDRBD. **Methods:** A total of 60 subjects (20 iRBD, 20PDRBD and 20 healthy controls) were recruited from the Movement Disorder and Sleep Centers in Cagliari. RBD and PD diagnosis was made according to current criteria. The study included 1-night video-polysomnography recording, neuropsychological assessment and [123I]-FP-CIT dopamine transporter (DAT) scan where a semi-quantitative-age-adjusted basal nuclei values BasGanV2 algorithm was used. Startle Reflex was acquired by means of SR-HLABTM EMG and latency and amplitude measured. All indices will be compared between groups by 2-way analyses of variance (ANOVAs).

Results: 20PDRBD patients (M=18; mean age: 67.8±7.5 yrs, mean education 9.1±4.1 yrs), 20 iRBD patients (M=17; age:70.5±8.2; edu: 8.7±4.1 yrs.) and 20 sex- and age-matched control were enrolled. Among iRBD patients, n=15 had abnormal DAT-Scan and n=6 were found to have a Mild Cognitive Impairment. An alteration of the startle reflex (latency prolongation) was observed in iRBD and PDRBD, compared to healthy controls (ANOVA 1-way p<0.05), while no difference in amplitude was found.

Conclusion: Startle reflex is altered in both iRBD and PDRBD patients. Changes in iRBD may indicate an early expression of the neurodegenerative process underlying this disorder at the brainstem level, persisting in PDRBD. Startle Response might represent a tool to explore brainstem neurophysiology in RBD.

Disclosure: Nothing to disclose

EPR2233

Investigation on neurexin 1 alpha antibodies in narcolepsy and other hypersomnias

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Background and aims: Neurexin 1 alpha (NRXN1) has been suggested as a possible autoantigen in narcolepsy patients. Our aim was to investigate the frequency of antibodies (abs) against NRXN1 in a group of patients with narcolepsy and other sleep disorders using a newly established cell-based assay.

Methods: Sera from 59 type 1 (NT1) and 15 type 2 (NT2) narcolepsy patients, 10 patients with idiopathic hypersomnia and 11 patients with hypersomnia but otherwise normal sleep studies (sEDS) were studied. Human embryonic kidney cells were transiently transfected with human NRXN1 encoding plasmid, incubated with patients' sera for 1 hour at 1:100 dilution and then fixed. Binding of antibodies was detected by fluorescently-labelled secondary antibodies to human IgG and the different IgG subclasses. A non-linear visual scoring system was used from 0 to 4; samples scoring ≥1 were considered positive. End-point titers were established on positive samples.

Results: 3 out of 95 sera (3.1%) tested positive with end-point titers between 1:500 and 1:2500. Subclass analysis showed that antibodies were IgG1. Positive cases included 1 male NT1 patient and two female sEDS patients. None of them had an acute onset of the disease and all were sampled far from onset.

Conclusion: Antibodies to NRXN1 are very rare in patients with narcolepsy.

Disclosure: Nothing to disclose

EPR2234

Do Depression and Anxiety Depend on Insomnia Phenotypes in Patients with Epilepsy?

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Background and aims: Insomnia is a frequent co-morbidity in patients with epilepsy (PWE). It also accompanies depression and anxiety. 2 main insomnia phenotypes are recognized: sleep-onset (SOI) or sleep-maintenance (SMI). We aimed to study the relationship of insomnia phenotypes with depression and anxiety in PWE.

Methods: 2 groups of participants were interviewed at a sleep center: epilepsy patients with insomnia group (EIG) and patients with insomnia group (IG). We tested them using Hamilton depression and anxiety rating scales (HAMD, HAMA) and Pittsburgh Sleep Quality Index (PSQI). Participants were classified into predominantly SOI or SMI phenotype subgroups according to clinical interview and specific points in HAMD.

Results: We interviewed 175 PWE, 90 of them had insomnia comprising EIG – mean age-37.5, F-43.3% (SOI-32.2%, SMI-67.8%). Data from IG consisting of 31 insomnia patients were also studied, mean age-41.1, F-61.3% (SOI-16.1%, SMI-83.9%). In EIG mean scores for HAMA, HAMD, and PSQI for SOI/SMI subgroups were respectively: HAMA 13.5/22.2, HAMD 11.9/8.7, PSQI 8.2/12.3 ($p < 0.05$). Interestingly, no differences were found between SOI/SMI subgroups in IG: HAMA 19.4/17.4, HAMD 12.6/15.4, PSQI 14.2/14.8 ($p > 0.05$).

Conclusion: Our results show that sleep-maintenance insomnia was associated with higher rates of depression, anxiety and poor sleep quality in epilepsy patients compared to sleep-onset phenotype. We did not find similar relationship within insomnia population. This is the 1st report supporting that depending on insomnia phenotype depression and anxiety are influenced differently in epilepsy patients.

Disclosure: Nothing to disclose

EPR2235

Pitolisant in the Treatment of Patients With Narcolepsy: A 2-Year, Prospective, Observational, Single-Center Study

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Background and aims: The efficacy of pitolisant, a selective histamine H3 receptor inverse agonist, in adults with narcolepsy was demonstrated in randomized, placebo-controlled trials. This study evaluated long-term use of pitolisant in clinical practice.

Methods: This prospective, open-label, 2-year, observational study was conducted at a major narcolepsy center in Germany and enrolled adults with a diagnosis of narcolepsy who had no prior treatment with pitolisant. Assessments included excessive daytime sleepiness (Epworth Sleepiness Scale [ESS]), weekly rate of cataplexy (WRC), and health-related quality of life (Short-Form Veterans RAND [VR-36]).

Results: The study enrolled 147 patients: mean age, 29.9 years; 57.1% female, 65.3% with cataplexy, and 66.7% with disrupted nighttime sleep. Most patients received concomitant narcolepsy medications (63.3% at baseline; 79.6% at month 24). Mean ESS score decreased from 16.2 at baseline to 12.6 at Month 24. Mean WRC was reduced by 31% at Month 24. Significant improvement in quality of life was noted on VR-36 subscales that assess general health perception, vitality, and social function. In all, 38 patients (25.8%) discontinued from the study before Month 24: 15.0% for lack of efficacy and 10.8% due to adverse events. The most common adverse events were disrupted nighttime sleep (29.3% of patients), headache (15.5%), and nausea (12.2%).

Conclusion: These real-world data show that long-term treatment with pitolisant (usually with 35.6mg/d) was efficacious for reducing EDS and cataplexy and improving quality of life in patients with narcolepsy. Treatment was generally well tolerated.

Disclosure: Writing support funded by Harmony Biosciences, LLC.

EPR2236

Discovery of a novel, orally available orexin 2 receptor-selective agonist, TAK-988, as a potential therapeutic drug for narcolepsy.

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Background and aims: The loss of orexin-producing neurons in lateral hypothalamus is associated with narcolepsy type 1 (NT1). Orexin 2 receptor (OX2R), but not orexin 1 receptor (OX1R), knockout (KO) mice show clear narcolepsy-like phenotypes. Selective activation of OX2R may be effective for treatment of narcolepsy. In this study, we characterized in vitro and in vivo profiles of a novel, orally available OX2R-selective agonist, TAK-988.

Methods: A calcium mobilization assay in Chinese hamster ovary (CHO) cells stably expressing human OX2R was used to assess OX2R-agonistic activity. To investigate the activation of OX2R-downstream signals, inositol monophosphate contents, beta-arrestin recruitment, and phosphorylation of extracellular signal-regulated kinase 1/2 and cAMP response element-binding protein were measured in CHO cells stably expressing ProLink-tagged human OX2R and beta-arrestin2-beta-gal-EA fusion protein. Electrophysiological studies were conducted to assess the activation of physiological OX2R on histaminergic neurons in the mouse tuberomammillary nucleus (TMN). Electroencephalogram/electromyogram recordings with wild-type (WT) mice and OX2R KO mice were performed during sleep phase to evaluate TAK-988 mediated arousal effects.

Results: TAK-988 activated OX2R (EC50 value: 2 nM) in the calcium mobilization assay, and induced OX2R-downstream signaling similar to orexin peptides in vitro. TAK-988 also activated physiological OX2R on histaminergic neurons in the mouse TMN in vitro. Oral administration of TAK-988 promoted wakefulness in WT mice, but not in OX2R KO mice, confirming its OX2R selectivity in vivo.

Conclusion: The orally available TAK-988, OX2R agonist may have potential as a new treatment option for individuals with NT1 as well as other hypersomnia disorders with normal orexin levels.

Disclosure: Nothing to disclose

EPR2237

The Vitamin D Receptor Gene FokI Polymorphism is associated with susceptibility to Sleep Disorders

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Background and aims: Immune-mediated mechanisms are thought to be implicated in some Sleep Disorders (SD). Vitamin D is a pleiotropic hormone with specific functions in the Immune and the Central Nervous System (CNS). It acts through a nuclear receptor (Vitamin D Receptor - VDR) expressed in all immune cells including microglia. Low vitamin D levels have been reported in narcoleptic patients. Function and expression of VDR is influenced by several known polymorphisms. One of these, FokI, has been recently associated with obstructive sleep apnea syndrome in a Greek population. Our aim was to investigate whether FokI polymorphism is associated with SD susceptibility and presentation in a Portuguese cohort.

Methods: We studied 133 SD patients (39 Narcolepsy Type1; 28 Narcolepsy Type 2 and 66 with Hypersomnia) followed at the Sleep Outpatient Clinic of HSA/CHP and 446 healthy individuals. The clinical picture was assessed by night PSG+Day MSLT. FokI was genotyped using a pre-designed TaqMan allelic discrimination assay.

Results: A statistically significant higher frequency of the TT genotype was observed in SD patients (16.5% vs. 10.1%, p=0.027, OR (95% CI)=1.77(1.02-3.07)) relative to controls. This difference was particularly relevant in Narcolepsy Type 1 patients (p=0.04; OR=2.30).

Conclusion: The FokI T allele translation product has lower transcriptional activity and results in a longer and less abundant transcript with a negative impact in the efficiency of transduction of the vitamin D signal. Thus, it is possible that individuals with the TT genotype could be prone to unbalanced T-cell responses leading to the development of immune-mediated sleep disorders.

Disclosure: Nothing to disclose

EPR2238

Narcolepsy type 1 features through the lifetime: age impact on clinical phenotype

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Background and aims: Narcolepsy type 1 (NT1) is a chronic neurological disorder typically arising during adolescence and young adulthood. Nonetheless, NT1 clinical picture is mostly known in adults after a long delay in diagnosis. The present study was therefore set to characterize NT1 clinical pictures in different age groups of patients.

Methods: A total of 106 consecutive NT1 subjects underwent clinical and polysomnographic examinations and completed the Epworth Sleepiness Scale (ESS). Clinical features of core narcolepsy symptoms were evaluated through semi-structured interview. Patients belonging to 5 age groups (childhood, adolescence, early and late adulthood and old age) were contrasted.

Results: The ESS showed a significant increase with age, while the duration of total daytime sleep (min/day) was lower in elderly subjects and in younger adults, the latter also complaining more automatic behaviors, compared to other age groups.

As cataplexy triggers, “anger” and “meeting someone unexpectedly” were reported in the majority of adult and elderly patients, but only sporadically in patients’ <11 years-old. Children presented increased occurrence of cataplexy (>1/day in 95% of cases) and reported a time-of-day effect on cataplexy frequency (65%).

Conclusion: EDS and cataplexy variably presented in NT1 at different age, a finding that may contribute to the long diagnostic delay and the high misdiagnosis rate.

Disclosure: Nothing to disclose

EPR2239

Motor patterns of Disorders of Arousal (DoA) in adults. A video-polysomnographic analysis of 300 episodes

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Background and aims: Disorders of Arousal (DoA) are NREM parasomnias typically considered as self-limited childhood manifestations. It is now clear that DoA can persist in adults, often presenting with distinctive characteristics. Nevertheless, few video-polysomnographic (VPSG) studies described the semeiology of DoA episodes in adulthood.

Methods: We reviewed 93 nocturnal VPSG recordings of 40 adult patients (>15 years). We scrutinized the semeiology of the episodes recorded, classifying them into 3 groups according to 3 semeiological motor patterns with increasing intensity and complexity: Simple Arousal Movements (pattern I or SAMs), characterized by head flexion/extension, head flexion/extension and limb movement or head flexion/extension and partial trunk flexion/extension; Rising Arousal Movements (pattern II or RAMs), characterized by a complete trunk flexion with patient sitting up in bed; Complex Arousal with Ambulatory Movements (pattern III or CAMs) characterized by Sleepwalking. The V-PSG recordings were compared to those of 15 healthy controls.

Results: 300 episodes were recorded: 248 (82%) SAMs, 34 (11%) RAMs, and 18 (7%) CAMs. Episodes lasted 33±35 seconds as a mean. Movements tended to halt temporarily during 64% episodes. Explorative behaviours were frequently observed. We recorded 983 sleep-related movements in the healthy controls. Only 8 of them were characterized by head flexion/extension but in the context of a body position change.

Conclusion: We identified 3 specific motor patterns in DoA patients never hitherto reported and not observed in healthy controls. Identification of these patterns could be important for the diagnosis and serve as the basis for a new definition of DoA in adults.

Disclosure: Nothing to disclose

EPR2240

Neurophysiology of parasomniasG. Mayer¹, A. Heidebreder², D. Krefting³¹Department of Neurology, Hephata-Klinik Treysa, Schwalmstadt, Germany; ²Medical University of Innsbruck, Innsbruck, Austria; ³Institut für Medizinische Informatik, Universitätsmedizin Göttingen, Göttingen, Germany**Background and aims:** The pathophysiology of NREM parasomnias is not well understood.

The study aims were to re-investigate in a large sample of patients with NREM parasomnia the consistency of several hypotheses from recent literature: Fragmentation of 1st sleep cycles, delayed built up and decay of slow wave sleep, decrease of slow wave sleep, increase of slow wave activity prior to events, topography of sleepwalking (SW) events, neuronal networks involved in SW, differences in SW events followed by sleep stage vs wake.

Methods: 196 SW (ICSD 2/3 criteria) were compared to 197 from the SIESTA group (110 matches). Sleep staging was performed according to Rechtschaffen & Kales. Time delay stability (TDS) was used to investigate brain connectivity.**Results:** SW had more stage N3, no change in N3 latency, N3 increased with age, N3 phases were less, but longer than in controls. Wake after sleep onset was increased in the 1st sleep cycles, number of awakenings was slightly increased at night, transition from N3-wake was increased, and reduced from stage N3-N2. Transition probabilities showed more change from N2-N3-wake and wake-N2. TDS connectivity showed more elevated link ratios between frontal and central locations and central and occipital locations in SW. TDS connectivity 3 and 6 minutes prior to SW showed a tendency to lower link ratios in the low frequency domain fronto-occipital.**Conclusion:** Our data confirm for SW: higher stability of N3, higher N3 pressure, increased number of awakenings from N3, dissociated connectivity fronto-occipital, increased WASO compared to controls.**Disclosure:** Nothing to disclose

EPR2241

Altered pharmacokinetics of sodium oxybate in narcolepsy type 1 patients after gastric bypass surgeryM. Moresco¹, S. Mohamed¹, A. Perrone¹, F. Pizza², M. Contin¹, R. Riva¹, G. Plazzi²¹IRCCS Istituto delle Scienze Neurologiche, Bologna, Italy;²Department of Biomedical and Neuromotor Sciences, Università di Bologna - Alma Mater Studiorum, Bologna, Italy**Background and aims:** We investigated pharmacokinetics of sodium oxybate (SO; Xyrem[®]) in 2 narcolepsy type 1 (NT1) patients developing side effects after gastric bypass surgery (enuresis, morning nausea and dizziness).**Methods:** 4 NT1 patients (2 underwent gastric bypass and 2 were controls) on SO stable dose for at least 12 months. Each subject took 2 56mg/kg doses of SO 4 hours apart. SO concentrations were determined from blood samples [1] at 0, 0.75, 1.5, 2, 3, 4 hours following first dose, and at 4.75, 5.5, 6.5, 8, 9 hours after the second.**Results:** Mean (\pm SD) maximum SO (gamma-hydroxybutyric acid) blood concentrations (C_{max}) were 79.4 \pm 7.5 μ g/ml and 44.65.6 μ g/ml after 1st dose; 127.3 \pm 20.2 μ g/ml and 79.3 \pm 0.9 μ g/ml after the 2nd dose for patients with gastric bypass and controls, respectively. Residual morning SO levels at 8 hours from the 1st dose were 58.6 \pm 18.8 μ g/ml in gastric resection patients vs 9.1 \pm 7.3 μ g/ml in controls. Maximum time needed to reach the 1st dose C_{max} was 1.5h in gastric bypass patients and 0.75h in controls. Mean area under the plasma concentration-time curve (AUC_{0-9h}) was doubled in patients with gastric bypass vs controls: 656.6 \pm 18.9 vs 275.7 \pm 31.1 [(μ g/ml) x h] respectively.**Conclusion:** Gastrointestinal alterations particularly impaired gastric emptying and increased intestinal transit time [2], which might result in prolonged exposure of the drug to intestinal mucosa accounting for the higher extent of SO absorption and explaining the occurrence of the side effects observed in our patients with gastric bypass.**Disclosure:** Nothing to disclose

EPR2242

Spectrum of motor manifestations during REM sleep in idiopathic REM sleep behavior disorder

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Background and aims: Abnormal motor activity in rapid eye movement (REM) sleep is a major video-polysomnographic (video-PSG) feature of idiopathic REM sleep behavior disorder (iRBD). The diagnosis is based on complex nature of the movements visible at the video recording during video-PSG, but more discreet motor manifestations can be observed as well. The aim was to perform a systematic video analysis of movements during REM sleep.

Methods: Motor manifestations identified at the video during video-PSG in 34 iRBD patients aged 67.5±7.1 years were classified into 4 categories according to clinical severity (elementary, excessive, scenic and violent). In addition, topographic distribution, brief and slow character of movements, association with vocalization, subsequent wakefulness and emotional subtext were determined for each motor event.

Results: An average of 123.8±118.6 motor events were identified in REM sleep. Of these, 67.8% were classified as elementary, 9.1% as excessive, 22.4% as scenic and 0.7% as violent. Violent manifestations were observed in 32.4% of patients. Brief movements were more frequent than slow (p=0.001). Vocalization occurred in 38.2% of patients. Movement caused wakefulness in 8.8% of patients and in 20.6% was at least once associated with distinct emotion.

Conclusion: This study shows extensive variability in a large amount of motor phenomena registered in REM sleep in iRBD. Elementary events represent the vast majority. Although violent manifestations were captured in relative minority, they were detected in 32% of patients.

Disclosure: This work was supported by grants: Charles University grant GAUK 64216, Czech Science Foundation grant GACR 16-07879S and Ministry of Health of the Czech Republic grant 16-28914A.

EPR2243

Rest-wake activity and sleep patterns among patients with acute ischemic stroke

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Background and aims: Non-breathing sleep disorders (non-SBD), which may negatively affect neurological course and recovery after stroke, are common but underinvestigated. The aim of our study was to analyse rest-wake activity and sleep patterns among patients with acute ischemic stroke.

Methods: Patients hospitalized in Hospital of Lithuanian University of Health Sciences within 2-7 days after 1st stroke symptoms were investigated with questionnaires, polysomnography (PSG), actigraphy for rest-wake activity and exposure to light, and thermochrone for body temperature.

Results: We included 27 patients (17 males) with an age median of 67.5 [range: 39÷82] and a NIHSS score of 4 [1÷16], due to a stroke in the anterior (78%) or posterior (22%) circulation. Based on PSG data, 17 (63%) patients were diagnosed with SBD, 7 (25.9%) – with periodic limb movement disorder, and 2 (7.4%) – with insomnia. Actigraphy analysis suggested the presence of an impaired diurnal rhythm in 7 (25.9%) patients, insomnia - 5 (18.5%) and hypersomnia - 13 (48.1%). The average for bed time was 21h: 25min: 34sec [17:40:00÷23:56:54], get up time - 7:01:34 [4:26:45÷11:48:35], total sleep time - 7:34:47 [3:39:00÷11:16:52], sleep efficiency - 77.1% [44.7÷91.79], number of awakenings during night sleep - 42.6 [26.43÷113]. Patients with more severe stroke had a significantly more delayed actigraphy-based sleep onset, worse sleep efficiency and earlier get up time.

Conclusion: Preliminary results of this ongoing study suggest that stroke patients frequently present sleep-wake rhythm disturbances, fragmented and insufficient night-sleep and hypersomnia.

Disclosure: Nothing to disclose

EPR2244

Sleep disturbances and risk of stroke in general population in Russia/Siberia: gender features. WHO epidemiological program Monica-psychosocial

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Background and aims: There are a few studies describing gender differences a risk of stroke in general population depending on sleep quality. The aim was to determine the gender differences in the effect of sleep disorders on risk of stroke in an open population 25-64 years in Russia/Siberia over 16 years of follow-up.

Methods: Under the 3rd screening of WHO program MONICA -Psychosocial a random representative sample of both gender aged 25-64 years in Novosibirsk was examined in 1994 (n=1346, male 48.8%, mean age 44.9±0.4 years). The sleep assessment was performed using the Jenkins Sleep Questionnaire. There were 35 cases of new-onset stroke in women and 22 in men from 1994 to 2010. This longitudinal survey performed in frame budgetary issue #AAAA-A17-117112850280-2.

Results: In an open population aged 25-64 years 48.6% of men and 65.9% of women had sleep disorders (p<0.001). In univariate analysis risk of stroke was higher in men HR=3 (95%CI 1.2-7.6; p<0.05) than in women HR=1.9 (95%CI 1.03-3.7; p<0.05). Multivariate analysis revealed in men with SD 2.8-fold risk of stroke (95%CI 1.1-7.1; p<0.05) and women HR=2,7 (95%CI 1.4-5.42; p<0.01). Stroke risk was higher in men with lower educational level and SD. There was an increase in the risk of stroke in women with a college education and SD HR=3.7 (95%CI 1.1 - 11.9; p<0.05).

Conclusion: Our results demonstrated men with sleep disorders had higher risk of stroke than women. Social gradient increases cardiovascular risk in urban inhabitants with sleep disorders unequally.

Disclosure: Nothing to disclose

Monday, May 25 2020

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EPR3001

A Cost-Benefit Analysis of Routinely Performed Transthoracic Echocardiography in the Setting of Acute Ischemic Stroke

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Background and aims: The role of transthoracic echocardiography (TTE) in the management of acute ischemic stroke remains controversial. This study was undertaken to assess the cost vs benefit of “routine” TTE.

Methods: We examined a consecutive series of patients who were hospitalized for acute ischemic stroke and underwent TTE. We sought to determine the frequency with which the results of TTE led to a new diagnosis of cardioembolism and at least potentially influenced short or long-term clinical outcome. We recorded the direct cost associated with TTE.

Results: There were 1076 patients in the study group, all of whom underwent TTE. TTE identified an unsuspected source of possible/probable cardioembolism in 62 patients (6%), confirmed an initially suspected source (primarily endocarditis) in an additional 13 (1%) and produced findings that stimulated subsequent testing diagnostic of possible/probable cardioembolism in 7 patients (<1%). TTE results potentially influenced clinical outcome in a total of 48 patients (4%). With a total direct cost of \$1.51 million, the mean cost per case wherein TTE results potentially influenced clinical outcome was \$31,375. Diagnostically and therapeutically, TTE was most beneficial in 67 patients under the age of 55 who presented with “cryptogenic” stroke, identifying patent foramen ovale in 21 (31%); closure was performed in 19.

Conclusion: The utility of TTE in the setting of acute ischemic stroke is modest, with its yield greatest in younger patients with cryptogenic stroke. Given the greater sensitivity of transesophageal echocardiography in detecting PFO and evaluating the aortic arch, TTE’s role in stroke diagnosis would appear to be limited.

Disclosure: Nothing to disclose

EPR3002

Factors associated to lobar hemorrhage and death risk after transient focal neurological episodes in cerebral amyloid angiopathy: a systematic review and individual participant data meta-analysis.

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Background and aims: Transient focal neurological episodes (TFNE) are a frequently overseen presentation of cerebral amyloid angiopathy (CAA) whose prognostic implications are still not well described. This study aims to examine factors associated to further development of lobar hemorrhage (LH) and to death after a first event of TFNE due to CAA.

Methods: Systematic review and individual participant data meta-analysis of TFNE in CAA. 2 systematic searches in Pubmed and Embase were performed. This study was conducted following the PRISMA guidelines.

Results: 49 studies and 231 TFNE cases were included according to predefined inclusion criteria from the initial 1619 records. Motor symptoms were present in 39.4% of TFNE cases. Convexity subarachnoid hemorrhage and cortical superficial siderosis (CSS) were detected in 78.9% and 68% of individuals, respectively. Follow up was performed in 167 patients (median 13 months). LH during follow-up was the most frequent adverse event (41% of patients). Motor symptoms (OR 2.50, IC95% 1.32-4.71) and antithrombotic use during follow-up (OR 3.64, IC95% 1.53-8.64) constituted the main risk factors for LH. A total of 19.3% patients died during follow-up being incident LH during follow-up and CSS the main risk factors for death (OR 2.88, IC95% 1.28-6.48; OR 3.28, IC95% 1.17-9.23, respectively).

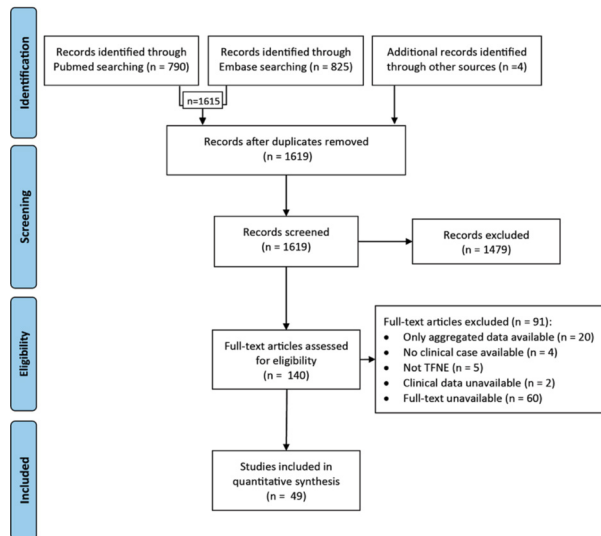


Figure 1. Flow diagram.

Flow Diagram

Conclusion: CAA patients presenting with TFNE are subject to a particularly high risk of morbidity and mortality. Motor symptoms and use of antithrombotics may play a role increasing bleeding risk while CSS and LH act as risk factors for death. These results provide new prognostic information regarding these episodes.

Disclosure: Nothing to disclose

EPR3003

1-year prognosis of transient ischemic attacks with nonfocal symptoms

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Background and aims: A few studies suggested an increased risk of stroke or coronary heart disease in patients with transient ischemic attacks (TIA) presenting with accompanying nonfocal symptoms. We aimed to assess the vascular prognosis of TIA patients with and without accompanying nonfocal symptoms.

Methods: Observational study of consecutive patients with TIA referred to a TIA Clinic from March 2004 to March 2011. Primary outcome was the composite of any event: stroke, TIA, myocardial infarction (MI) or vascular death in the 1st year of follow-up; 2ndary outcomes included individual components of the primary outcome. Cumulative risk of recurrent events was calculated using Kaplan-Meier curves. Hazard ratios were calculated with Cox regression.

Results: 429 TIA patients were enrolled, 100 (23.3%) with nonfocal symptoms. Most common nonfocal symptoms were cardiac and vegetative signs, and nonrotatory dizziness. In the 1st year after TIA, the primary outcome occurred in 65 patients (16.0%; 95% CI, 12%-19%): stroke, in 28 patients; TIA, in 31 patients; MI and vascular death in 2 patients each. The frequency of the composite outcome was similar in patients with or without nonfocal symptoms (16 events (17.0%; 95% CI, 10-24%) vs. 49 events (15.7%; 95% CI, 12-20%); $p=0.430$). There were no significant differences in the frequency of any of the secondary outcomes between patients with or without nonfocal symptoms.

Conclusion: Nonfocal symptoms were reported by almost one-fourth of TIA patients, but their occurrence did not increase the risk of vascular events at one year of follow-up.

Disclosure: Nothing to disclose

EPR3004

Association of post-stroke sleep wake disturbances with endothelial dysfunction, arterial stiffening and decreased heart rate variability

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Background and aims: Sleep-wake disturbances (SWD) and cardiovascular parameters, such as arterial stiffness, endothelial function and heart rate variability (HRV), are known to affect cardio-cerebrovascular risk and outcome. In this study, we investigated the interaction and the temporal development of these factors after acute stroke.

Methods: The Sleep Deficiency & Stroke Outcome Study, prospectively assessed 438 stroke patients recording demographic, anthropometric, stroke and sleep (questionnaires, respirography, actigraphy) characteristics. In a randomly selected subset of 64 patients, EndoPAT-derived cardiovascular features (endothelial dysfunction, arterial stiffness, HRV) were evaluated at admission, 3 and 12 months after stroke.

Results: Using mixed effect linear models adjusted for age, gender and medical and stroke history, different associations between cardiovascular parameters and specific SWD were observed (Figure 1). SWD were prevalently associated with EndoPAT-derived cardiovascular parameters generally accepted as carrying negative cardiovascular prognosis. We observed the association of endothelial dysfunction with fatigue, longer time with oxygen saturation below 90% and longer sleep duration, the association of arterial stiffening with excessive daytime sleepiness and shorter sleep duration and the association of decreased heart rate variability with fatigue, insomnia and restless leg syndrome. Although sleep quality and sleep duration improved after stroke (p=0.032 and p=0.019, respectively), EndoPAT-derived cardiovascular parameters remained constant over time.

Conclusion: These data suggest an association between EndoPAT-derived cardiovascular parameters and specific SWD, which may contribute to the negative relation between SWD and stroke outcome.

Disclosure: Nothing to disclose

Cardiovascular feature	Endothelial function	Arterial stiffness	HRV			
	EndoPAT-derived parameter	Reactive hyperemia index	Augmentation index	Standard deviation of NN intervals	Triangular index	Low to high frequency ratio
Sleep characteristics	Sleep quality (Pittsburgh sleep quality index)	+				
	Fatigue (Fatigue severity scale)	-		-		
	Excessive daytime sleepiness (Epworth Sleepiness Scale)	+	+			
	Insomnia (Insomnia Severity Scale)				-	
	Restless leg syndrome					+
	Oxygen desaturation index					
	Time with oxygen saturation below 90%	-	-			
Demographic parameters	Lowest oxygen saturation	+				-
	Sleep duration	+	-			
Anthropometrics	Age			+	+	-
	Gender			+	+	-
Comorbidities	Body mass index			-	-	+
	Hypertension	-		-	-	
	Atrial Fibrillation	+	+	+		
	Coronary artery diseases			+	+	-
	Previous stroke	-		+	+	-
	Diabetes	+	+	+	+	
	Migraine	-				
	Depression		+			
	Apathy			-	-	
	Smoking	-	+			-
Stroke characteristics	Stroke or transient ischemic attack	-		+	+	-
	TOAST stroke subtype	+				
	Wake-up stroke	+	+	+		

Figure 1. Associations between EndoPat-derived cardiovascular findings and SWD. Positive and negative significant associations are represented with “+” and with “-“, respectively.

EPR3005

Risk factors for carotid plaque progression

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Background and aims: Carotid plaque progression belongs to factors increasing stroke risk. The aim was to identify factors influencing carotid plaque progression.

Methods: The ANTIQUE study (Clinical Trials NCT02360137) participants completed sonographic controls during 3 years were enrolled to analysis. Duplex sonography of cervical arteries was performed in 6-month intervals with measurement of plaque width in carotids. Plaque width measurement error (ME) was set as 99th percentile of difference between 2 measurements of in 2-week interval. Stable and progressive plaques were defined as plaque width difference between initial and final measurements <1ME and >2ME, resp. Univariate and multivariate logistic regression analysis (LRA) was performed to identify factors (age, gender, body mass index, blood pressure, carotid plaque width, arterial hypertension, diabetes mellitus, coronary heart disease, atrial fibrillation, myocardial infarction, stroke, vascular surgery/stenting, smoking, alcohol use) influencing the plaque progression.

Results: Totally 1391 patients (466 males, age 67.2±9.2 years) were enrolled to the analysis. Stable plaques in both carotids were detected in 332 patients. Progressive plaque in at least 1 carotid artery was detected in 255 patients. Higher age (66.7 vs. 69.5 years), male gender (37.7% vs. 49.4%), greater plaque width (2.61 vs. 3.12mm), coronary heart disease (19.6% vs. 28.6%), vascular surgery/stenting in history (11.1% vs. 22.8%) and smoking (9.9% vs. 17.3%) were more frequently present in patients with progressive plaque (p<0.05 in all cases). Multivariate LRA identified only plaque width (OR=1.850) as the independent factor influencing plaque progression.

Conclusion: Carotid plaque width (corresponding with stenosis severity) is the independent risk factor for plaque progression.

Disclosure: Supported by the Ministry of Health of the Czech Republic grant No. 17-31016A.

EPR3006

CT Scan Reevaluation Prior to Mechanical Thrombectomy in Large Vessel Occlusion Patients Transferred from a Primary Stroke Center: an unneeded safety check-point?

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Background and aims: The benefit of mechanical thrombectomy (MT) is time-dependent but inadequate selection of patients may lead to futile and riskful recanalizations. In patients transferred from a primary stroke center (PSC) with acute ischemic stroke due to large vessel occlusion (LVO-AIS) it is uncertain whether computed tomography (CT) scan reevaluation in comprehensive stroke center (CSC) is beneficial or harmful. We aimed to compare clinical outcomes of patients submitted to CT scan reevaluation in CSS prior to MT with patients headed directly to the angio-suite.

Methods: We conducted a retrospective study in a prospectively designed cohort of a CSS. We included consecutive patients admitted to our center from 1/1/2016 to 31/12/2018, transferred from a PSC with LVO-AIS. Group differences were assessed by χ^2 or Fisher exact test for categorical variables, Student t test and Mann-Whitney U test for continuous variables as appropriate. We performed a logistic regression to estimate the probability of modified Rankin Scale (mRS) 0-2 according to CT reevaluation.

Results: We included 363 patients. In 66.8% a CT scan was performed before MT. We found no difference between CT or no-CT patients except for hypertension which was higher in CT group (p=0.025). The median door-to-groin time increased from 41 to 106 minutes (p<0.001) from no-CT to CT. Recanalization rate, hemorrhagic transformation and 90-day mRS were similar in both groups (OR:0.881; CI95%:0.557-1.393; p=0.588)

Conclusion: CT scan prior to MT delayed considerably recanalization but no difference was found in both safety and effectiveness outcome measures between groups.

Disclosure: Nothing to disclose

EPR3007

Subacute Blood-Brain Barrier Permeability after an Acute Ischemic Stroke is associated with Good Clinical Outcome

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Background and aims: The dynamics of blood-brain barrier (BBB) after an acute ischemic stroke (AIS) are multiphasic. An early increase in permeability is associated with edema, hemorrhagic transformation and poor clinical outcomes. Animal models indicate that a later, subacute stage of increased BBB permeability might have a positive effect representing neurovascular remodeling and neoangiogenesis. However, its clinical impact is still uncertain. Our aim was to evaluate the association between BBB permeability at day 7 after an AIS and the patients' clinical outcomes.

Methods: We included consecutive patients with nonlacunar AIS in the territory of a middle cerebral artery with ages ranging from 18 to 80 years. We used modified Rankin Scale score at 3 months as a measure of clinical outcome. Neuroimaging was performed at day 0 and 7 by Magnetic Resonance Imaging, including assessment of BBB permeability in the infarct lesion by dynamic contrast enhancement with quantification of the volume transfer coefficient (K_{trans}). We performed an ordinal regression model between mRS and BBB permeability adjusting for the baseline variables associated with good outcome and including infarct volume as a covariate.

Results: We included 45 patients; mean age 70.0 ± 10.0 years. BBB permeability in the subacute stage showed a nonsignificant reduction in comparison with day 0: K_{trans} : 0.0158 (SD:0.0092) vs. 0.0163 (SD:0.081), $p=0.756$. Permeability of BBB at day 7 was independently associated with improved clinical outcome (OR: 0.897; 95%CI 0.816–0.986; $p=0.025$).

Conclusion: We found subacute BBB permeability to be associated with good clinical outcome.

Disclosure: Nothing to disclose

EPR3008

Correlation between transcranial contrast ultrasound and transesophageal echocardiography in detection of right-to-left cardiac shunt

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Background and aims: Patent foramen ovale (PFO) is the most common type of right-to-left cardiac shunt (RLS) and together with atrial septal aneurysm (ASA) further increases the risk of ischemic stroke. In order to detect RLS we compared sensitivity of contrast transesophageal echocardiography (c-TEE) to sensitivity of contrast-enhanced transcranial Doppler ultrasound (c-TCD). Influence of vascular risk factors was also observed.

Methods: Retrospective cross sectional study included 58 individuals, treated at Neurology Clinic CCS in Belgrade, with positive c-TCD followed by c-TEE examination in patients with transient ischemic attack (TIA) and/or stroke. Intima-media thickness (IMT) and presence of carotid plaques, degree of stenosis, as well as possible deep venous thrombosis (DVT) were obtained via an ultrasound. From patients' medical history we collected the following data: hypertension; diabetes mellitus; dyslipidemia and smoking habits.

Results: c-TEE confirmed RLS detected by c-TCD in 6.9% patients. We found that there exists a correlation between smoking and total number of microembolic signals (MES) without Valsalva maneuver (VM) ($p<0.05$) as well as between presence of DVT (registered in 5.2% patients) and: total number of MES ($r=0.303$, $p<0.05$); number of MES in the right middle cerebral artery ($r=0.293$, $p<0.05$); and number of MES without VM ($r=0.273$, $p<0.05$). Positive correlation was found between number of MES without VM and interatrial septal defects (PFO and ASA) ($r=0.262$, $p<0.05$); the existing RLS ($r=0.303$, $p<0.05$), and between IMT and the time of occurrence of MES ($r=0.334$, $p<0.05$).

Conclusion: c-TCD and c-TEE are complementary methods for RLS detection which represent an important etiological factor of ischemic stroke and TIA in younger patients.

Disclosure: Nothing to disclose

EPR3009

Thrombo-inflammation is a driving force of stroke progression into the penumbra in mice

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Background and aims: In acute ischemic stroke upon a major cerebral artery occlusion, infarcts rapidly grow from the core into the penumbra before recanalization which encompasses brain tissue that receives residual blood flow from collaterals which eventually fails. The underlying mechanisms are unknown.

Methods: To address underlying mechanisms mice underwent filament occlusion of the middle cerebral artery (MCAO) for up to 4 hours. Infarct development was compared between sham-treated mice, and mice in which the platelet glycoprotein (GP) receptor Ib which facilitated tethering to the vessel wall was blocked. Moreover, Rag1^{-/-} mice lacking immune cells underwent the same procedures. Infarct volumes were measured by TTC-staining.

Results: Blocking of platelet GPIb ameliorated ischemic brain damage under MCA occlusion compared to sham-treated mice at all occlusion times tested (mean infarct volume 45.4mm³ versus 82.5mm³ at 3h). Inhibition of GPIb reduced T-cell infiltration into ischemic brains pointing to thrombo-inflammation as an underlying mechanism. Accordingly, Rag1^{-/-} mice lacking immune cells were similarly protected from infarct progression under occlusion during MCAO (35.3 mm³ versus 73.2 mm³).

Conclusion: As principal finding we show that it is possible to retard infarct progression into the penumbra under MCA occlusion in mice by either blocking platelet GPIb or by immune cell deficiency. Thus similar thrombo-inflammatory processes underlying ischemia/reperfusion injury (Stoll & Nieswandt, Nat Rev Neurol 2019; 15:473-481) are operative already at the hyperacute stroke stage under vessel occlusion. These findings pave the way for novel treatment strategies targeting thrombo-inflammation to salvage the penumbra before recanalization.

Disclosure: Funded by the German Research Foundation project number 374031971 CRC/TR240

EPR3010

Computed Tomographic Perfusion abnormalities in acute migraine with aura: Predictors and differential diagnosis with Transient Ischemic Attacks

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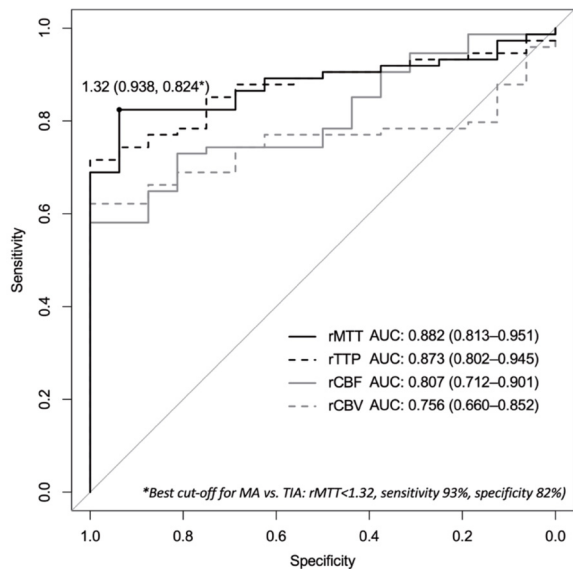
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Background and aims: Migrainous aura (MA) accounts for up to 10% of “stroke mimics” and can present cerebral perfusion abnormalities. We aimed to compare perfusion CT (PCT) findings in acute MA and transient ischemic attacks (TIA).

Methods: We retrospectively studied patients admitted to our hospital between 2002 and 2014 for the suspicion of acute ischemic stroke, undergoing PCT and receiving a final diagnosis of MA. We visually assessed PCTs for the presence and extension of focal hypoperfusion (FHP). We performed a quantitative analysis for mean-transit-time (MTT), time-to-peak (TTP), cerebral blood flow (CBF) and volume (CBV), measured as ratio between the visually hypoperfused region and the healthy side. MA patients with FHP were compared with consecutive TIA patients showing FHP.

Results: Of 47 patients with MA (median age=33 years, 55% females), 16 (34%) displayed FHP. MA patients with FHP, compared to MA patients without FHP, had similar headache and aura features, but less frequently a history of MA (1/16[6.2%] vs. 14/31[45.2%], p=0.010). Compared to 74 TIA patients with FHP (median age=69 years, 43% females), hypoperfusion in MA patients more frequently involved multiple arterial territories or a whole hemisphere and had less pronounced increase in rMTT (1.2 vs. 1.8, p<0.001) and rTTP (1.1 vs. 1.2, p<0.001) and decrease in rCBF (0.8 vs. 0.6, p<0.001). rMTT displayed the best discriminative ability to differentiate MA from TIA (Figure).

ROC curves for different PCT parameters to differentiate migranous aura from TIA



ROC curve analysis for PCT parameters in differentiating MA and TIA

Conclusion: Focal perfusion abnormalities in acute MA often involve multiple unilateral arterial territories and hypoperfusion is less pronounced than in TIA. MA can be best differentiated from TIAs by lesser rMTT increase.

Disclosure: Nothing to disclose

EPR3011

Aphasia after acute stroke in a prospective, randomized, clinical and experimental controlled noninvasive study with an ipad-based app (Neolexon®): study protocol of the Lexi Study

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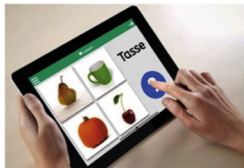
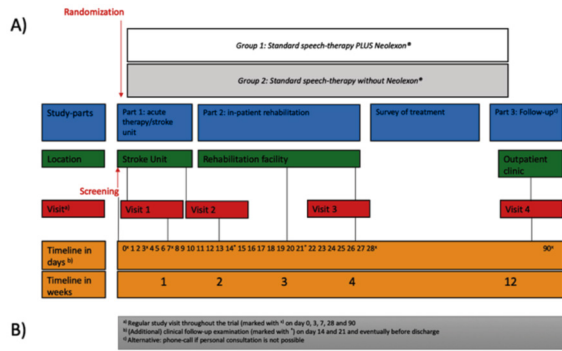
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Background and aims: Treatment of aphasia is still challenging for physicians, therapists and patients. So far there is proven evidence for “traditional” logopedic therapy. However, digital age potentially offers the opportunity to work more efficiently and cost-effectively. Neolexon® is a commercial tablet-based software for treatment of aphasia.

Methods: A sample size of 140 patients, 70 for each group will be included. Prospective, randomized, parallel group, open-label, clinical and experimental controlled non-invasive trial. Adult German native speakers suffering from acute aphasia after stroke are included. Computer-generated, blocked and stratified randomization by aphasia severity will assign patients to 1 of 2 groups: either 4 weeks of standard logopedic treatment vs. logopedic treatment with Neolexon® additionally. Both groups will also have self-training. Severity of aphasia will be assessed using the Bielefelder Aphasia Screening (BIAS), Aphasia Bedside Test (AABT) and Aphasia Check List (ACL). Follow-up will be assessed after 3 months.

Results: The primary endpoint is defined as a significant difference between aphasia severity comparing the 2 groups. Differences in quality of life, Beck Depression Inventory (BDI) and modified Ranking Scale (mRS) will be evaluated as secondary outcome parameters.

Conclusion: This trial will determine whether Neolexon® is superior to standard logopedic therapy. Subgroups with the greatest response to Neolexon® will be described.



This photo has been approved by Neolexon® for commercial use, publication, distribution, use, editing and transfer - in digital and print form by the photographer or by third parties.

Figure 1

Disclosure: This study is in part funded by Boehringer Ingelheim Pharma GmbH & Co.KG. The funder has no influence on the trial and will not have any impact on participant recruitment, data and statistical analysis or writing the protocol. The company Neolexon® supports the study by granting licenses for the app free of charge. The company also has no influence on the study planning nor the patient treatment and evaluation of the study data.

Cerebrovascular diseases 6

EPR3012

Distribution patterns of dilated perivascular space in moyamoya disease

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Background and aims: The pathogenesis of dilated perivascular space (DPVS) is still unclear. Blood-brain barrier (BBB) dysfunction may be involved in the development of DPVS. BBB dysfunction is also closely related to the pathogenesis of moyamoya disease (MMD). The purpose of this study was to investigate the distribution pattern of DPVS in MMD and to determine whether it is related to cerebral vascular status.

Methods: 51 patients with MMD were included. DPVS were graded in basal ganglia (BG) and centrum semiovale (CS) on T2 weighted imaging, using a validated 4-point semi-quantitative score. Cerebral vascular status on MR angiography (MRA) was graded using a validated MRA scoring. DPVS and MRA grading were classified as high (score >2) or low (score ≤2). Asymmetry of DPVS and MRA grading was defined as a difference of greater than 1 grade between the cerebral hemispheres.

Results: The CS-DPVS was showed in all of the enrolled patients. Out of those, 44 (88%) had high degree of CS-DPVS. The BG-DPVS was showed in 25 (50%), all with low degree of BG-DPVS. The asymmetry of CS-DPVS (26%) and MRA grade (42%) were significantly correlated to each other (Kendall's tau-b 0.604, p<0.001). The CS-DPVS degree was not associated with MRA degree (Kendall's tau-b -0.008, p=0.951) and age (p=0.378).

Conclusion: Our results showed that DPVS in MMD was predominantly observed in the CS and that the asymmetry of DPVS scores between cerebral hemispheres was associated with the asymmetry of the MRA grade.

Disclosure: This study was supported by Research Institute for Convergence of biomedical science and technology Grant (30-2020-015), Pusan National University Yangsan Hospital.

EPR3013

A Cost-Benefit Analysis of Mechanical Thrombectomy Generated Via a “Brain Attack” Protocol

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The advent of mechanical thrombectomy for acute ischemic stroke and the corresponding increase in the therapeutic window has produced a paradigm shift in stroke management. While mechanical thrombectomy per se appears to represent a cost-effective treatment intervention, in this study we sought to assess the cost-benefit associated with implementation of a thrombectomy-relevant “brain attack” protocol.

Methods: For a period of 1 year we prospectively evaluated patients treated according to our institution's brain attack protocol. We recorded the frequencies with which RAPID CT perfusion imaging, CT angiography (CTA), catheter-based cerebral arteriography and mechanical thrombectomy were performed and calculated their direct costs. Assuming a number needed to treat (NNT) of 4 to achieve functional independence, we calculated the mean direct cost required to achieve a thrombectomy-related positive clinical outcome.

Results: We evaluated 872 brain attack patients. RAPID CT perfusion imaging and CTA were performed in 384 cases (44%), catheter-based cerebral arteriography in 80 (9%) and mechanical thrombectomy in 48 (5.5%). The direct cost associated with these procedures totaled \$2.186 million. With the NNT of 4 applied to the 48 patients undergoing mechanical thrombectomy, the mean cost of achieving a thrombectomy-related positive outcome was \$182,000.

Conclusion: By ICER criteria, these findings suggest that aggressive use of a thrombectomy-relevant brain attack protocol may represent a borderline cost-effective intervention for acute ischemic stroke. Minimizing the frequency with which CTA that demonstrates no large vessel occlusion is performed or reducing the cost of that procedure would represent the most effective means of improving cost-effectiveness

Disclosure: Nothing to disclose

EPR3014

Anticoagulation treatment in secondary prevention of stroke: the RESTAIC study.

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Background and aims: Our aim is to explore the differences in long-term outcomes according to the type of oral anticoagulant (OAC) in secondary stroke prevention.

Methods: A prospective, multicentric, registry including ischemic stroke patients who were discharged under OAC for secondary prevention of stroke. 3 months follow-up was scheduled at outpatient clinic with subsequent annual phone interviews for 3 years. Principal outcomes: stroke recurrences, intracranial hemorrhage, major bleeding, and mortality. Patients were classified into 3 study groups according to the OAC at discharge: Vitamin K antagonist (VKA), Factor Xa inhibitor (FXa-I) and direct thrombin inhibitor (DTI).

Results: A total of 242 patients with OAC were included and 196 completed the 3-year follow-up evaluation. The reason for OAC treatment was the presence of a cardioembolic source in 241 patients (99.6%). Up to 77 patients (31.8%) were treated with OAC before the index stroke, 62 of them with VKA. At hospital discharge 106 were treated with FXa-I (43.8%), 96 with VKA (39.66%), and 40 with DTI (16.53%). The cumulative incidence at 3 years was 17% for stroke recurrence, 1.6% for intracranial hemorrhage, 4.9% for major hemorrhage and 22% for all-cause mortality; without differences between OAC groups. During the follow-up, 36 patients changed the OAC, mostly for stroke recurrence (12.32% of all causes). No differences among groups were found in OAC changes.

Conclusion: OAC treatment in 2ndary prevention of stroke has a lower risk of bleeding complications than stroke recurrence without differences among the type of OAC.

Disclosure: Nothing to disclose

EPR3015

Predictors of malignant middle cerebral artery infarction after mechanical thrombectomy.

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Background and aims: Several predictors have been described to early diagnose malignant middle cerebral artery infarction (MMI) and select patient for hemispherectomy. Nevertheless, few studies have asses them among patients with acute ischemic stroke undergoing mechanical endovascular thrombectomy (MET). The overall objective in this study was to evaluate these predictors in patients undergoing MET in the purpose to guide the medical care in the acute phase.

Methods: We selected patients from a prospective local database which reference all patients eligible for treatment with Alteplase thrombolysis and/or mechanical endovascular thrombectomy in acute stroke. We investigated demographic, clinical, and radiological data. Multivariate regression analysis was used to identify clinical and imaging predictors of MMI.

Results: In 32 months, 66 patients were included. 18 (27.3%) developed MMI. Malignant evolution was associated with: severity of neurological deficit and level of consciousness at admission, infarct size in DWI sequence and involvement of other vascular territories. Study groups didn't differ in terms of successful reperfusion. 2 variables were identified as independent predictors of MMI: DWI infarct volume ($p < 0.001$) and time before recanalization ($p = 0.018$). A decision tree based on these 2 factors was able to predict malignant evolution with high specificity (100%) and sensibility (73%).

Conclusion: Our study proposes a practical decision tree including DWI lesion volume and delay before recanalization to early and accurately predict MMI in a subgroup of patients with MCA infarction undergoing MET regardless to the status of reperfusion.

Disclosure: Nothing to disclose

EPR3016

Predictors of intracranial hemorrhage caused by arteriovenous malformation

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Background and aims: Cerebral arteriovenous malformation (AVM) is the most common cause of hemorrhagic stroke in young adults. The role of different factors in the pathophysiology AVM and stroke risk stratification remains unclear. The aim of this study to identify potential biomarkers for AVM stroke risk stratification.

Methods: This observational prospective cohort study included 382 patients with bAVM. Patient's demographics, clinical, neuroimaging data, and angioarchitectural characteristics were analyzed. A univariate analysis was performed, and factors with potential physiological significance that showed at least a trend toward significance were added to a multivariate logistic regression model.

Results: Deep brain location (hazard ratio [HR] 3.25, 95% CI 1.30 to 8.16), high flow AVM (HR 1.05, 95% CI 1.03 to 1.08), single draining vein (HR 1.95, 95% CI 2.01 to 4.15), exclusive deep venous drainage (HR 3.25, 95% CI 1.01 to 5.67), vein stenosis or varices (HR 2.25, 95% CI 1.8 to 3.19), aneurysm on feeding artery (HR 1.01, 95% CI 1.01 to 2.58), occurrence of silent intralesional microhemorrhage (according to neuroradiological assessment) (HR 5.38, 95% CI 2.64 to 10.96) were independent predictors of subsequent hemorrhage. Annual hemorrhage rates on follow-up ranged from 0.8% for patients without determined hemorrhagic risk factors to 39.1% for those harboring all these risk factors.

Conclusion: Knowing the risk factors for hemorrhagic AVM presentation is crucial for selecting appropriate therapeutic strategies. Our results allow to work out design of future trials for optimise management of unruptured AVM. Received information might improve identification of patients at risk.

Disclosure: Nothing to disclose

EPR3017

Influence of new DWI MRI lesions on cognitive functions after carotid endarterectomy

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Background and aims: Effect of carotid endarterectomy (CEA) on cognitive functions is unclear. The aim was to assess changes in cognitive functions following CEA and influence of new ischemic lesions on diffusion-weighted magnetic resonance imaging (DW-MRI) after CEA.

Methods: Patients without dementia or psychiatric disease including depression were included to the study after signing the Informed consent. In all patients The Addenbrooke's Cognitive Examination-Revised (ACE-R), Mini Mental State (MMSE), Clock Drawing Test (CDT) and Speech Fluency Test (SFT) were performed prior to CEA, 24 hours, 30 days and 1 year after CEA. Demographic data, history of vascular disease, diabetes, smoking, medication, clinical status, new lesion on DWI and changes in cognitive tests were collected and statistically analysed.

Results: Totally 37 (15.0%) out of 247 patients (177 males, age 67.4±7.5 years, 116 symptomatic stenoses) had new ischemic lesions on control DW-MRI. Cognitive tests (median value) in patients with/without DW-MRI lesions prior to CEA, 24 hours, 30 days and 1 year after CEA were: ACER 83/85, 83/90, 87/90, 85,5/90 points; MMSE 27/28, 27/29, 28/29, 27/29 points; CDT 5/5, 5/5, 4/5, 5/5 points; SFT 9/10, 10/10, 10/11, 10/11 points. No significant differences between patients with and without new ischemic lesion were found. Significant improvement was detected in MMSE 24 h after CEA (p=0.011) and CDT 30 days after CEA (p=0.038) compared to results prior to CEA.

Conclusion: New ischemic lesions on DW-MRI after CEA have no influence on cognitive functions in 1-year follow-up.

Disclosure: Supported by the Ministry of Health of the Czech Republic grant No. 17-31016A

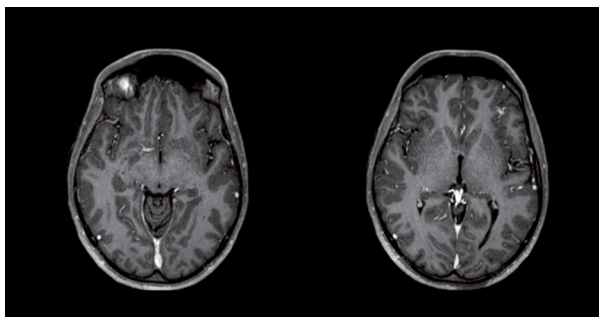
EPR3018

A novel mutation in ENG gene in an Italian family with hereditary hemorrhagic telangiectasia and polymicrogyria

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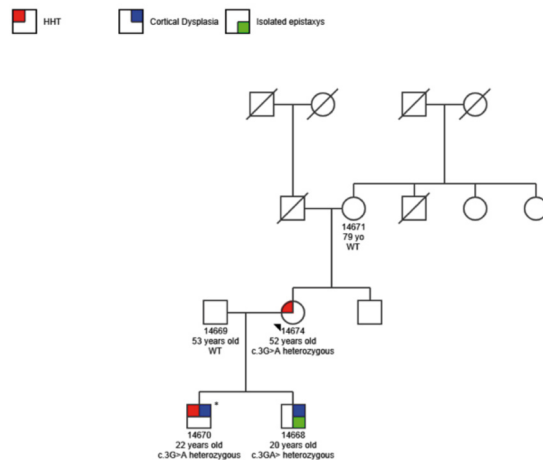
Background and aims: Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant condition primarily caused by mutations in genes involved in the maintenance of the endothelial homeostasis such as Endoglin (ENG). Main clinical features include recurrent epistaxis, telangiectases and systemic arteriovenous malformations (AVMs). Cortical development malformations have rarely been reported in association with the classical phenotype. **Methods:** Herein, we describe a case of a 22-years-old-male presenting with sudden onset of slurring of speech and left-sided weakness. He suffered from symptomatic epilepsy and recurrent epistaxis from childhood. Brain MRI showed a right frontal recent ischemic lesion as well as and multiple supratentorial cerebral arteriovenous malformations (cAVMs) and focal polymicrogyria. No atrial septum defects were found despite the evidence of a right to left vascular shunt at transcranial Doppler ultrasound. Chest CT revealed multiple pulmonary AVMs as the obvious source of paradoxical embolism. Given the consistent family medical history and the complex phenotype, genetic testing was performed and revealed a novel heterozygous mutation c.3G>A (p. Met11Ile) in ENG gene, which was likewise found in patient's brother and mother.



Brain MRI - Axial T1 weighted sequence with gadolinium showing left frontal cAVM and multifocal polymicrogyria involving the left cerebral hemisphere



Pulmonary angiography showing multiple AVMs. A large pulmonary arteriovenous malformation located in the left lower lobe.



Pedigree. Proband = *. WT = wild type.

Results: The patient underwent endovascular embolization of the largest AVMs and was started on a full dose treatment of low-molecular-weight heparin for six months. **Conclusion:** We described a novel mutation in ENG gene associated with CAVMs and symptomatic polymicrogyria. If associated with epistaxis, HHT must be ruled out in young patients presenting with acute cerebral ischemic event of unknown origin.

Disclosure: Nothing to disclose

EPR3019

Posterior circulation ischaemic strokes: efficacy, timing and functional outcome of endovascular treatment versus intravenous thrombolysis in a population-based retrospective study.

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Background and aims: Beyond the Guidelines, few studies proved the efficacy of endovascular treatment (EVT) in posterior circulation ischaemic strokes (PCI) compared to IV thrombolysis (IVT), as well as ideal timing of treatment. To retrospectively compare functional outcomes at 90 days between IVT versus EVT in our population of PCI. To assess predictive factors of good outcome (modified Rankin Scale ≤ 2), favourable outcome (modified Rankin Scale ≤ 3), and mortality.

Methods: From the Italian Registry of Endovascular Treatment and the local database of the Safe Implementation of Thrombolysis in Stroke – International Stroke Thrombolysis Register, 182 patients admitted to our hospital between 2006 and 2019 with posterior circulation vessels' occlusion on neuroimaging were selected: 91 underwent IVT, while 91 EVT (37 IVT plus EVT, 54 direct EVT).

Results: Statistically significant difference in the odds of favourable outcome was found (OR=2.08; 95% CI: 1.04-4.14; P=0.38) in favour of IVT group. On multivariate logistic regression analysis, age and NIHSS at onset were strong independent predictors of either good or favourable outcome (OR=1.05; 95% CI: 1.02-1.08; P=0.000; OR=1.08; 95% CI: 1.05-1.12; P=0.000, respectively); successful recanalization in EVT group (achieved in 76.4%) was shown to be predictive of favourable outcome (OR=2.98; 95% CI: 1.03-3.62; P=0.043). Time to treatment was predictive outcome.

Conclusion: Age, NIHSS at onset and recanalization were predictors of favourable outcome in our population of PCI.

Disclosure: Nothing to disclose

EPR3020

Basilar Artery Occlusion ischaemic strokes: outcomes and predictive factors of intravenous thrombolysis versus endovascular treatment in a population-based retrospective study.

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Background and aims: Pending the results from the BASICS trial, there is no consensus regarding the efficacy of endovascular treatment (EVT) compared to IV thrombolysis (IVT), and the optimal time of treatment, in Basilar Artery Occlusion acute ischaemic strokes (BAOs). To retrospectively compare functional outcomes at 90 days between IVT versus EVT in our population. To assess predictors of good outcome (modified Rankin Scale ≤ 2), favourable outcome (modified Rankin Scale ≤ 3), and mortality.

Methods: From the Italian Registry of Endovascular Treatment and the database of the Safe Implementation of Thrombolysis in Stroke - International Stroke Thrombolysis Register, 82 patients admitted to our hospital between 2006 and 2019 with BAOS on neuroimaging were selected: 23 received IVT, 59 EVT (24 IVT plus EVT, 35 direct EVT).

Results: No statistically significant differences in the odds of good and favourable outcome, as well as mortality, between IVT versus EVT groups were found (OR=8.53; 95% CI: .30-2.41; P=0.764; OR=1.48; 95% CI: 0.56-3.90; P=0.424; OR=1.62; 95% CI: 0.48-5.52; P=0.441, respectively). On multivariate logistic regression analysis, age and NIHSS at onset were strong independent predictors of good and favourable outcome. Successful recanalization in EVT group (achieved in 77.6%) was independent predictor of mortality (OR=40.98, P=0.002), but neither of good nor favourable outcome. Time to treatment was not predictive of any primary outcomes.

Conclusion: Further evidences are needed to clarify the optimal acute management of BAOs.

Disclosure: Nothing to disclose

EPR3021

Development and Validation of 3-month Major Post-stroke Prediction Nomogram after Acute Ischemic Stroke Onset

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Background and aims: The early detection of major post-stroke depression (PSD) is essential to optimize patient care. The Post-stroke Depression Prediction Nomogram was needed to develop and validate for early identification of acute ischemic stroke (AIS) patients with increased 3-month major post-stroke depression risk.

Methods: The early detection of major post-stroke depression (PSD) is essential to optimize patient care. The Post-stroke Depression Prediction Nomogram was needed to develop and validate for early identification of acute ischemic stroke (AIS) patients with increased 3-month major post-stroke depression risk.

Results: 11.57% (31/268) patients showed MDD at 3 months after stroke onset. The final logistic regression model included age, NIHSS score on admission, baseline calcium-phosphorus product and serum globulin. The model had acceptable discrimination, based on an C-statistics of 0.80 (95% CI, 0.747~0.846), with 87.10% sensitivity and 61.60% specificity. Furthermore, we transformed the model to nomogram, an easy-to-use risk assessment tool.

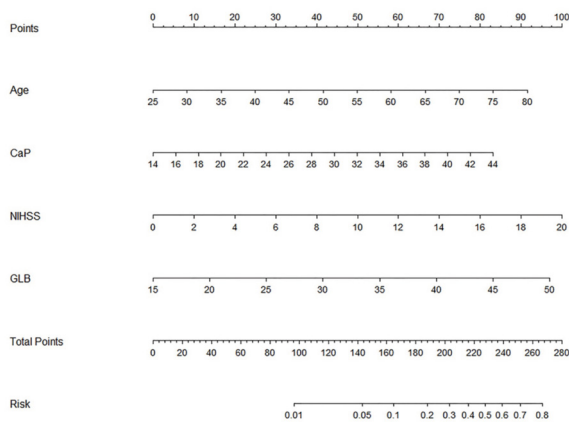
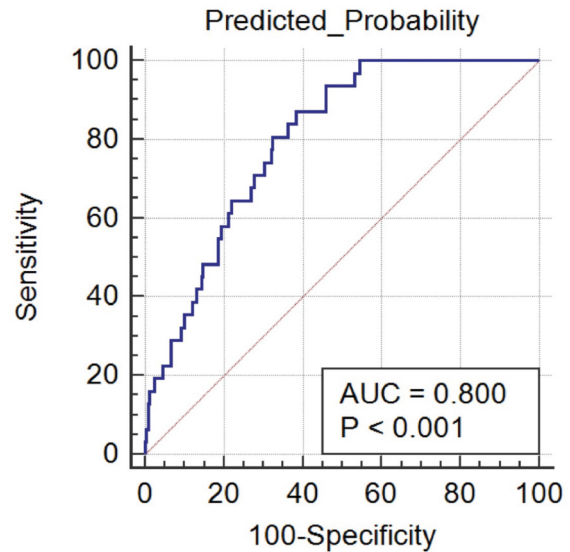
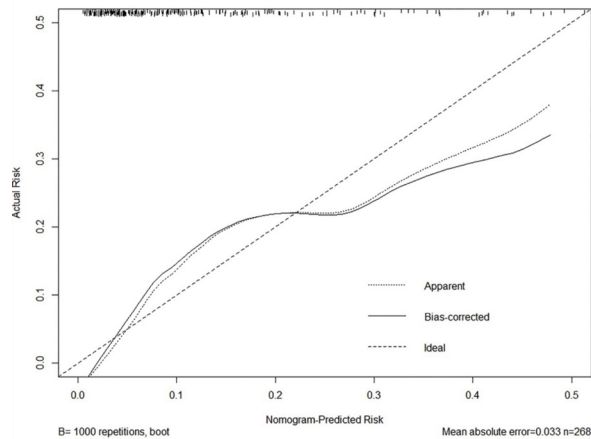


Figure 1. Nomogram to predict the risk of 3-month major PSD after stroke onset



ROC curve was plotted to show the performance of the nomogram. C-statistic was 0.80 (95% CI, 0.747~0.846), with 87.10% sensitivity and 61.60% specificity. Cutoff value was 0.083, which was obtained from the multivariate logistic regression equation with stepwise backwards method.



Calibration plots of the nomogram for major 3-month PSD prediction.

Conclusion: Age, baseline NIHSS score, serum globulin and calcium-phosphorus product were independent predictors of 3-month major PSD. Nomogram, as an effective clinical tool with good predictive performance, facilitate the early assessment of 3-month major PSD risk after stroke onset.

Disclosure: Nothing to disclose

EPR3022

Endovascular thrombectomy in patients with acute ischemic stroke and dementia

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Background and aims: Dementia and stroke are leading causes of disability and dependency worldwide. Numerous studies demonstrated success of endovascular thrombectomy (ET) in acute ischemic stroke (AIS). None of the studies had cognitive impairment or dementia listed as exclusion criteria, however, some studies had an upper age limit (80 or 85 years). Due to intracerebral lesions present in neurodegenerative or vascular cognitive impairment, patients with dementia might have different risks and outcomes after ET. Our aim was to analyze use and outcomes of ET for AIS in patients with pre-existing dementia.

Methods: Nation-wide longitudinal cohort study 2007–2017 from the Swedish national dementia registry (SveDem) and the Swedish national stroke registry (Riksstroke). Patients with dementia who suffered an AIS will be compared with matched non-dementia AIS patients. Access to ET and its outcomes at discharge from hospital and at three months post-stroke (death, residency and modified Rankin Scale score –mRS) will be examined. Odds ratios (ORs) and 95% CI will be calculated using logistic and ordinal logistic regressions.

Results: Final results will be presented at the congress. There were 802 ET of which 43 (5.4%) were performed in patients with dementia. Approximately half of the patients (~400) received intravenous thrombolysis and ET. 20 patients (2.5%) suffered postprocedural brain hemorrhage.

Conclusion: Our hypotheses are that (1) patients with dementia have a worse access to ET, but adjustments for pre-stroke functional independence might explain this difference, and (2) there are no differences in post-procedural intracranial hemorrhages and death, however, patients with dementia have poorer functional outcomes.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 3

EPR3023

Validation of the “Zihlschlacht Planning and Organisation Score” in patients with Parkinson’s disease

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Background and aims: This pilot study examined whether the “Zihlschlacht Planning and Organisation Score” (ZPOS) may represent a valid tool to assess the planning and organisational skills in patients with Parkinson’s disease (PD) with the aim to detect dysexecutive symptoms early in neuropsychological assessment and to avoid confounding with memory deficits in case of poor recall.

Methods: 37 inpatients with PD (22 male, 15 female; age 69.9±8.5 years; disease duration 9.7±6.6 years, Hoehn&Yahr stage 3.0±0.8) performed a neuropsychological assessment including for example the Rey-Osterrieth Complex Figure Test (ROCF) and the planning test as reported by Kohler and Beck (2018). The ZPOS represents a novel approach to evaluate executive function by analyzing with what precision and in what order configurational elements of the ROCF (i.e., the rectangle with 2 centerlines and 2 diagonals) are copied. The ZPOS is calculated by analysing 6 specific items of the copying procedure.

Results: We observed a significant correlation between the ZPOS subscale “precision” containing four items and the planning test ($r=0.49$, $p=0.001$), while correlation with the total ZPOS showed a trend toward significance ($r=0.26$, $p=0.06$). Besides we found a significant correlation between ROCF recall and the total ZPOS ($r=-0.49$, $p=0.001$) and its subscale “precision” ($r=-0.49$, $p<0.001$), respectively.

Conclusion: The ZPOS and the subscale “precision” may feature suitable screening tools for executive function in PD. Besides our results provide further evidence of a possible correlation between executive function and visual memory. Further research is required to delineate the usefulness of the ZPOS in PD and other neurological patients in more detail.

Disclosure: Nothing to disclose

EPR3024

Occupational burnout-like syndrome in early-onset Alzheimer’s disease

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Background and aims: Early-onset Alzheimer’s disease (EOAD) differentiates from late-onset AD by a predominant and early involvement of the parietal neocortex with hippocampal sparing, leading to non-amnesic syndromes. We aimed to identify the inaugural symptoms leading to a medical consultation in EOAD patients.

Methods: We retrospectively collected the clinical history of patients younger than 62 years referred to our memory clinic for cognitive dysfunction during the last year. Among 91 patients, 31 were diagnosed with AD based on clinical and biological criteria (cerebrospinal fluid biomarkers). Their mean age was 55±3.8 years.

Results: 11 EOAD patients (35%) were initially diagnosed with an occupational burnout syndrome, while logopenic aphasia or visuo-spatial deficit were observed in the remaining 20 patients (65%). In the burnout syndrome subgroup, the delay between the 1st symptoms and neurological examination was 2.6±1.1 years and the initial Mini-Mental State Examination score was 19.6±4.6/30. The neuropsychological assessment showed a severe working memory deficit, associated with mild cognitive cortical parietal syndrome. Visual inspection of brain MRI and FDG-PET showed bilateral parietal atrophy and a severe focal hypometabolism of associative parietal cortices.

Conclusion: We describe for the 1st time a new clinical presentation of EOAD mimicking an occupational burnout syndrome. The severe inaugural working memory deficit due to early cortical parietal damage leads to an inability to carry out concurrent professional tasks, and to severe anxiety, in the absence of overt aphasia or episodic memory deficit. It is crucial to consider this clinical phenotype in the definition of EOAD to avoid delayed diagnosis.

Disclosure: Nothing to disclose

EPR3025

Psychiatric and cognitive features of psychogenic non epileptic seizures and psychogenic neurological deficits

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Background and aims: The psychological mechanisms underlying psychogenic neurological impairments or seizures are poorly understood with a lack of well-established evidence-based treatments. The goal of this study is to assess the psychological profile of patients with psychogenic non-epileptic seizures and neurological deficits, and explore their cognition.

Methods: Prospective study including patients with a confirmed psychogenic non-epileptic seizure or psychogenic neurological deficit, recruited from neurology emergencies of Ibn Rochd University Hospital. Psychological assessment was performed by Hamilton scale of anxiety and depression (mild score if <17, moderate when 18-24, and severe when 25-30). MoCA was used for cognitive evaluation. Statistical methods included multivariate analysis with non-parametric regression and fisher's exact test.

Results: Among 27 patients, mid-age was 37.6 years (18-62), 70% were women. 37% had a psychogenic non-epileptic seizure and 63% a psychogenic neurological deficit. In the 1st group, Hamilton anxiety scale mean score was 29 versus 22 for depression. In the 2nd group, Hamilton anxiety scale mean score was 27 versus 20 for depression. 75% of all patients had a severe anxiety (without significant difference between the 2 groups). 50% of the psychogenic deficit patients had a severe depression versus only 25% of patients in the psychogenic non-epileptic seizure patients (p=0.02). MoCA mean score was 22.8, with no significant difference between both groups.

Conclusion: Anxiety seems to be the most predominant psychiatric impairment for our patients with an impact on some cognitive functions (memory, attention). These findings should enable us to wellknow our patients' difficulties and offer them the accurate therapeutic care.

Disclosure: Nothing to disclose

EPR3026

Neuropsychological indicators of subjective cognitive decline progression

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Background and aims: Neuropsychological indicators to identify cases of subjective cognitive decline (SCD) exist but their discriminant values are still unknown. Our objective was to examine early neuropsychological indicators that could discriminate between people in whom SCD progressed to mild or major neurocognitive disorder (NCD) and people in whom SCD remained stable.

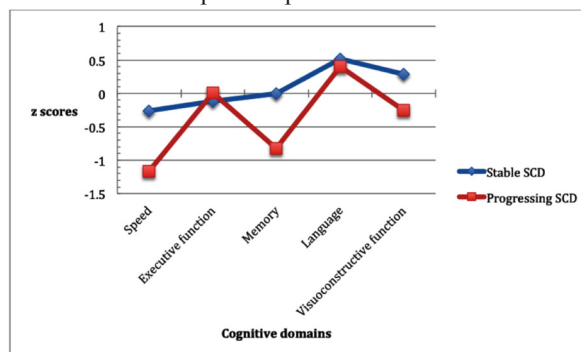
Methods: We retrospectively included patients from the memory center at Amiens University Medical Center with SCD and who had undergone 3 or more neuropsychological assessments at least 6 months apart. The relationship between changes in domain-specific scores and global cognitive score (GCS), as a function of final status was examined using a generalized linear mixed model.

Study participants, n	80
Gender, male, n (%)	34 (42.5)
Age, mean [95%CI]	64.07 [61.68 – 66.47]
MMSE score, mean [95%CI]	28.22 [27.78 – 28.65]
Time between visits 1 and 3, day, mean [95%CI]	1413.1 [1266.984 – 1559.29]
Educational level	
Primary education, n (%)	15 (18.8%)
Secondary education, n (%)	32 (40%)
Tertiary education, n (%)	33 (41.3%)

Abbreviation: CI: Confidence interval; MMSE: Mini-Mental State Examination.

Characteristics of the study population.

Results: Among the 80 patients with SCD, 11 had progressed to a NCD. When considering the GCS, the effect of final status was significant as a result of the lower score measured at the initial assessment. The combination of age, memory (sum of total recall), and action speed scores at the first assessment predicted the progression of SCD with a sensitivity of 91%, a specificity of 78%, a negative predictive value of 98% and a positive predictive value of 40%.



Differences in cognitive domain z scores between “stable SCD” and “progressing SCD” groups of patients.

Conclusion: The present results should help physicians to identify cases of SCD at risk of progression by examining early neuropsychological indicators.

Disclosure: Nothing to disclose

EPR3027

Sensitivity and Specificity of the ECAS in Parkinson's Disease and Huntington's Diseases

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Background and aims: The study aims to investigate psychometric properties of the ECAS, recently validated in the Italian language, in Parkinson's (PD) and Huntington's (HD) diseases. In particular, the sensitivity and specificity of the ECAS in highlighting HD and PD cognitive-behavioural features and in differentiating between these two populations and from healthy controls (HC) were evaluated.

Methods: Participants were administered the ECAS, together with other cognitive screening tools (FAB, MoCA, RME) and psychological questionnaires (BDI, STAI/Y, I-DAS). Patients' possible changes in behaviour were evaluated by carers interview (ECAS Carer Interview). 73 PD, 38 HD patients and 49 HC were recruited at the San Luca Hospital, IRCCS Istituto Auxologico Italiano and at CSS-Mendel and LIRH Foundation site, Rome. Correlations between the ECAS and traditional cognitive measures, together with core clinical features were analysed.

Results: The ECAS distinguished between HD patients and HC ($p < 0.001$) and between the 2 clinical syndromes ($p < 0.001$) with high sensitivity and specificity. Even if diagnostic accuracy of the ECAS in distinguishing between PD and HC was very low ($p = 0.05$), the PD cognitive phenotype was very well described by the ECAS. Convergent validity of the ECAS against other traditional cognitive screening was observed, as well as correlations with psychological aspects and typical clinical features, especially for the HD group.

Conclusion: The ECAS represents a rapid, feasible and sensitive tool, useful also in different neurodegenerative disorders affecting verbal-motor abilities other than ALS. Clinical applications in these neurodegenerative conditions require further investigations.

Disclosure: Nothing to disclose

EPR3028

The brain mechanisms for the use of objects

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Background and aims: We described new paradigms developed to elucidate the brain mechanisms that are involved in object manipulation to establish whether changes in goal-directed and habitual actions in healthy volunteers and patients with limb apraxia.

Methods: In a novel experiment I developed (Rounis et al. 2017, Figure 1), participants grasped a cup from its open or closed end to lift or turn it. We measured reaction times and error rates when a group of 18 healthy volunteers, and 22 patients with limb apraxia.

In a follow-up experiment (Rounis et al. in preparation, Figure 2) 25 healthy participants performed the same task while being scanned with fMRI.

Conclusion: These results are consistent with the evidence that there is a circuit that is involved in grasping (AIP-PMv) (Murata 2000) and a circuit that is involved in the movement of the object, that is in object use (IP – inferior frontal gyrus) (Fogassi 2009).

Disclosure: Nothing to disclose

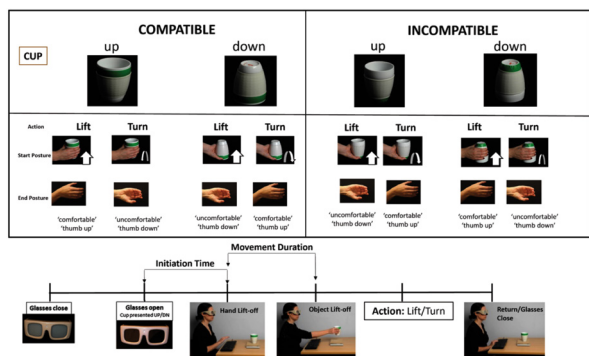


Figure 1 Behavioural Study

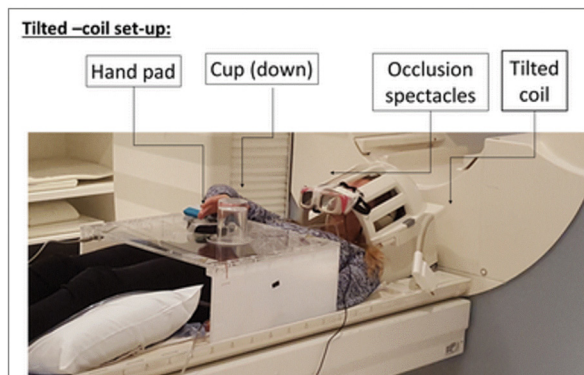


Figure 2 fMRI study

Results: We found that the movements were quicker if the cup was to be grasped by the open (wide) rather than the closed (narrow) end, consistent with the notion that objects ‘afford’ particular actions: a cup is for drinking, hence a preference for its open end. Patients were compromised in non-afforded actions. We identified activations in left anterior intraparietal, and superior temporal areas and in the dorsal premotor area (in incongruent tasks).

EPR3029

The role of executive cognition in the prediction of HIV medication adherence

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Background and aims: Suboptimal medication adherence in HIV infection is associated to drug-resistant strain development and viral replication. The aim of the present study is to explore whether neuropsychological tests of Executive Functions predict antiretroviral adherence among HIV individuals beyond and above demographic variables, disease characteristics, motor and overall cognitive functioning.

Methods: 105 HIV-positive individuals completed a comprehensive executive function test battery, along with measures of verbal memory, motor functioning, processing speed, visuospatial perception, picture naming and overall cognitive performance. Medication adherence was assessed via a visual analogue self-report scale recording the amount of prescribed doses taken during the past month. A stepwise linear regression was conducted to examine the ability of executive test performance to predict medication adherence. Subsequently, executive test variables were entered at the final step of a hierarchical regression model in order to assess their additional predictive power on medication adherence.

Results: Performance on two executive cognition measures was associated with medication adherence, explaining 16.2% of the variance. In the hierarchical regression model, 20.1% of the variance in medication adherence reports was explained by treatment complexity, memory performance, age and education, whereas the addition of executive performance added unique variance, increasing the amount of variance explained through the model to 30.3%.

Conclusion: Evaluation of executive functioning suggests a promising tool in order to increase the predictive ability of medication adherence among HIV-positive individuals.

Disclosure: Greek State Scholarship Foundation (I.K.Y.)

EPR3030

Subjective perception of driving ability in patients with Mild Cognitive Impairment (MCI) and mild Alzheimer's Disease (AD)

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Background and aims: Driving ability of patients with neurodegenerative diseases interferes with their everyday functionality and is subjected to neurological evaluation. We examined the self perception of patients with MCI or mild AD regarding their driving ability and their driving habits through a specially developed questionnaire.

Methods: We examined the answers of 40 patients with MCI (27 Males, Mean Age 67-year-old), 14 patients with AD (14 Males, Mean Age 74-year-old) and 63 cognitively healthy individuals (33 Males, Mean Age 48-year-old). Questions referred to driving skills, driving ability and driving habits under difficult conditions.

Results: Both MCI and AD patients recognize increased difficulties (compared to the control group, after controlling for confounding factors) during the last 5 years in driving under certain conditions (night, rain, unfamiliar routes, highways, long distances). AD patients avoid driving under the above-mentioned conditions compared to healthy individuals. However, driving frequency under these conditions does not differ between the MCI patients and the control group. No statistically significant differences were found regarding the subjective evaluation of driving skills between the patients and the control group.

Conclusion: Although, cognitively impaired patients do not recognize impairment of their driving skills, they do realize their difficulties under difficult conditions. Thus, AD patients avoid driving under these conditions, as a compensatory mechanism. This finding is important and highlights the need of objective evaluation of driving ability of patients with (even mild) cognitive impairment along with the utility of targeted questionnaires.

Disclosure: This study is part of the PhD project with title "Evaluation of driving behavior in patients with MCI, Dementia or Parkinson's Disease: Diagnostic and Prognostic Markers", funded and supported by Onassis Foundation.

EPR3031

Cognitive Impairment in Multiple Sclerosis: A Multiparametric Structural and Functional MRI Study

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Background and aims: We applied a multiparametric MRI approach to investigate the association between cognitive impairment in multiple sclerosis (MS) patients and specific patterns of structural and functional MRI abnormalities.

Methods: 100 healthy subjects (HC) and 297 MS patients underwent 3D T1-weighted, diffusion tensor, dual-echo and resting-state (RS) scans at 3.0 Tesla. Patients also underwent a neuropsychological evaluation. Grey matter (GM) atrophy, white matter (WM) microstructural abnormalities and RS functional connectivity (RS-FC) of the default mode network (DMN) were investigated using voxel-wise approaches.

Results: 89 MS patients were cognitively impaired (CI). Compared to HC, cognitively preserved (CP) patients had significant GM atrophy of deep GM nuclei, in regions of fronto-temporo-parietal and occipital lobes, cingulate cortex, and hippocampus, bilaterally. Additional widespread GM atrophy in supratentorial regions and cerebellum were found in CI patients. Compared to CP, CI patients had atrophy in the thalamus, caudate nucleus, hippocampus, cerebellum, bilaterally and left supplementary motor area (SMA). Compared to HC, CP patients had decreased fractional anisotropy (FA) of supratentorial WM tracts, while CI patients had additional decreased FA of infratentorial WM tracts. Compared to HC, CP patients had reduced RS-FC in left SMA. CI patients had additional reduced RS-FC in left posterior and middle cingulate cortex, right inferior parietal lobule (IPL) and increased RS-FC in left IPL and right middle frontal gyrus. Compared to CP, CI patients had reduced RS-FC in the left posterior cingulate cortex and right IPL.

Conclusion: Structural abnormalities of critical CNS structures combined with functional maladaptive mechanisms contribute to explain CI in MS patients.

Disclosure: Nothing to disclose

EPR3032

Comparison of longitudinal changes of cerebral small vessel disease markers and cognitive function between subcortical vascular mild cognitive impairment with and without NOTCH3 mutation: a 5-year follow-up study.

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Background and aims: In this study, we compared the longitudinal changes in cognition and cerebral small vessel disease (CSVD) markers between subcortical vascular mild cognitive impairment (svMCI) patients with and without NOTCH3 mutation [NOTCH3(+) svMCI vs. NOTCH3(-) svMCI].

Methods: We prospectively recruited patients with svMCI between September 2008 and September 2011 and screened for NOTCH3 mutation by sequence analysis for mutational hotspots in the NOTCH3 gene. Patients were annually evaluated for 5 years.

Results: Among 63 svMCI patients, 9 (14.3%) patients had either known mutations or possible pathogenic variants. Thirteen of 63 patients converted to dementia on follow-up; 1/9 (11.1%) among NOTCH3 (+) svMCI patients and 12/54 (22.2%) among NOTCH3(-) svMCI patients. Cox regression model showed that dementia risk was not significantly different between NOTCH3(+) and NOTCH3 (-) svMCI patients after controlling for age, sex, education, and PiB positivity ($p=0.763$; adjusted hazard ratio, 0.723; 95% confidence interval, 0.088–5.926). Linear mixed effect models testing the interaction effect of NOTCH3 mutation and time showed that NOTCH3 (+) svMCI group had much greater increases in the number of microbleeds [β (SE)=0.66 (0.29), $p=0.025$] and lacunes [β (SE)=0.42 (0.16), $p=0.008$].

Conclusion: The rate of increases in microbleed and lacune counts was much greater in NOTCH3 (+) svMCI patients compared to NOTCH3 (-) svMCI patients. In spite of a much greater increase of lacune and microbleed counts in NOTCH3 (+) svMCI patients, there were no significant differences in dementia conversion rate and neuropsychological score changes over 5 years between the 2 groups.

Disclosure: Nothing to disclose

Epilepsy 3

EPR3033

Long-Term Safety and Efficacy of Cannabidiol (CBD) Treatment in Dravet Syndrome: Results Overall and for Patients Completing 1–3 Years of an Open-Label Extension (GWPCARE5)

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Background and aims: We assessed the long-term safety and efficacy of add-on CBD in patients with Dravet syndrome (DS) in the 3rd interim analysis of the open-label extension (OLE; GWPCARE5; NCT0224573) of two randomised controlled trials (RCTs; GWPCARE1 [parts A/B], GWPCARE2).

Methods: Patients who completed either RCT could enter this OLE, in which they received plant-derived highly purified CBD medicine (Epidyolex[®]; 100mg/mL oral solution). Primary endpoint: safety (n=315). 2ndary endpoints: median percentage change from baseline in convulsive and total seizure frequency overall (n=287) and patients completing 1, 2, and 3 years (n=214, 113, and 55). **Results:** 95% (315/330) of eligible patients with DS enrolled. Median follow-up was 61 weeks (18 days–184 weeks); Mean age was 10 years; 97% <18 years; 50% male. Patients were taking a median 3 concomitant antiepileptic drugs at baseline; 68% were on clobazam, 67% valproate, and 38% stiripentol. Mean modal CBD dose was 22mg/kg/day overall and ranged from 21–24mg/kg/day over follow-up for 3-year completers. 43% (135/315) of patients withdrew. Adverse events (AEs) occurred in 97% of patients and serious AEs in 41%; 9% discontinued due to AEs. Aspartate/alanine aminotransferase levels >3× upper-limit-of normal occurred in 21%. There were 4 deaths; none deemed treatment-related by the investigator(s). Median percentage reduction in convulsive seizure frequency during 12 week visit windows over 156 weeks was 45–73% overall; and 49–56%, 57–67%, and 57–77% for 1-, 2-, and 3-year completers.

Conclusion: Long-term treatment with add-on CBD in patients with DS produced sustained seizure reductions, with no new safety concerns.

Disclosure: This trial was sponsored by GW Pharmaceuticals.

EPR3034

Long-Term Effects of Concomitant Anti-Seizure Medications (ASMs) During Adjunctive Perampanel Treatment in Paediatric Patients (Aged 4-

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Background and aims: We report a post hoc analysis of long-term (1-year) perampanel safety and efficacy by concomitant ASM use in paediatric patients (aged 4–<12 years) with partial-onset seizures (POS; with/without secondarily generalised seizures [SGS]) or primary generalised tonic-clonic seizures (PGTCS) from Study 311 (NCT02849626).

Methods: Cumulative data from all enrolled patients were included (23 weeks [Core Study]; 52 weeks [Core/Extension]). Treatment-emergent adverse events (TEAEs) and efficacy (median percent reduction in seizure frequency/28 days; 50% responder rates) were assessed.

Results: Of 180 patients, 35 (19.4%), 100 (55.6%) and 45 (25.0%) received 1, 2 or 3 baseline ASMs, respectively. Most common concomitant ASMs were levetiracetam (32.2%), valproic acid (30.0%), clobazam (26.7%), lamotrigine (25.0%), topiramate (16.1%) and carbamazepine (13.9%); patients could receive >1 of these. TEAEs are presented in Table 1. Median percent reductions in seizure frequency/28 days are shown in Figures 1/2. At Weeks 40–52, POS, SGS and PGTCS 50% responder rates were: 1 ASM, 78.9% (15/19), 87.5% (7/8) and 75.0% (3/4); 2 ASMs, 63.3% (38/60), 81.8% (18/22) and 66.7% (4/6); 3 ASMs, 48.3% (14/29), 72.7% (8/11) and 33.3% (1/3), respectively. For the most common ASMs, 50% responder rates at Weeks 40–52 ranged from: POS, 50.0% (topiramate [8/16]; valproic acid [18/36]) to 64.5% (levetiracetam [20/31]); SGS, 63.6% (lamotrigine [7/11]) to 100.0% (carbamazepine [4/4]); PGTCS, 0.0% (carbamazepine [0/0]) to 100.0% (valproic acid [3/3]).

Table 1. Overview of TEAEs and most common TEAEs (occurring in ≥15% of patients in any ASM group) by number and most common concomitant baseline ASMs (Safety Analysis Set)

n (%)	Number of baseline ASMs			Most common baseline ASMs					
	One (n=35)	Two (n=100)	Three (n=45)	Levetiracetam (n=58)	Valproic acid (n=54)	Clobazam (n=48)	Lamotrigine (n=45)	Topiramate (n=29)	Carbamazepine (n=25)
Any TEAE	33 (94.3)	89 (89.0)	40 (88.9)	55 (94.8)	47 (87.0)	41 (85.4)	40 (88.9)	25 (86.2)	20 (80.0)
Serious TEAEs	4 (11.4)	16 (16.0)	16 (35.6)	12 (20.7)	13 (24.1)	11 (22.9)	9 (20.0)	7 (24.1)	3 (12.0)
TEAEs leading to discontinuation	4 (11.4)	13 (13.0)	5 (11.1)	8 (13.8)	7 (13.0)	3 (6.3)	6 (13.3)	4 (13.8)	1 (4.0)
Most common (≥15%) TEAEs									
Somnolence	9 (25.7)	26 (26.0)	14 (31.1)	14 (24.1)	17 (31.5)	19 (39.6)	12 (26.7)	5 (17.2)	4 (16.0)
Nasopharyngitis	7 (20.0)	18 (18.0)	18 (40.0)	15 (25.9)	10 (18.5)	17 (35.4)	8 (17.8)	6 (20.7)	6 (24.0)
Dizziness	4 (11.4)	14 (14.0)	6 (13.3)	9 (15.5)	11 (20.4)	4 (8.3)	9 (20.0)	2 (6.9)	5 (20.0)
Pyrexia	8 (22.9)	13 (13.0)	8 (17.8)	9 (15.5)	7 (13.0)	9 (18.8)	7 (15.6)	1 (3.4)	5 (20.0)
Vomiting	8 (22.9)	15 (15.0)	4 (8.9)	11 (19.0)	7 (13.0)	5 (10.4)	5 (11.1)	1 (3.4)	5 (20.0)
Irritability	7 (20.0)	10 (10.0)	7 (15.6)	8 (13.8)	8 (14.8)	2 (4.2)	7 (15.6)	4 (13.8)	1 (4.0)
Influenza	5 (14.3)	10 (10.0)	8 (17.8)	7 (12.1)	7 (13.0)	6 (12.5)	8 (17.8)	5 (17.2)	6 (24.0)
Headache	4 (11.4)	5 (5.0)	6 (13.3)	9 (15.5)	2 (3.7)	3 (6.3)	7 (15.6)	0 (0.0)	2 (8.0)
Balance disorders	0 (0.0)	4 (4.0)	3 (6.7)	3 (5.2)	2 (3.7)	1 (2.1)	0 (0.0)	5 (17.2)	0 (0.0)

A TEAE is defined as an AE that emerges from the date of first dose of study drug to 28 days after the last end date of dose in prescribed dose entity, having been absent at pretreatment or recurred during treatment, having been present at pretreatment but stopped before treatment, or worsened in severity during treatment relative to the pretreatment state, when the AE is continuous.

Patients with ≥2 TEAEs in the same system organ class or with the same preferred term are counted only once for that system organ class or preferred term.

AE, adverse event; ASM, anti-seizure medication; TEAE, treatment-emergent adverse event.

Table 1. Overview of TEAEs and most common TEAEs (occurring in ≥15% of patients in any ASM group) by number and most common concomitant baseline ASMs (Safety Analysis Set)

Figure 1. Median percent reduction in seizure frequency per 28 days from baseline by number of baseline ASMs for (A) POS*, (B) SGS* and (C) PGTCs (Full Analysis Set)

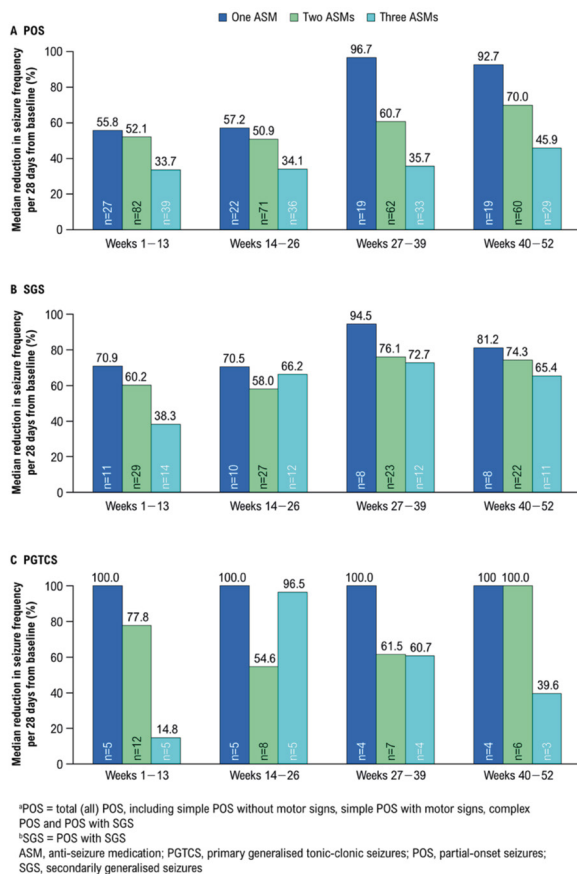


Figure 1. Median percent reduction in seizure frequency per 28 days from baseline by number of baseline ASMs for (A) POS, (B) SGS and (C) PGTCs (Full Analysis Set)

Figure 2. Median percent reduction in seizure frequency per 28 days from baseline by most common concomitant ASMs for (A) POS*, (B) SGS* and (C) PGTCs (Full Analysis Set)

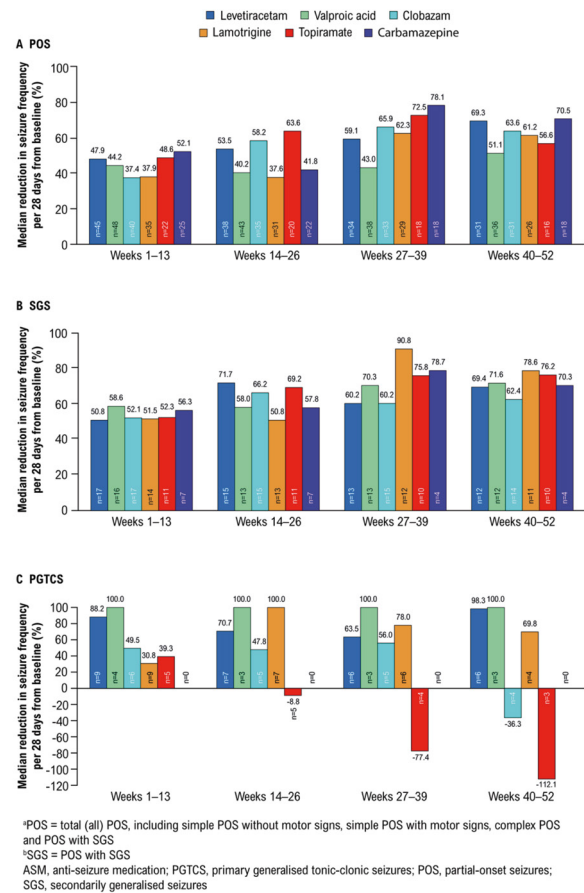


Figure 2. Median percent reduction in seizure frequency per 28 days from baseline by most common concomitant ASMs for (A) POS, (B) SGS and (C) PGTCs (Full Analysis Set)

Conclusion: Long-term (1-year) adjunctive perampanel was generally well tolerated and efficacious in paediatric patients with POS (with/without SGS), irrespective of baseline ASMs; sample size was too small for PGTCs to draw conclusions.

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EPR3035

Withdrawn

EPR3036

Natural history of Lafora disease: systematic review of literature and metanalysis.

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Background and aims: Lafora Disease (LD) natural history has been described only in case reports and small series of patients to date. Here we present a systematic review of all the available cases reported in literature, aiming to better define LD course and possibly enucleate prognostic factors, in view of the release of specific therapies in the next future.

Methods: 2 independent reviewers extracted the relevant data from articles selected by using PubMed/MEDLINE database. We included in statistical analysis only genetically confirmed LD cases.

Results: Of 699 citations, 62 studies with a total of 252 cases (214 families) were identified. Mean age at disease onset was 13.8±3.5 years. EPM2A was mutated in 83 families (38.8%), while EPM2B in 131 (61.2%). Mean duration of the disease in 62 deceased cases was 8.2±5.7 years (9.9±9 years in 19 EPM2A cases and 7.5±3.2 years in 43 EPM2B cases). Loss of autonomy (grade 3 of disability scale) occurred after a mean of 6.4±5.6 years from onset (4.8±4.9 years for 20 EPM2A cases and 7.1±5.7 years for 45 EPM2B cases).

Conclusion: Our preliminary analysis suggests that despite mean disease duration appears globally shorter in EPM2B mutated cases, overall survival in LD could vary widely even between cases with the same altered gene, suggesting that mutation type could play a major role. EPM2A cases seems to spend more time in a severe disability state than EPM2B cases. Even if a prospective study is still needed to further characterize the disease, here we have described for the first time a large LD cohort.

Disclosure: Nothing to disclose

EPR3037

Safety of Cenobamate as Adjunctive Treatment for Uncontrolled Focal Seizures: Results from a Large, International, Safety Open-Label Study

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Background and aims: Cenobamate is a novel antiepileptic drug (AED) with a unique, complementary, dual mechanism of action which has shown a significant seizure frequency reduction, including seizure freedom, in 2 well-controlled studies. Among the first 953 adults exposed to cenobamate, three confirmed cases of drug reaction with eosinophilia and systemic symptoms (DRESS) occurred. This study was designed to assess whether a slower titration and lower starting dose would reduce the incidence of DRESS.

Methods: This ongoing, open-label study enrolled epilepsy patients 18–70-year-old with uncontrolled focal onset seizures taking stable doses of 1-3 AEDs. Increasing daily doses of cenobamate were administered (12.5, 25, 50, 100, 150, and 200mg) at 2-week intervals. Further increases to a maximum dose of 400mg/day by 50mg/day increments every other week were allowed. A key objective was to assess the rate of DRESS after 6 months. Hypersensitivity reactions were reviewed monthly.

Results: 1,340 patients were dosed (2,192 patients/year; July 2019 data cut-off). No cases of DRESS occurred. The most frequent AEs (incidence ≥10%) were somnolence (30.8%), dizziness (26.8%), fatigue (18.8%) and headache (15.5%). Serious AEs occurred in 14.2% of patients, severe AEs in 10.2% and TEAEs leading to discontinuation in 13.1%.

Conclusion: Long-term treatment with adjunctive cenobamate was generally safe and well tolerated, with the most common TEAEs being CNS-related. This study shows preliminary evidence that reducing the starting dose and slowing the titration rate of cenobamate to 2w intervals might mitigate the risk of DRESS.

Disclosure: Study 021 (NCT02535091) was sponsored by SK Life Science, Inc. and the analyses supported by Arvelle Therapeutics International GmbH

EPR3038

Transient and terminal asystoles in focal epileptic seizures: results of continuous ECG monitoring

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Background and aims: Cardiac arrhythmias and conduction disorders in patients with epilepsy are presumably one of the main causes of sudden unexpected death in epilepsy (SUDEP), and they can be identified by long-term ECG monitoring. The aim of this study was to determine the nature and frequency of bradycardia and asystole in patients with persistent epileptic seizures, despite the ongoing antiepileptic therapy, over a long period of time using a loop ECG recorder.

Methods: 193 patients with persistent epileptic seizures were implanted with subcutaneous ECG recorders programmed to record bradycardia, cardiac pauses, ventricular/atrial tachyarrhythmias. The recording was also activated by the patient with the onset of epileptic seizures.

Results: About 6000 ECG fragments were recorded during 36 months of monitoring. More than half of the patients showed changes in heart rhythm in the ictal period, but only 13 (6.7%) of patients in the form of bradycardia and asystole. During the entire follow-up period, 5 (2.6%) patients died due to SUDEP. Analysis of postmortem records showed that at the time of death, bradycardia with subsequent cardiac arrest was recorded on the ECG, however, during the entire previous follow-up period, no rhythm and conduction disturbances were observed. On the other hand, the asystoles recorded in a number of patients in the ictal period were reproducible from seizures to seizures and had a transient nature.

Conclusion: Transient asystoles during seizures and terminal asystole at the time of death indicate not only different pathophysiological mechanisms underlying these types of bradiarrhythmias, but also different prognostic value.

Disclosure: Nothing to disclose

EPR3039

Myocardial ischemia in patients with epilepsy

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Background and aims: Patients with epilepsy (PWE) are at increased risk for unexpected death. The determination of causes of death in seizure- and epilepsy-related death is challenging.

The aim of the study was to employ myocardial perfusion imaging (MPI) to evaluate the risk of cardiovascular events in epileptic patients.

Methods: MPIs with ^{99m}Tc tetrofosmin stress – rest single photon emission computer tomography (^{99m}Tc - SPECT) was performed in 28 patients with epilepsy and 32 age-matched individuals. MPI was assessed using 17 segment polar map and with a scale of 0 to 4 scoring. Abnormal MPI was considered when summed stress score was ≥ 4 .

Smoking, hypertension, diabetes mellitus, dyslipidemia, obesity and family history of coronary artery disease were recorded as risk factors for myocardial infarction in both groups. Clinical data of PWE were also recorded.

Results: 28 PWE (F/M: 6/22) with a mean age of 56.86 ± 10.54 and 32 controls (F/M: 7/25) with a mean age of 55.06 ± 9.34 (p: NS) were recruited. PWE had 2.36 ± 1.12 of the aforementioned risk factors vs 2.62 ± 1.04 for the controls (p: NS). They were suffering from pharmacoresistant epilepsy for 26.48 ± 18.50 years and were under a median number of 2 antiepileptic drugs. 18 PWE had abnormal MPI (64.28%) vs 14 controls (43.72%), $p=0.028$.

Conclusion: In a PWE the elevated stress and sympathetic response to the seizure may trigger an acute coronary event. As shown by the results of our study, PWE may suffer from concurrent cardiac disease, a potential explanation for sudden death.

Disclosure: Nothing to disclose

EPR3040

Improving access to ‘first suspected seizure’ services: A Quality Improvement Project in an epilepsy clinicP. Smith¹, M. Pierri²¹Cardiff, ²Epilepsy Unit, University Hospital of Wales, Cardiff, United Kingdom

Background and aims: The diagnosis of a 1st suspected seizure is essentially clinical, with emphasis upon the history and eyewitness account. Some causes of blackouts are life threatening, and for many people blackouts threaten work, education, driving and social interaction. The UK target for specialist assessment of 1st suspected seizures is 2 weeks following referral. Many busy epilepsy services have difficulty maintaining such rapid access.

Methods: We reviewed the 12 months baseline data before the intervention. We process-mapped referrals to the epilepsy service and identified ‘quick wins’; we then conducted iterative quality improvement cycles using ‘Plan–Do–Study–Act’ (PDSA) over 6 months, noting changes to the waiting times following each intervention. Noting several quick wins, we established a weekly multidisciplinary team (MDT) meeting to discuss and triage all referrals into the epilepsy service. We increased the proportion of telephone follow-up (improving patient convenience and shortening consultations), increased numbers seen in the nurse led clinics, and increased discharges to ‘open appointments’.

Results: We reviewed the data at 6 months and at 24 months after starting the interventions. The waiting time for 1st seizure referrals fell from 7–10 weeks (baseline) to consistently below 2 weeks at 6 months and 24 months. The MDT discussed a mean of 28.5 patients weekly. We increased the proportion of telephone review appointment from 8% (baseline) to 29% at 24 months.

Conclusion: Through MDT triage of all referrals to the service, and by freeing space in the routine review epilepsy clinic, we sustainably reduced specialist assessment waiting times following a first suspected seizure.

Disclosure: Nothing to disclose

EPR3041

Long-term epilepsy outcome of post-anoxic refractory status epilepticus after aggressive treatmentL. Tinti¹, S. Beretta¹, A. Coppo², E. Bianchi³, C. Zanchi¹, D. Carone¹, A. Stabile¹, G. Padovano¹, E. Sulmina², A. Grassi², G. Bogliun¹, G. Foti², C. Ferrarese¹, A. Pesenti⁴, E. Beghi⁵, L. Avalli²¹Epilepsy Center, Department of Neurology, San Gerardo Hospital ASST Monza, University of Milano Bicocca, Monza, Italy, ²Department of Intensive Care, University of Milano Bicocca, Monza, Italy, ³Neuroscience, IRCCS Mario Negri Institute for Pharmacological Research, Milan, Italy,⁴Department of Anesthesia, Critical Care and Emergency, IRCCS Ospedale Maggiore Policlinico, Milan, Italy,⁵Neuroscience, IRCCS-Istituto di Ricerche Farmacologiche “Mario Negri”, Milan, Italy

Background and aims: Studies on neurological prognosis after cardiac arrest usually assess functional status, while data about long-term sequelae such as epilepsy are limited.

Methods: 166 consecutive patients with cardiac arrest, in a coma for more than 24 hours, were electroencephalogram (EEG) monitored and enrolled in a previously published study on aggressive treatment of post-anoxic status epilepticus (Beretta et al, Neurology 2018). Patients were classified in the acute phase using four mutually exclusive patterns: continuous and/or reactive EEG (pattern A, 76 patients), status epilepticus by Salzburg criteria (pattern B, 36 patients), generalized periodic discharges (pattern C, 13 patients), discontinuous and unreactive EEG (pattern D, 41 patients). 77 survived at 6 months and were retrospectively contacted by phone calls. A standardized questionnaire assessed the following outcomes: new seizures, new diagnosis of epilepsy after cardiac arrest, seizures before cardiac arrest, usage of antiepileptic drugs (AEDs), Cerebral Performance Category (CPC) score.

Results: 63 patients were contacted, while 14 patients were lost at follow-up (median follow-up: 70 months, range 43–100). Only 2 patients (3.2%) were on long-term AED, both presented pattern B during the acute phase. 1 patient was seizure-free, the other developed chronic focal epilepsy and Lance-Adams syndrome. No pattern A patient developed epilepsy. As regards prognostic indicators, pattern B survivors and non-survivors differed especially by rates of basal EEG reactivity in the acute phase ($p=0.006$).

Conclusion: Although both anoxic insults and status epilepticus are considered risk factors for further seizures, epilepsy was a rare outcome in our population of aggressively treated post-anoxic patients.

Disclosure: Nothing to disclose

EPR3042

Epidemiology, clinical presentation, aetiology, neurophysiological findings, treatment and outcome of nonconvulsive status epilepticus in adults: a 7-year retrospective, hospital-based study

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Background and aims: Nonconvulsive Status Epilepticus (NCSE) comprises a group of heterogenous disorders with different presentations, prognosis and treatment. Clinical diagnosis remains challenging. The aim of this study was to characterise the epidemiology, presentation, aetiology, neurophysiological findings, treatment and outcome of NCSE.

Methods: A retrospective descriptive study was performed on patients diagnosed with NCSE between 2012 and 2019 in Hospital Beatriz Ângelo (Portugal). Patients diagnosed in intensive care were excluded. We applied the 2015 International League Against Epilepsy Definition and Classification of Status Epilepticus and 2015 modified Salzburg Consensus Criteria.

Results: Total number of patients was 67 (24-93 years; 39 female), 23 had previous history of epilepsy and 19 had dementia. 11 patients presented as NCSE with coma and 56 without coma (51 focal with impaired consciousness, 4 aphasic status and 1 aura continua). In 55 (82%) patients NCSE had an acute precipitating cause or was remotely provoked. EEG fulfilled direct diagnostic criteria (>2,5Hz epileptiform discharges) in 34% of patients and 66% required an additional minor criterion (51% with <2,5Hz epileptiform discharges and 15% with rhythmic delta/theta activity). In 46% of patients only one antiepileptic drug was necessary; coma was induced in 5 patients; 12 patients had sequelae and 14 patients died.

Conclusion: In our population, NCSE was frequently the first epileptic manifestation. Clinical features were diverse and often subtle and EEG was frequently essential to the diagnosis. In the majority of patients a cause was identified. Although its treatment was relatively easy, NCSE had a high morbidity-mortality rate.

Disclosure: Nothing to disclose

EPR3043

Seizure onset zone and seizure networks: Multiple SISCOm hyperperfusion areas and surgical outcome

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Background and aims: In presurgical evaluation of drug refractory epilepsy subtraction ictal SPECT co-registered with MRI (SISCOm) is a diagnostic tool applied in case of discordant results, non-lesional MRI or for planning of intracranial electrodes. We recently described high reliability with a high rate of overlapping results in multiple SISCOms. Here, we correlate surgical site and postsurgical outcome to multiple SISCOms hyperperfusion areas.

Methods: All patients undergoing resective epilepsy surgery were screened for the study. Those with additional results of multiple SISCOms were included. Results of multiple SISCOms including overlap and correlation maps as well as single SISCOm results were compared to surgical site, histology and postsurgical outcome according to Wieser classification.

Results: So far, 9 patients with multiple SISCOms underwent resective surgery. Site of surgery was concordant to overlapping SISCOm activation in 4 patients. In 2 patients only 1 of the SISCOms showed hyperperfusion areas concordant with site of surgery and in 3 patients hyperperfusion areas in SISCOm were discordant. Median postsurgical follow up at time of abstract submission was less than 1 year. Outcome data will be provided on the poster therefore.

Conclusion: In this preliminary analysis of multiple SISCOms hyperperfusion areas, less than 50% of cases showed correlation to site of surgery. Together with single SISCOm results, 66% were localizing. Seizure control over one year will be reported for the presentation. Multiple SISCOms analysis compared to surgical outcomes will contribute to the understanding of network effects responsible for good surgical outcomes.

Disclosure: Nothing to disclose

EPR3044

Treatment Guidelines for Five Rare Neurodevelopmental Disorders: A Targeted Literature Review

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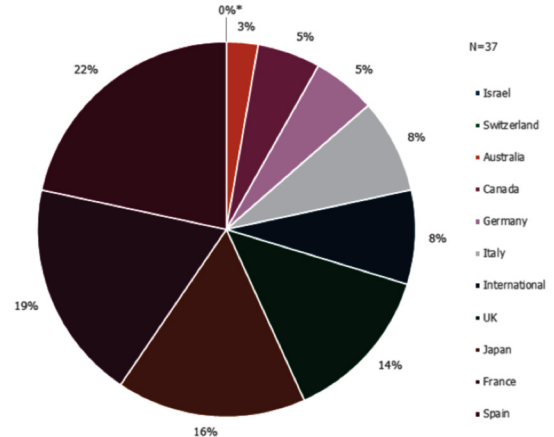
Background and aims: Lennox-Gastaut syndrome, Dravet syndrome and CDKL5 deficiency disorder (CDD) are rare epileptic disorders characterised by severe seizures in early childhood. Severe seizures are also common in the rare genetic conditions tuberous sclerosis complex and Rett syndrome. Due to seizure severity and unique treatment needs, high-quality treatment guidelines are required to optimise care. This review aimed to characterise methods of development, availability and content of treatment guidelines for these disorders.

Methods: A targeted literature review of treatment guidelines was conducted in February/March 2019 by manually searching online rare disease and guideline databases, and health technology assessment body/regulatory agency websites from target countries, defined using pre-specified eligibility criteria (Table 1; no date limit applied). Search terms, developed for each condition, were translated into appropriate languages to identify guidelines specifically for use in countries of interest. Guideline development methodology, geographical focus and treatment recommendations were extracted from guidelines using a pre-determined extraction grid.

	Inclusion criteria	Exclusion criteria
Population	Patients with the following epileptic conditions: <ul style="list-style-type: none"> • Dravet syndrome • Lennox-Gastaut syndrome • Tuberous sclerosis complex • Rett syndrome • CDKL5 deficiency disorder 	Conditions other than those listed
Intervention	Any	None
Outcomes	The document must have discussed the management of the conditions of interest in terms of pharmacological treatment pathways for routine seizure control	<ul style="list-style-type: none"> • Documents that did not discuss the management in terms of pharmacological treatment pathways • Emergency medication and surgical guidelines
Publication type	Guidelines or guidance documents	Publications other than guidelines
Other considerations	Specifically produced for use in: <ul style="list-style-type: none"> • EU5 countries (UK, Germany, Spain, Italy, France) • Japan • Australia • Switzerland • Israel • Canada International guidelines (i.e. guidelines produced for multiple countries that included or potentially included the countries of interest, or guidelines that did not specify which countries they pertained to)	Produced specifically for use in countries that were not of interest

Sources searched included: Guideline Central, National Organization for Rare Disorders, International League Against Epilepsy, Orphanet, Websites of National Health Technology Assessment (HTA) bodies for countries of interest were also searched.

Table 1. Eligibility criteria



*No treatment guidelines were identified for Israel and Switzerland. Two guidelines identified for Canada were developed specifically for the provinces of Ontario and British Columbia. Two Spanish guidelines were developed specifically for Andalusia. One Italian guideline was developed specifically for Tuscany.

Figure 1. Geographical focus of treatment guidelines

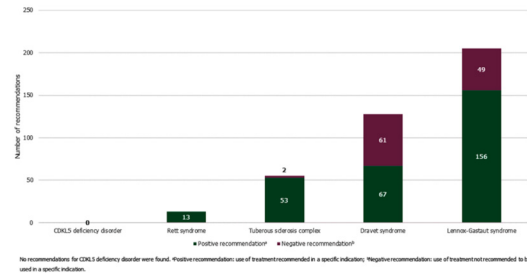


Figure 2. Positive and negative treatment recommendations by indication

Conclusion: There is a need for international collaboration to develop further high-quality and comprehensive consensus-based treatment guidance for these five neurodevelopmental disorders.

Disclosure: This study was funded by GW Pharmaceuticals; editorial services were provided by Costello Medical; R. Chin, has provided consultancy and speaker services, and has participated in events and studies, for GW Pharmaceuticals, Eisai, Zogenix and Neopharm Group; A. Mingorance, has provided consultancy to Encoded Therapeutics, F. Hoffmann-La Roche, GW Pharmaceuticals, Neurelis, Ovid Therapeutics, and Praxis Precision Medicines; I. Newell, employee of Costello Medical; B. Ruban-Fell, employee of Costello Medical; J. Evans, employee of Costello Medical; K. Vyas, employee of GW Pharmaceuticals; C. Nortvedt, employee of GW Pharmaceuticals; S. Amin, has no potential conflict of interest.

Headache and pain 5

EPR3045

Real-world evidence data characterizing the use of the monoclonal antibody Erenumab in daily clinical routine in Germany from the treating physician's perspective

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Background and aims: Erenumab, the first-in-class fully human monoclonal antibody against the CGRP receptor, has demonstrated efficacy and safety in clinical studies. This data collection now aims to collect first real-world data by characterizing the use of erenumab in clinical practice from the point of view of treating physicians in Germany.

Methods: Data from 70 headache centers across Germany has been collected by an online survey from July-December 2019. First, the use of erenumab is characterized from the treating physician's perspective with regards to therapy decision, patient profiles and quality of life of the patients. Second, each center documented 10-20 individual episodic and chronic migraine patients who had already completed 3 months of treatment with erenumab for their treatment effects and satisfaction with outcome.

Results: An interim analysis of 109 patients showed that on average there was a reduction of 8 migraine days under erenumab therapy. Physicians reported that 75% of their patients already had a response after the 1st injection. Based on observations during patient visits, physicians noted that 80% of the patients felt a reduction of intensity of migraine attacks and in general, they rated 80% of the patients as 'much improved' and 'very much improved' on the global impression score. The full data set including >700 erenumab patients will be available for EAN congress.

Conclusion: The TELESCOPE study provides real world data for erenumab in Germany regarding treatment routines, typical patient profiles and the effect on daily functioning and quality of life, both outcomes with great impact on migraine patients.

Disclosure: This study has been funded by Novartis Pharma GmbH.

EPR3046

Microstructural abnormalities precede cutaneous allodynia in patients with migraine.

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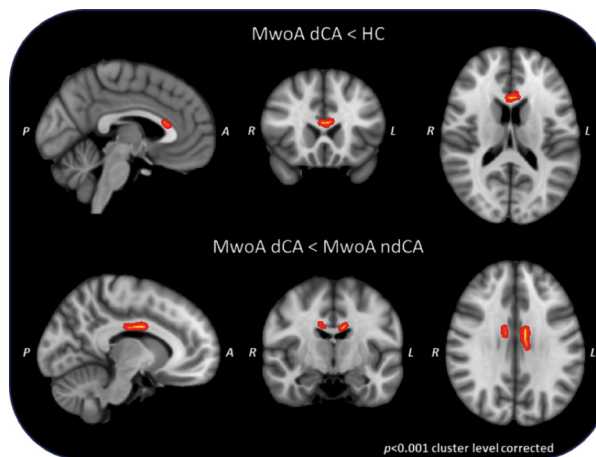
Background and aims: Cutaneous allodynia (CA) is complained by 2/3 of patients with migraine without aura (MwoA). CA is a clinical symptom of central nociceptive pathway sensitization and an independent predictor for migraine chronification.

We aim to investigate structural brain abnormalities could precede the development of CA in patients with MwoA.

Methods: 37 patients with MwoA were recruited and underwent MRI scan. All patients have been followed over a 3-years period and divided into 2 sub-groups based on CA development. In this way, 20 patients with MwoA who have developed CA (MwoA dCA) and 17 patients with MwoA who have not developed CA (MwoA ndCA) has been identified and compared with 19 sex- and age-matched healthy controls (HC).

Tract-based spatial statistics (TBSS) method was applied to investigate white matter alterations.

Results: TBSS analysis revealed a reduced fractional anisotropy (FA) of the corpus callosum (CC) in patients with MwoA dCA when compared with MwoA ndCA and HC. No significant correlations have been found between the TBSS changes observed in the CC and any clinical parameters of disease severity.



Reduced fractional anisotropy (FA) of the corpus callosum (CC) in patients with MwoA dCA when compared with both MwoA ndCA and HC

Conclusion: Our data showed microstructural changes in patients with MwoA. FA abnormalities are more evident in patients with MwoA dCA when compared with patients with MwoA ndCA. Reduced FA of CC has been previously reported in patients with MwoA with comorbidities known to be related to migraine chronification (depression and medication overuse headache). Based on this observations we speculate that our findings might represent a negative prognostic biomarker able to identify phenotype of patients more prone to migraine chronification.

Disclosure: Nothing to disclose

EPR3047

Changes in Acute Migraine-Specific Medications after Initiating Erenumab: Results from a Real-World Retrospective Cohort Study in the United States

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Background and aims: Overuse of acute migraine-specific medications (AMSMs) can potentially complicate migraine management. Erenumab, a calcitonin gene-related peptide antagonist, significantly reduces the use of AMSMs in migraine patients. We aimed to examine the real-world changes in AMSMs use among patients prescribed erenumab in the United States.

Methods: We conducted a retrospective cohort study using data from IQVIA's open source pharmacy and medical claims databases. Patients aged 18 years or older were included if they had completed an adequate trial of erenumab (≥ 3 claims) from 1 May 2018 to 30 April 2019 (1st claim was the index date) with data continuity in the 12 months prior to and ≥ 6 months following the index date. Post-index change in AMSMs use (triptans and ergotamine derivatives used both pre-and-post-index) included discontinuation (no refills for ≥ 60 days after the last post-index fill) and change (post-pre index) in units (tablets/pills) filled.

Results: We identified 43,185 patients who received ≥ 3 doses of erenumab (female, 85.8%; average [standard deviation (SD)] age, 47 [12.9] years). After initiation of erenumab, AMSMs were discontinued in 36.8% (8556/23,222) patients with both pre- and post-index use (triptans, 35.9% [8021/22,338]; ergotamines, 60.5% [535/884]). AMSMs units changed in 80.0% (18,571/23,222) patients; for triptans, in 80.7% (18,034/22,338), and in 60.7% (537/884) for ergotamines, with an overall mean [SD] change of -1.2 [6.6] units for triptans and -0.4 [6.9] units for ergotamines

Conclusion: In this US-focused real-world study, a proportion of patients completing an adequate trial of erenumab discontinued and/or reduced consumption of their AMSMs.

Disclosure: This study was funded by Amgen Inc., Thousand Oaks, CA, USA. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance outstanding.

EPR3048

Sustained Benefits of OnabotulinumtoxinA Treatment in Chronic Migraine: Results from a PREEMPT Pooled Analysis

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Background and aims: Determine proportion of individuals with chronic migraine (CM) that achieved <15 monthly headache days (MHDs) following continuous onabotulinumtoxinA treatment.

Methods: Observed data from PREEMPT (24-week, 2 onabotulinumtoxinA cycle, randomized, double-blind placebo-controlled phase, followed by 32-week, 3 onabotulinumtoxinA cycle, open-label phase) were pooled for analysis. To assess MHD reductions (<15), several time periods were analyzed: 1) end of double-blind (21-24 weeks) or open-label (53-56 weeks); 2) any 3 consecutive months of double-blind (1-24 weeks) or entire study (1-56 weeks); and 3) all months end of double-blind (13-24 weeks; termed 'treatment-controlled CM') or entire open-label (25-56 weeks; termed 'sustained treatment-controlled CM'). Proportion of participants (double-blind: onabotulinumtoxinA vs. placebo; open-label: onabotulinumtoxinA only) achieving each classification, with mean MHDs, presented as exploratory post-hoc analyses with Bonferroni correction (significance $p \leq 0.008$).

Results: 1384 participants randomized to onabotulinumtoxinA (n=688) or placebo (n=696) in double-blind; most continued to open-label (n=607 onabotulinumtoxinA/onabotulinumtoxinA, n=629 placebo/onabotulinumtoxinA). A higher proportion of onabotulinumtoxinA-treated individuals compared to placebo achieved <15 MHD and had lower mean MHDs[SD] last month of double-blind (67.4% [n=363/539] vs. 58.0% [n=322/555], $p=0.001$; 6.9 [4.0] vs. 7.7[4.1], $p=0.021$, respectively), any 3 consecutive months of double-blind (61.2% [n=359/587] vs. 52.3% [n=315/602], $p=0.002$; 8.3 [3.5] vs. 8.9 [3.5], $p=0.022$), and/or treatment-controlled CM end of double-blind (56.3% [n=334/593] vs. 48.3% [n=290/600], $p=0.006$; 6.5 [3.6] vs. 7.2 [3.4], $p=0.007$). In onabotulinumtoxinA-treated, 79.8% (n=319/400) achieved <15 MHD last month of open-label (mean MHDs[SD]: 4.9 [4.1]), 73.3% (n=440/600) any 3 consecutive months of entire study (7.7 [3.9]), and/or 59.9% (n=333/556) sustained treatment-controlled CM for entire open-label (4.5[3.2]).

Conclusion: In PREEMPT, a high proportion of onabotulinumtoxinA-treated individuals achieved sustained treatment-controlled CM for the entire observed open-label phase.

Disclosure: This study was sponsored by Allergan plc.

EPR3049

Cognitive networks disarrangement in patients with migraine predicts cutaneous allodynia.

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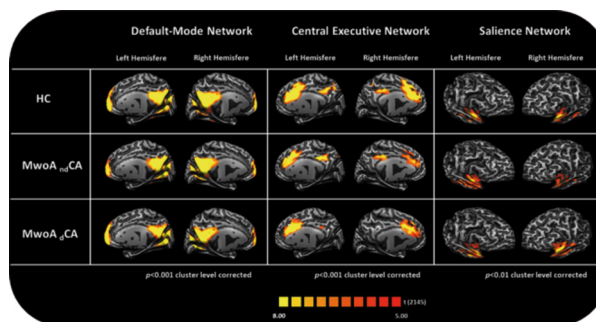
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Background and aims: 2/3 of patients with migraine without aura (MwoA) complain cutaneous allodynia (CA) during the attacks. CA is a clinical sign of central nociceptive pathway sensitization and independent predictor for migraine chronification. We aim to investigate whether abnormalities of the functional connectivity (FC) of the brain cognitive networks (default mode network (DMN) and the central executive network (CEN)) could predict the development of CA in patients with MwoA.

Methods: 37 patients with MwoA were recruited and underwent fMRI. All these patients have been followed over a 3 years' period and then divided into 2 groups based on whether or not CA was developed. Then, we compared FC within the cognitive network in 20 patients with MwoA who have developed CA (MwoA dCA) versus 17 patients with MwoA who have not developed CA (MwoA ndCA) and 19 sex- and healthy controls (HC).

Results: We observed a significantly reduced FC of both DMN (within anterior cingulate cortex (ACC), medial frontal gyrus (MFG) and insula) and CEN (posterior cingulate cortex (PCC)/precuneus) and in patients with MwoA dCA when compared with both patients with MwoA ndCA and HC.



Conclusion: The reduced FC of PCC/precuneus (key hub of DMN involved in multisensory integration) could subtend an abnormal integration of inputs from different sensory modalities and, subsequently, the development of CA. The reduced FC of ACC and MFG (central hubs of CEN involved in pain perception and in executive functions) could reflect a subclinical impairment of complex executive functions making these patients more prone to the development of migraine attacks.

Disclosure: Nothing to disclose

EPR3051

Effects of galcanezumab on health-related quality of life in patients with treatment-resistant migraine: Results from CONQUER study

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Background and aims: The CONQUER study assessed health outcome measures with galcanezumab in patients with treatment-resistant episodic (EM) or chronic migraine (CM). Treatment resistance was defined as previous failure with 2 to 4 standard-of-care migraine preventive medication categories in the past 10 years due to inadequate efficacy and/or safety/tolerability reasons.

Methods: In the study, patients with treatment-resistant migraine (EM or CM) were randomized 1:1 to receive galcanezumab (GMB) 120mg/month (with 240mg loading dose) or placebo (PBO) during a 3-month double-blind period. Migraine Disability Assessment (MIDAS) and European Quality of Life 5-Dimensions 5-Levels (EQ-5D-5L) scores were collected at baseline and Month 3. Migraine-Specific Quality of Life Questionnaire v2.1 (MSQ) was collected at baseline and monthly. Treatment comparisons were done at Month 3 using mixed model repeated measures (in case of repeated measures) and analysis of covariance models (single post-baseline measure).

Results: Baseline values for all scores were balanced between PBO and GMB groups (Table 1). In the intent-to-treat population (N=462) and in subpopulations with EM (N=269) and CM (N=193), there were significantly greater mean improvements from baseline with GMB versus PBO for MSQ total and all domain scores (all $p < 0.0001$), and MIDAS total scores (intent-to-treat [$p < 0.0001$], EM [$p = 0.0002$], CM [$p = 0.0142$]) (Table 2). Mean improvement with GMB versus PBO on EQ-5D-5L visual analog scale was significant ($p = 0.03$) in the intent-to-treat population (Table 2).

Table 1: Baseline scores in different patient populations

	Intent-to-treat population ^a		EM subpopulation ^b		CM subpopulation ^c	
	PBO	GMB	PBO	GMB	PBO	GMB
Age, mean (SD)	45.67 (12.33)	45.87 (11.34)	46.28 (11.75)	45.91 (11.21)	44.84 (13.09)	45.81 (11.60)
Female, n (%)	202 (87.83)	195 (84.05)	117 (88.64)	112 (81.75)	85 (86.73)	83 (87.37)
Race – White, n (%)	182 (81.61)	183 (81.70)	115 (88.46)	118 (88.72)	67 (72.04)	65 (71.43)
Migraine headache days/month, mean (SD)	13.01 (5.73)	13.44 (6.08)	9.20 (2.65)	9.47 (2.98)	18.14 (4.67)	19.17 (4.68)
Duration of migraine illness, years, mean (SD)	23.76 (13.86)	22.73 (13.24)	22.90 (13.05)	21.72 (12.72)	24.92 (14.86)	24.18 (13.88)
Scores, Mean (SD)						
MSQ role function-restrictive	43.95 (18.49)	45.81 (16.00)	46.54 (17.14)	48.55 (14.72)	40.47 (19.73)	41.86 (17.01)
MSQ role function-preventive	63.04 (19.64)	63.84 (19.12)	64.66 (18.74)	64.74 (19.63)	60.87 (20.68)	62.53 (18.38)
MSQ emotional function	51.91 (26.73)	54.80 (24.59)	57.42 (25.10)	59.51 (22.86)	44.49 (27.17)	48.00 (25.52)
MSQ total score	51.11 (18.44)	52.89 (16.27)	54.05 (17.12)	55.53 (15.61)	47.16 (19.48)	49.08 (16.51)
MIDAS total score	50.96 (45.50)	50.90 (45.96)	37.14 (26.17)	41.31 (34.31)	69.56 (57.90)	64.73 (56.20)
EQ-5D-5L VAS score	73.15 (18.23)	72.65 (18.70)	76.92 (16.91)	75.34 (17.55)	68.07 (18.78)	68.77 (19.70)

^aAll patients who were randomized and received at least 1 dose of investigational product; ^bAll patients with EM who were randomized and received at least 1 dose of investigational product; ^cAll patients with CM who were randomized and received at least 1 dose of investigational product

CM=chronic migraine; EM=episodic migraine; EQ-5D-5L=European Quality of Life 5-Dimensions 5-Levels; GMB=galcanezumab; MIDAS=Migraine Disability Assessment; MSQ=Migraine-Specific Quality of Life Questionnaire v2.1; PBO=placebo; SD=standard deviation; VAS=Visual Analog Scale

Baseline scores in different patient populations

Table 2: Mean change from baseline at Month 3 in health-related quality of life measures in different patient populations

Scores, LS mean change (SE)		Intent-to-treat population ^a		EM subpopulation ^b		CM subpopulation ^c	
		PBO	GMB	PBO	GMB	PBO	GMB
MSQ	Role function-restrictive	10.68 (1.34)	23.21 [†] (1.35)	11.88 (1.80)	23.39 [†] (1.79)	6.71 (1.99)	20.61 [†] (2.05)
	Role function-preventive	7.68 (1.19)	17.53 [†] (1.20)	8.94 (1.56)	18.44 [†] (1.55)	5.37 (1.83)	15.27 [†] (1.88)
	Emotional function	12.02 (1.60)	24.02 [†] (1.61)	11.58 (2.08)	22.52 [†] (2.06)	11.09 (2.57)	24.38 [†] (2.63)
	Total score	10.08 (1.25)	21.67 [†] (1.26)	10.91 (1.67)	21.70 [†] (1.66)	7.67 (1.86)	20.17 [†] (1.91)
MIDAS	Total	-3.30 (3.28)	-21.10 [†] (3.32)	-2.58 (3.68)	-18.96 ^{**} (3.63)	-1.68 (6.19)	-20.27 [*] (6.40)
EQ-5D-5L	VAS score	-0.09 (1.29)	3.38 [*] (1.31)	-0.83 (1.63)	2.90 (1.63)	NA	NA

[†] $p < 0.05$, ^{**} $p < 0.01$, ^{††} $p < 0.0001$ versus placebo

^aAll patients who were randomized and received at least 1 dose of investigational product; ^bAll patients with episodic migraine who were randomized and received at least 1 dose of investigational product; ^cAll patients with chronic migraine who were randomized and received at least 1 dose of investigational product

CM=chronic migraine; EM=episodic migraine; EQ-5D-5L=European Quality of Life 5-Dimensions 5-Levels; GMB=galcanezumab; LS=least squares; MIDAS=Migraine Disability Assessment; MSQ=Migraine-Specific Quality of Life Questionnaire v2.1; NA=not available; PBO=placebo; SE=standard error; VAS=Visual Analog Scale

Mean change from baseline at Month 3 in health-related quality of life measures in different patient populations

Conclusion: Patients with treatment-resistant migraine treated with GMB reported improvements in daily functioning and patient perception of health state, and decreased disability compared to PBO.

Disclosure: This study was sponsored and funded by Eli Lilly and Company

EPR3052

Benefit of Migraine Prevention with Erenumab in Patients Receiving Background Standard-of-Care Acute Treatment

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Background and aims: Erenumab is approved for migraine prevention in adults. Its benefit in patients using acute migraine-specific medications (AMSMs, e.g. triptans) has not been established. Here we assess the effect of erenumab (erenumab-aooe in the US) on AMSM use in patients with episodic (EM) and chronic migraine (CM).

Methods: A post hoc analysis of a subgroup with ≥4 days of AMSM use during the 4-week baseline period of 2 pivotal trials in EM (STRIVE, NCT02456740) and CM (NCT02066415) compared preventive treatment (erenumab 70 and 140mg) plus AMSM use with AMSM use alone (placebo arm); all patients continued AMSMs as needed. Change from baseline in monthly migraine days (MMD), monthly AMSM usage days, Headache Impact Test-6 (HIT-6) and Migraine Disability Assessment (MIDAS) scores (EM, averaged over Months 4–6; CM, Month 3) were assessed.

Results: The analysis included 428 EM (erenumab 70mg, n=136; erenumab 140mg, n=144; AMSM use alone, n=148) and 457 CM (n=122; n=135; n=200, respectively) patients. Erenumab plus AMSMs significantly reduced MMD and monthly AMSM use days compared with AMSM use alone in EM and CM (Table). HIT-6 and MIDAS scores were also significantly reduced.

Outcome measures	Episodic migraine		Chronic migraine	
	Erenumab 70 mg + AMSM n=136	Erenumab 140 mg + AMSM n=144	Erenumab 70 mg + AMSM n=122	Erenumab 140 mg + AMSM n=135
MMD*	-2.1 [-2.8, -1.4]	-2.9 [-3.6, -2.2]	-2.2 [-3.4, -0.9]	-3.3 [-4.5, -2.1]
Monthly AMSM days*	-1.9 [-2.5, -1.3]	-2.6 [-3.2, -2.0]	-2.5 [-3.6, -1.4]	-3.6 [-4.7, -2.5]

Data indicates difference in LSM (95% CI). *p<0.001
MMD, Monthly migraine days; AMSM, Acute migraine-specific medication

Benefit of erenumab in patients using acute migraine-specific medications

Conclusion: This study demonstrated that preventive treatment with erenumab plus AMSMs as needed significantly reduced MMD, AMSM use, and disability compared with AMSMs alone. These findings suggest a clinical benefit of effective prevention with erenumab over acute treatment alone in patients using AMSMs at baseline.

Disclosure: Amgen Inc., Thousand Oaks, CA, USA, funded this study. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance outstanding.

EPR3053

Biomarker for fibromyalgia – are we (already) there?

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Background and aims: Evidence is increasing for peripheral mechanisms underlying pain in fibromyalgia syndrome (FMS) including small fiber pathology and systemic immune alterations.

Methods: We investigated 156 patients with FMS and applied 5 clinical small fiber tests including skin biopsy, quantitative sensory testing, corneal confocal microscopy, pain-related evoked potentials, and microneurography. We further withdrew blood and generated keratinocyte cultures from skin punch biopsies to assess potential systemic and local microRNA signatures.

Results: We found small fiber pathology in a subgroup of FMS patients including morphological, functional, and electrophysiological properties. In 63% of patients, skin innervation was abnormal and associated with disease severity. In blood and keratinocyte miRNA analysis we found 69 versus 41 deregulated microRNAs. We identified fatty acid synthesis and factor forkhead box protein O1 (FOXO1) (blood) and extracellular matrix receptor (keratinocytes) signaling as potential key pathways. miR-576-5p was validated as a distinguishing microRNA between FMS and healthy controls (p<0.001) and FMS and patients with depression with pain as disease controls (p<0.01).

Conclusion: Our data further support small nerve fiber impairment in FMS subgroups as potential peripheral contributor to FMS pain, and that the extent of small fiber impairment may reflect FMS severity. We further provide hints for systemic and local miRNA alterations in FMS that may be instrumental as diagnostic signatures and for targeted treatment.

Disclosure: Nothing to disclose

EPR3054

Pharmacokinetics, safety and tolerability of lasmiditan in healthy elderly subjects

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Background and aims: Lasmiditan is a 5-hydroxytryptamine 1F receptor agonist approved for the acute treatment of migraine in adults. Unlike triptans, it lacks coronary vasoconstrictor activity, and can be used in patients with cardiovascular disease. We compared the pharmacokinetics, safety and tolerability of lasmiditan in elderly and young healthy subjects.

Methods: 2 randomized, double-blind, crossover studies were conducted. In the 1st, elderly subjects (≥ 65 years) received lasmiditan 200mg and placebo; young subjects aged 18-45 years received open-label lasmiditan 200mg. Plasma samples were taken for pharmacokinetic analysis. As unexpected BP elevations occurred in elderly subjects, a non-inferiority study was conducted to assess BP using ambulatory monitoring. Elderly subjects received lasmiditan 100 and 200mg, and placebo. Non-inferiority (margin 10mmHg) for baseline subtracted peak hourly mean systolic BP (SBP) for lasmiditan versus placebo was determined.

Results: Study 1: maximum lasmiditan concentrations and time to maximum concentrations were not significantly different between elderly (n=18) and young (n=17) subjects. The geometric least squares mean ratio for lasmiditan area under the concentration versus time curve from zero to infinity (elderly:young) was 1.26 (90% confidence interval, 1.03-1.55). Study 2 (n=36): the difference in peak hourly mean SBP change for both lasmiditan doses versus placebo was <10 mmHg at all time points ($p < 0.0001$ for all comparisons). Lasmiditan was generally well tolerated.

Conclusion: Exposure to lasmiditan 200mg was 26% higher in elderly than young subjects but this was clinically irrelevant. Lasmiditan was non-inferior to placebo regarding elevation of BP in elderly subjects. Therefore, lasmiditan dose adjustment is not necessary in the elderly.

Disclosure: All authors are full-time employees and minor shareholders of Eli Lilly and Company.

Infectious diseases 2

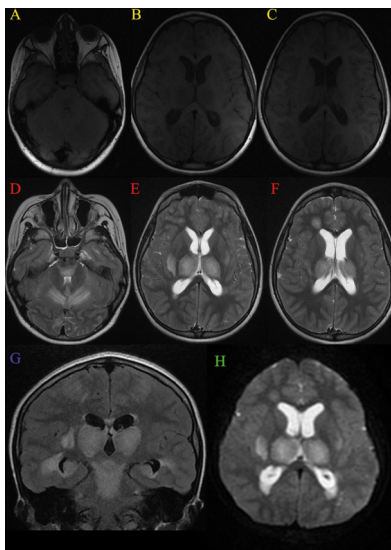
EPR3055

Acute necrotizing encephalopathy in childhood - Case seriesN. Elsaid¹, A. Saied¹, Z. Ahmed², F. Sherif²¹Neurology, Mansoura University, Faculty of Medicine, Mansoura, Egypt, ²Radiology, Mansoura University, Faculty of Medicine, Mansoura, Egypt

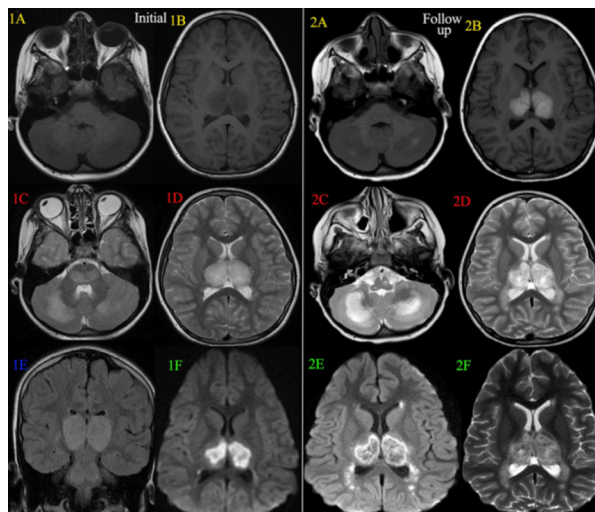
Background and aims: Acute necrotizing encephalopathy (ANE) is an under-recognized clinic-radiologic disorder characterized by rapid alteration of consciousness, seizures and nonspecific symptoms following or accompanying respiratory or gastrointestinal infection and high fever with radiological symmetric lesions in the magnetic resonance imaging involving the thalami, brainstem, cerebellum, and white matter. This disease has global distribution but more commonly seen in immune-competent East Asian infants and children. The condition carries a poor prognosis with high morbidity and mortality rates.

Methods: Case presentation of three recently encountered cases of ANE. In an attempt to increase the recognition of ANE, we present the clinical, laboratory and MR imaging findings of these three patients.

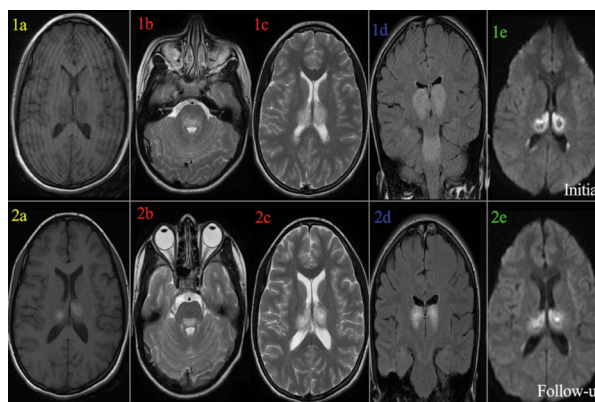
Results: Three children recently presented with rapid neurological deterioration and fever after prodromal respiratory symptoms. Magnetic resonance imaging examination performed showed symmetric lesions involving the thalami and brainstem. Based on the temporal evolution of the clinical symptoms and MRI findings, the diagnosis of ANE was considered. Also, they carried a relatively bad prognosis based on the MR prognostic score and the ANE severity scale. Unfortunately, 2 cases died and the third was discharged in a vegetative state.



Case 1 MRI showing bilateral lesions involving the thalami, dorsal pons, midbrain, right basal ganglia and right frontal lobe; hypo-intense on T1(A-C), hyper-intense in T2 (D-F) and FLAIR coronal view (G), with evidence of restricted diffusion in DWI (H)



Case 2 initial(1) & 10 d follow up(2) MRI show low SI in both thalami in T1(1a,1b) with follow up evidence of hemorrhage(2a,2b). Initial(1c,1d) & follow up(2c,2d) T2 show high SI in the thalami, cerebelli & brain stem, same as in FLAIR(1e). Initial (1f) & follow up (2e) DWI show trilaminar appearance, apparent also in ADC(2f)



Case 3 initial(1) & 2 w follow up(2) MRI show low SI in both thalami in T1(1a) with follow up evidence of hemorrhage(2a). Initial(1b,1c) & follow up(2b,2c) T2 show high SI in the thalami and brain stem, same as in FLAIR(1d,2d). Initial (1e) & follow up (2e) DWI show peripheral concentric high SI & central low SI.

Conclusion: In conclusion, although ANE is a rare disease, it is a devastating disease that should not be underestimated.

Disclosure: Nothing to disclose

EPR3056

Inclusion of mechanical ventilation in severity staging of tuberculous meningitis improves outcome prediction

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Background and aims: Tuberculous meningitis (TBM) patients in any stage of British Medical Research Council (BMRC) scale if need mechanical ventilation (MV) are likely to have poor outcome. We report usefulness of BMRC, BMRC–MV and BMRC–HC (hydrocephalus) staging, and HAMSI scoring in predicting outcome of TBM
Methods: 197 TBM patients were retrospectively analyzed from a TBM registry of a teaching institute in India. The severity of meningitis was categorized using BMRC (stage I–III), BMRC–MV [I–IV (MV patients grouped as stage IV)] and BMRC–HC [I–IV (BMRC stage III with hydrocephalus grouped as stage IV)]. HAMSI scoring was categorized as <6 and >6. Outcome was defined at 6 months using modified Rankin Scale (mRS) as death, poor (mRS score >2) or good (mRS<2).

Results: 49 (25%) patients died. BMRC–MV stage IV had the highest predictive value for defining death with a sensitivity of 88% and specificity of 86%. 121 out of 158 (76.6%) surviving patients had good outcome at 6 months. BMRC–MV stage I–III had the highest predictive value for defining good outcome with a sensitivity of 93% and specificity of 61%.

Conclusion: In TBM, BMRC–MV staging has the best predictive value for defining death and disability

Disclosure: Nothing to disclose

EPR3057

Clinical characteristics, prognostic factors, and causes of death in adults with community-acquired pneumococcal meningitis

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Background and aims: We evaluated the clinical characteristics, prognostic factors, and cause of death in adult pneumococcal meningitis.

Methods: We included adults (≥16 years) with community-acquired pneumococcal meningitis from 2 large nationwide prospective cohort studies in the Netherlands (1998–2002, 2006–2018). Deaths were categorized independently by 2 physicians as neurologic or systemic. Missing data were imputed to perform a multivariable logistic regression analysis.

Results: A total of 1816 episodes in 1783 patients were included (median age 62, IQR 51–70). 11 of 336 (3%) patients between 1998–2002 and 1177 of 1437 patients (82%) between 2006–2018 received adjunctive dexamethasone. 363 patients (20%) died, 192 due to neurologic cause (54%; e.g. brain herniation (n=78)) and 166 due to systemic cause (46%; e.g. cardiorespiratory failure (n=72)). In patients ≥75 years old, mortality rate was 43%, and more commonly due to systemic causes compared to younger patients (63% vs. 39%, p<0.001). Dexamethasone treatment was associated with a lower rate of focal neurological abnormalities (19% vs. 25%, p=0.006), cardiorespiratory failure (28% vs. 41%, p<0.001), and mortality (30% vs. 15%, p<0.001). Dexamethasone decreased both neurologic (15% vs. 9%) and systemic causes of death (15% vs. 6%). Age ≥75 years, immunocompromising condition, higher heart rate, lower Glasgow Coma Scale score, cranial nerve palsy, CSF white cells <1,000/μL, CSF:blood glucose ratio <0.23, C-reactive protein >200mg/L, and thrombocytes <75,000units/L were associated with mortality in a multivariable model.

Conclusion: Pneumococcal meningitis is still associated with high mortality and morbidity rates. Death due to systemic causes increased with age.

Disclosure: Nothing to disclose

EPR3058

Withdrawn

EPR3059

Chorea and pancerebellar syndrome caused by cerebrospinal fluid HIV escape

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Background and aims: HIV neurotropism is one of the main problems associated to HIV infection. Central nervous system (CNS) is an ideal reservoir. Despite antiretroviral treatment, there could be direct lesion in the CNS caused by the virus, due to cerebrospinal fluid (CSF) HIV escape phenomena, which can be defined by duplication of the viral load in CSF with blood viral load of 50-500/ml.

Methods: Case report.

Results: 51-year-old man, HIV positive discovered in 2008. The patient started antiretroviral therapy (ART) with emtricitabine-tenofovir and raltegravir in 2009. Through years of consultations, no viral suppression was achieved (mean blood viral load of 200/ml), partially related to suboptimal therapeutic adherence. He was evaluated in early 2019 for chorea and pancerebellar syndrome, with mnemonic and behavioral impairment with 5 months progression. MRI revealed diffuse leukoencephalopathy. CSF analysis showed 12 cells (90% mononuclear) and viral load of 1600/ml (blood viral load of 228/mL) suggestive of CSF HIV escape phenomena. Other causes for neurologic symptoms were excluded. Test for antiretroviral therapy (ART) showed moderate to high levels of resistance. Therapeutics were changed for darunavir/cobicistat + dolutegravir. For symptomatic control, he also started a low dosage of haloperidol. Progressive clinical improvement was noticed after 2 weeks.

Conclusion: We described a rare case of chorea and cerebellar syndrome secondary to HIV escape in CSF. Here we can see two causes that contributed to the escape phenomena: non-adherence to therapy and resistance to ART.

Disclosure: Nothing to disclose

EPR3060

A systematic literature review to identify the named outcome measures used in the long-term follow up of encephalitis

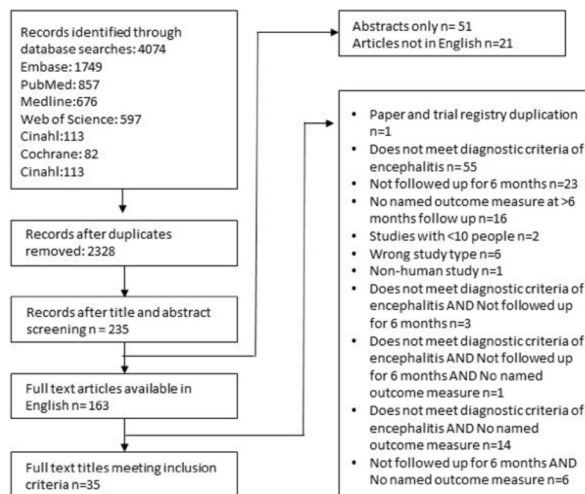
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Background and aims: Encephalitis is inflammation of the brain caused by infection or autoimmunity, from which most patients don't fully recover. Drawing conclusions in this field has been challenging due to the breadth of outcome measures used, which creates heterogeneous data across studies. This review details the outcome measures used in studying the long-term outcomes of encephalitis and will determine if these align with those that are important to patients.

Methods: A systematic literature review has been performed using Cochrane Library, Web of Science, Embase, PubMed, MEDLINE and CINAHL in June 2019. A single reviewer screened titles, abstracts and determined if shortlisted full-text articles met the inclusion criteria. Key data was collected from the included papers which has been included in a narrative summary.

Results: A total of 35 papers were included, in which 37 named outcome measures were assessed in a total of 3,133 patients. These broadly fall into five categories: physical, cognitive, mood, quality of life, and functional outcomes. The outcome measures used on most patients were Modified Rankin Score (mRS), Glasgow Outcome Score (GOS), Barthel index and Euro-QoL-5D, which were all used on over 1,000 patients each.



Prisma flow chart outlining the selection process for included articles.

Conclusion: Many variable outcome measures are used in encephalitis research and many assess narrow problems.

Excluding the Liverpool Outcome Score, the outcome measures used are not validated in encephalitis. Future research should focus on validating the outcome measures in use and developing a core-outcomes set or a composite outcome measure that assesses all important outcome domains to both clinicians and patients.

Disclosure: Nothing to disclose

EPR3061

Cerebrospinal fluid culture yield and timing of antibiotic treatment in patients with acute community-acquired bacterial meningitis

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Background and aims: Bacterial meningitis is a severe disease which requires timely diagnosis and treatment. We evaluated the association between timing of lumbar puncture and antibiotic treatment with respect to diagnostic yield in patients with community-acquired bacterial meningitis.

Methods: Adult patients (≥ 16 years) presenting to the emergency department who underwent a lumbar puncture for the suspicion of a central nervous system infection, included in 2 prospective cohort studies (2012-2015 single center study; 2017-2019 multi-center study), were analyzed. Bacterial meningitis was diagnosed based on microbiological evidence, or scored independently by 2 neurologists based on available clinical data.

Results: Of the 554 episodes included, 54 (10%) were clinically diagnosed with bacterial meningitis of whom 41 (76%) had an individual predictor of bacterial meningitis. Cerebrospinal fluid (CSF) culture remained negative in 33 episodes (61%). CSF PCR identified the pathogen in 5 additional episodes and blood culture in an additional 17 episodes, resulting in 17 (32%) bacterial meningitis patients without proven causative pathogen. A greater amount of time between the start of antibiotic treatment and lumbar puncture was associated with higher rate of negative CSF culture ($p=0.007$). CSF culture was positive in 89% if the lumbar puncture was performed within 1 hour, in 40% if performed between 1-6 hours, and in 33% if performed after 6 hours (tertiles, $p=0.034$).

Conclusion: Timing of antibiotic treatment prior to lumbar puncture is associated with the yield of CSF cultures. Results stress the importance of early lumbar puncture in patients with suspected central nervous system infection.

Disclosure: Nothing to disclose

Movement disorders 5

EPR3062

Clinical phenotyping and ethnicity: observational study of White and Asian population in the United Kingdom

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Background and aims: Ethnicity may be associated with different presentation of Parkinson's disease (PD) related to genetic, epigenetic, environmental, cultural and socioeconomic factors.

Methods: Therefore, in this cross-sectional multicenter study across London from a multi-ethnic PD population clinical profiles between Asian and White PD Patients were explored using a range of PD stage (Hoehn and Yahr, HY), motor function (Scopa-Motor), Nonmotor symptoms Scale (NMSS), and relevant biomarkers (MRI and DaTSCAN imaging).

Results: In total 146 White (58.9% males, age 67.2±12.7 years) and 54 Asian (66.7% males, age 66.4±11.4 years) patients were evaluated. There were no significant differences between the White and Asian population in terms of age, gender, disease duration, age at PD onset, Hoehn and Yahr and Levodopa Equivalent Daily Dose. Asians however had higher comorbidity (in particular arterial hypertension (46.3% versus 27.6%, $p < 0.05$) as well as greater motor impairment (SCOPA-Motor Scale Total 16.5±9.1 versus 21.0±11.4, $p = 0.008$) and worse overall non-motor burden on the NMSS scale (36.4±29.5 versus 62.0±52.8; $p = 0.016$). There were no differences in the burden of white matter changes on MRI scans. Dopamine receptor presynaptic imaging data suggested equivalent reduction on DaTSCAN uptake in the two groups.

Conclusion: Our data suggest higher disease burden, both from a motor and non-motor point of view in Asian patients with PD, and higher rates of comorbidity, which underlie these differences at least partly. The findings lay out grounds for a large-scale multicentre cohort study with a focus on specific biomarkers and ethnicity.

Disclosure: Parkinson's UK grant Kirby Laing grant

EPR3063

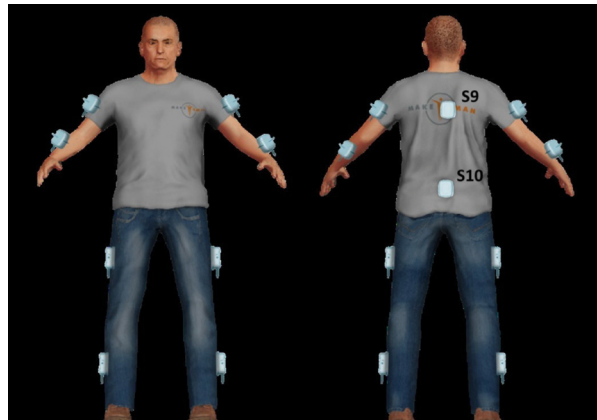
Transcranial direct current stimulation (tDCS) on PD patients with freezing of gait: a kinematic evaluation

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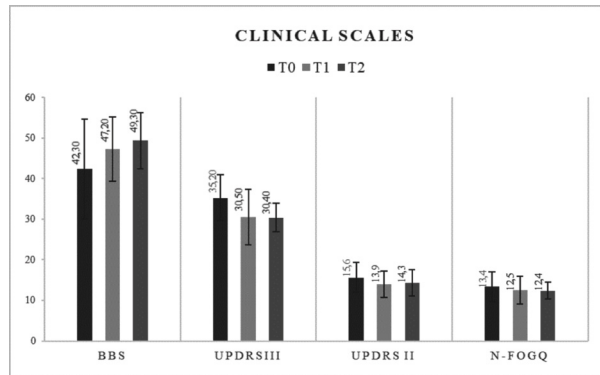
Background and aims: Freezing of gait (FOG) is one of the most disabling complication of Parkinson's disease (PD), being not only a motor problem but also arising from deficit in executive functions. Aim of our study is to evaluate the effectiveness of anodal tDCS of the dorsolateral prefrontal cortex (DLPFC) in PD patients presenting FOG. To avoid the rater score variability and the underrating of motor performance, we used Technology-based objective measures to evaluate the treatment response.

Methods: 10 patients underwent 20 minutes of electric current of 2mA on 10 separate visits. Unified Parkinson's Disease Rating Scale pars 2-3 (UPDRSII-III), Hoehn and Yahr (H&Y), New Freezing of Gait Questionnaire (N-FOGQ), Berg Balance Scale (BBS) were performed at baseline (T0), after last stimulation (T1) and at one-month follow-up (T2). Moreover, kinematic parameters of gait abnormalities were measured by means of wearable devices (MOVIT G1®) in order to obtain an objective evaluation.



Wearable devices's position

Results: Our preliminary results demonstrate a significant clinical improvement in the disturbance of balance and the severity of FOG episodes. The kinematic evaluation shows an improvement in parameters that measures number and duration of steps and velocity of legs and thighs. Furthermore, a high correlation is found between the amelioration of clinical and kinematic features.



Improvement in clinical scales

Kinematic features	Clinical item	ρ	p-value
TUG Test duration	UPDRSIII - Gait	0.52953068	0.00261942
TUG Walk duration	UPDRSIII - Gait	0.54234132	0.00196099
TUG Turn duration	UPDRSIII - Gait	0.51061797	0.00393683
TUG Average velocity thigh	UPDRSIII - Gait	-0.4247443	0.01930551
TUG Average velocity leg	UPDRSIII - Gait	-0.40529134	0.02629177
TUG Average velocity turn	UPDRSIII - Gait	-0.62640631	0.00021293
NW Step velocity	UPDRSIII - Gait	-0.38605316	0.03510726

Correlation between kinematic and clinical features (Spearman test)

Conclusion: Coherently with the hypothesis that cognitive executive circuit plays a role in FOG, we may consider anodal tDCS of the DLPFC as a potential adjunctive therapy in PD patients with FOG and disturbance of balance. Moreover, wearable devices can objectively quantifying a possible beneficial effect of a therapeutic intervention.

Disclosure: Nothing to disclose

EPR3064

The role of the London Handicap Scale in the evaluation of Parkinson's Disease patients before and after DBS-STN

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Background and aims: The London Handicap Scale (LHS) is a good measure of perceived-health status in PD. Handicap increases with disease duration and severity, and the identification of the affected subdomains at each disease stage may allow to adapt therapeutic interventions accordingly. Our aim was to characterize the handicap after 4.8years of DBS-STN.

Methods: 33 PD patients submitted to DBS-STN were evaluated after a mean of 4.8 years of surgery in 4 conditions (stimOFF/medOFF, stimON/medOFF, stimOFF/medON, stimON/medON), using MDS-UPDRS, HY and SE. Handicap (maximum LHS=0) and nonmotor symptoms (NMSS, NPI, MMSE, GDS), QoL (PDQ-8, EQ-5D) were also characterized.

Results: Mean age and age at DBS were 64.3 (\pm 9.9) and 59.4 (\pm 9.6)years, respectively. Median HY was 2 and median SE 90 (IQR,70-90). 78.8% of patients had independent gait.

Mean LHS score (4.8 years DBS-STN) was 0.707(\pm 0.207) and the most affected domains were Occupation, Mobility and Social Integration. Handicap was significantly correlated with age ($r=-0.358$), age at DBS ($r=-0.429$), independent gait ($r=0.600$), MDS-UPDRS-II ($r=-0.568$), MDS-UPDRS-I ($r=-0.527$), MDS-UPDRS-III ($r=-0.426$), SE ($r=0.562$), nonmotor symptoms(NMSS) ($r=-0.503$), depression (GDS) ($r=-0.491$), PDQ-8 ($r=-0.667$) and EQ-5D ($r=0.657$) (all $p<0.05$). Functional (SE) and gait dependence and depression were the independent predictors of handicap (adjusted $R^2=0.600$; $p=0.010$).

In a sample of 18 patients with LHS evaluation before and after surgery, handicap significantly improved after DBS [Δ LHS 0.213(\pm 0.185); $p=0.002$].

Conclusion: PD patients submitted to DBS-STN were mildly handicapped 5 years after surgery, which was determined by functional and gait dependency, and depression. The affected subdomains were Occupation, Mobility and Social integration. Compared to pre-DBS, handicap was still better after 5 years of surgery.

Disclosure: Nothing to disclose

EPR3065

Probabilistic response mapping in a cohort of mixed dystonia patients.

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Background and aims: Probabilistic outcome brain mapping is a promising tool to estimate the expected benefit of pallidal deep brain stimulation (DBS-GPi) in patients with dystonia. However, its validity and feasibility for isolated and combined dystonia needs to be established.

Methods: Registration of atlas, detection of leads and rendering of volume of tissue activated (VTA) were performed for each patient with generalized and cervical isolated or combined dystonia that underwent bilateral DBS-GPi between 2005-2015. Each patient-specific VTA was associated with the clinical improvement (percentage of dystonia score reduction). The correlation between predicted and real clinical benefit based on a VTA-atlas model was studied.

Results: We enrolled 21 patients with a mean follow-up of 3 years. Subjects with cervical dystonia had a superior clinical benefit on follow-up, but these results were not statistically significant (78% vs 62%, $p=0.098$). The proportion of non-responders was 9.4% and 24% patients had an excellent response (more than 80% of motor benefit) at 3-years follow-up. The volume with highest probability of good outcome was located within the ventroposterior GPi and adjacent subpallidal white matter. A correlation between real clinical improvement and the VTA-atlas model estimation was found. Considering clinical and demographic variables, we are able to explain 32% of the observed variance in DBS response according to this model ($r^2=0.32$; $P=0.042$).

Conclusion: There is a correlation between observed and predicted clinical improvement based on VTA-atlas model. These results emphasize the potential of probabilistic outcome brain mapping in refining the optimal therapeutic volume for pallidal neurostimulation.

Disclosure: Nothing to disclose

EPR3066

Progression of brain cholinergic dysfunction in patients with isolated REM sleep behavior disorder. A 11C-Donepezil PET study.

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Background and aims: Isolated REM sleep behavior disorder (iRBD) is widely considered a prodromal stage of parkinsonism, and we have previously reported the presence of reduced acetylcholinesterase activity, as measured by 11C-Donepezil PET, in the cortex but not in the basal ganglia of iRBD patients with no cognitive deficits. In this longitudinal study, we aimed to explore the temporal changes in acetylcholinesterase activity in the brains of iRBD patients.

Methods: We studied 11 polysomnography-confirmed iRBD patients with 11C-Donepezil PET, a marker of cholinergic function, twice over a 3-year period. The PXmod module of PMOD software 3.6 (PMOD technologies Ltd. Switzerland) was used to generate binding potential (BPND) images, using the Logan Reference Tissue model. The follow-up images were compared to the baseline images at a voxel level using Statistical Parametric Mapping (SPM) 12 (FIL Methods Group).

Results: The SPM analysis showed significant reduction ($p<0.04$, FWE corrected) in acetylcholinesterase activity from baseline to follow-up in the iRBD patients in several cortical regions (the frontal, parietal and occipital lobes, and the left temporal lobe), but also in both thalami as well as striatal areas of both hemispheres.

Conclusion: Our results suggest that the severity and extent of cholinergic dysfunction in the brains of iRBD patients increase significantly over a 3-year period. However, the clinical correlates of these changes remain to be investigated.

Disclosure: Nothing to disclose

EPR3067

Pre-motor manifestations, including psychotic features, in a rat model of Parkinson's disease based on human alpha-synuclein overexpression

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Background and aims: Amongst the non-motor symptoms of Parkinson's Disease (PD), neuropsychiatric, in particular psychotic manifestations, are amongst the most debilitating. Progress in understanding their pathophysiological basis, as well as their management, has been slow, in part due to the absence of relevant animal models.

Methods: Using humanized BAC transgenic alpha-synuclein (AS) rats (Nuber et al., 2013), we assessed motor function with the Beam Traversal and Footprinting tests; cognition with the Morris Water Maze test, mood with the Forced Swim and the sucrose preference tests, olfactory function with the buried pellet test, anxiety-like behavior with elevated plus-maze, and psychotic-like behavior with Prepulse Inhibition and locomotor activity in a novel environment. Fractionated Western immunoblotting was used to assess AS brain deposition, HPLC to assess striatal Dopamine levels and immunohistochemistry to assess dopaminergic neurodegeneration.

Results: AS BAC Tg rats manifested a pre-motor PD-like phenotype with age-dependent olfactory and cognitive deficits, as well as depressive behaviors. The most outstanding phenotype consisted of a psychosis-like profile, including an early and persistent hyperactivity in a novel environment that was reversed by antipsychotics, as well as a late-onset sensorimotor gating deficit, associated with a striatal hyperdopaminergic state. This neuropsychiatric phenotype was accompanied by an abundance of brain region-dependent aberrant AS aggregation pathology.

Conclusion: Our findings provide insight into region-specific perturbations that precede motor manifestations and support a role of an AS-mediated striatal hyperdopaminergic state in the generation of psychotic-like features prior to neurodegenerative phenocconversion. This situation has analogies to PD, where recent findings suggest that a premotor hyperdopaminergic state may occur.

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EPR3068

RFC1 intronic repeat expansions in multiple systems atrophy

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Introduction: Multiple Systems Atrophy (MSA) is difficult to diagnose in the early stages due to the clinical overlap of late-onset ataxia with autonomic features and MSA with cerebellar predominance and parkinsonian predominant phenotypes. With the recent identification of recessive, intronic repeat expansions in the RFC1 gene as a cause of late-onset ataxia, neuropathy, vestibular areflexia syndrome we hypothesised that there could be an overlap with the early stages of MSA or with atypical MSA and additional clinical features.

Methods: 2 MSA cohorts were investigated; 336 pathologically confirmed brain bank cases and 207 clinically diagnosed probable or possible MSA cases, both diagnosed according to MSA consensus criteria. These underwent genetic analysis and Southern blot confirmation of RFC1 expansions.

Results: 2 clinically diagnosed probable MSA cases were biallelic for the RFC1 expansion. They presented with typical rapid, progressive history and clinical features for MSA including progressive cerebellar ataxia, parkinsonism, autonomic dysfunction, but both also had a mild sensory neuropathy. No biallelic repeat expansions were identified in the pathologically confirmed MSA cohort.

Conclusion: We report that the clinical features of early MSA may overlap with RFC1 associated ataxia. We recommend adding RCF1 analysis to the initial screening of MSA patients, particularly those with an unusual phenotype, with a possible family history or any clinical signs of a peripheral neuropathy. With the advent of MSA therapeutic trials, initial screening to exclude other causes will be paramount to achieve the most accurate outcome.

Disclosure: Nothing to disclose

EPR3069

Long-term effectiveness and medication patterns (monotherapy vs polytherapy) with device-aided therapies: A retrospective analysis of an Israeli cohort of patients with advanced Parkinson's disease

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Background and aims: As Parkinson's disease (PD) progresses, some patients may not be adequately controlled with oral dopaminergic medication and may require device-aided therapies (DATs) such as levodopa-carbidopa intestinal gel (LCIG), continuous subcutaneous apomorphine infusion (CSAI), and deep brain stimulation (DBS). This study investigated treatment duration of LCIG vs CSAI, and medication patterns (mono- and combination therapies).

Methods: This retrospective cohort study used the Maccabi Healthcare Services database and identified advanced PD patients (≥18 years) treated with DATs since September 2009. Patients were excluded if they had <12 months of potential follow-up. Outcomes included treatment duration at 12 months, treatment persistence up to 60 months, and comedication profiles. Descriptive statistics were used.

Results: Of 161 patients identified (Table), LCIG had greater mean persistence rate (12 months: 87.0%; 36 months 81.5%) vs CSAI (12 months: 81.4%; 36 months: 59.4%) (Figure 1). Over the study, mean (95% CI) time to discontinuation (including death) for LCIG was 86.4 (73.3–99.6) months and 42.4 (27.7–57.1) months for CSAI (P=.046). There was a medication profile shift, with approximately half of patients in each group taking ≥4 PD medications before DAT initiation, whereas at last measurement, more patients had LCIG as monotherapy (LCIG: 29%; DBS: 13%; CSAI: 6%) or LCIG with only additional nighttime controlled-release levodopa (LCIG: 45%; DBS: 23%; CSAI: 12%) (Table, Figure 2).

Table. Patient Baseline Characteristics

Characteristic	LCIG (n = 62)	DBS (n = 76)	CSAI (n = 23)
Sex, n (%)			
Male	38 (61)	48 (63)	15 (65)
Age at PD diagnosis, years, median (IQR)	58.1 (49.5 – 66.4)	55.4 (49.8 – 61.7)	59.9 (55.9 – 67.0)
Age at DAT initiation, years, median (IQR)	69.4 (59.7 – 76.9)	65.3 (59.2 – 68.3)	68.9 (63.7 – 79.6)
Number of PD medications*			
0	1 (1.6)	2 (2.6)	—
1	5 (8.1)	6 (7.9)	2 (8.7)
2	7 (11.3)	16 (21.1)	6 (26.1)
3	13 (21.0)	14 (18.4)	2 (8.7)
≥ 4	36 (58.1)	38 (50.0)	13 (56.5)

Includes oral levodopa. CSAI, continuous subcutaneous apomorphine infusion; DAT, device-aided treatment; DBS, deep brain stimulation; IQR, interquartile range; LCIG, levodopa-carbidopa intestinal gel; PD, Parkinson's disease.

Figure 1

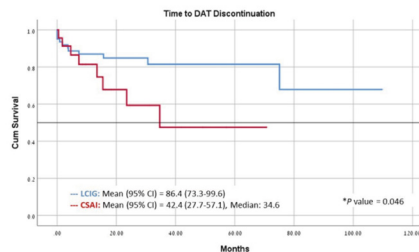
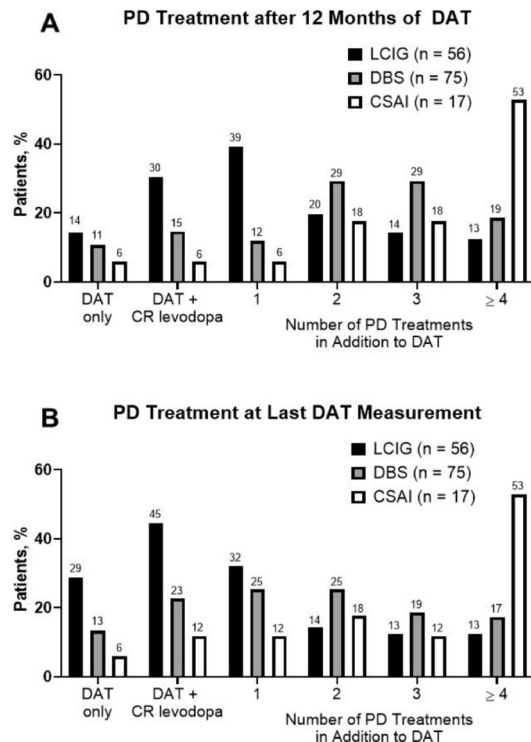


Figure 2



CR, controlled-release; CSAI, continuous subcutaneous apomorphine infusion; DAT, device-aided therapy; DBS, deep brain stimulation; LCIG, levodopa-carbidopa intestinal gel; PD, Parkinson's disease.

Conclusion: LCIG treatment was associated with higher persistence rates after 12 months and in the long-term vs CSAI. A higher proportion of patients on LCIG were on monotherapy vs DBS and CSAI.

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EPR3070

Burden of Care-Partners of People with Parkinson's disease: Findings from Parkinson's disease Real-World Impact Assessment (PRISM) Study

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Background and aims: The burden of care-partners of people with Parkinson's disease (PwP) is currently not well understood or reported. The PRISM study was a European survey of PwP and their care-partners. PRISM data on the characteristics and burden of the care-partners of PwP are presented here.

Methods: PRISM was a descriptive, exploratory, observational study with cross-sectional design, fielded through an online survey developed in collaboration with The Cure Parkinson's Trust (UK-based advocacy group) and an international scientific committee. Collecting data of PwP and their matched-samples care-partners through online channels may limit results interpretation. Care-partner burden was assessed using the Zarit Burden Inventory (ZBI). Multivariate analysis assessed associations between PwP/care-partner characteristics and ZBI total score.

Results: Between April-July 2019, data were collected from 256 care-partners of PwP from France, Germany, Italy, Portugal, Spain and the UK (Table). The majority of care-partners were female (65%) and partner/spouse to the PwP (82%). Care-partners spent a mean 22.5 hours/week caring for the PwP and the majority (55%) received no assistance from other caregivers. Care-partners reported mild-moderate burden (mean ZBI total score, 26.6); 72% reported that caring for PwP impacted their relationship, and 46% reported an impact on their sexual relationship. Multivariate analysis revealed that female care-partner gender, older PwP age, worse PwP's PDQ-39 mobility score, more PwP's non-motor symptoms, higher hours of care/week, and being a sibling care-partner were associated with higher care-partner burden (Figure).

Table. Characteristics and burden of care-partners of PwP

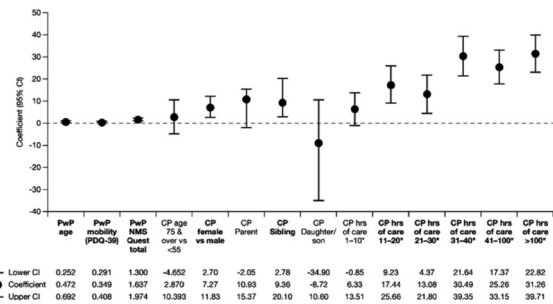
Characteristic	N=256
Female gender, %	65
Partner/spouse of PwP, %	82
Hours of care to PwP/week	
N	214
Mean (SD)	22.5 (24.6)
Median	14
ZBI total score*	
N	246
Mean (SD)	26.6 (17.6)
Median (range)	25 (0-83)
Burden severity by ZBI total score*	
N	246
Severe (ZBI total score >60), %	3
Moderate/severe (ZBI total score 41-60), %	20
Mild/moderate (ZBI score 21-40), %	34
Little/no burden (ZBI ≤20), %	43
Assistance from others in caring for PwP	
N	242
Family member, %	30
Friend, %	13
Paid nurse, %	3
Other paid caregiver, %	12
Severity of impact of caring for PwP on relationship	
N	239
Extreme, %	5
Very much, %	16
Moderate, %	25
Slight, %	24
Not at all, %	28

*Assessed over previous month. PD, Parkinson's disease; PwP, people with Parkinson's disease; SD, standard deviation; ZBI, Zarit Burden Inventory

Table

Figure. Multivariate analysis of variables associated with ZBI total score (previous month; N=236).

*Hours of care referenced to 0 hours of care. CI, confidence interval; CP, care-partner; NMSQuest, Non-Motor Symptoms Questionnaire; PDQ-39, Parkinson's Disease Questionnaire-39; PwP, patient with Parkinson's disease; ZBI, Zarit Burden Inventory



Figure

Conclusion: PRISM provides valuable information on meaningful factors affecting burden of care-partners in PD.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPR3071

Possible effects of metformin therapy on motor and non-motor features of diabetic patients with Parkinson's disease (PD): an exploratory study using the Parkinson's Progression Markers Initiative (PPMI) cohort

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Background: There is growing evidence for the benefits of metformin to counteract age-related diseases such as cancer, cardiovascular disease, and neurodegenerative diseases 1.

Objective: To evaluate the association between metformin treatment and the motor and non-motor clinical features among denovo PD patients with diabetes mellitus (DM).

Methods: This retrospective cohort study examined the effects of long-term metformin therapy (>2 years) on baseline PD clinical features among denovo PD patients with DM using the PPMI cohort. From the original PD cohort, 19 patients with a diagnosis of DM were selected and stratified into 2 groups: 1) Taking metformin for >2 years, 2) Not taking metformin. Additionally, we explored whether Metformin Cumulative Doses (Daily dose x years of treatment) could be associated with clinical features.

Statistical analysis: Categorical variables were expressed as proportions and compared using Fisher's test. Due to small group sizes, non-normal distribution of some variables, non-parametric tests (Chi-square, Mann-Whitney and Spearman correlation) were used for group comparisons and correlation analyses. The P-value<0.05 was considered statistically significant. Post-hoc correction for multiple comparisons was not applied given the exploratory nature of the study.

Results: DM patients taking Metformin showed lower baseline score in MDS-UPDRS total and performed better in Benton Judgment of Line Orientation, Symbol Digit Modalities and Semantic Fluency Total.

Conclusion: This observational analysis provides a soft footprint of metformin use and possibly better motor and cognitive scores in diabetic PD. Further studies of metformin in denovo or prodromal PD could provide a rationale for repurposing metformin.

Disclosure: Nothing to disclose

EPR3072

Independent domains of daily-life activity in patients with neurological gait disorders

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Background and aims: Alterations in daily-life activity and mobility are common in neurological patients. Quantitative assessment of daily-life mobility commonly yields a complex pattern of mobility measures that yet complicates clinical interpretability. Here, we applied factor analysis with the aim to classify clinical meaningful domains of daily mobility in patients with neurological gait disorders.

Methods: Daily-life activity and mobility of 315 individuals (55 healthy, 75 sensory ataxia, 78 cerebellar ataxia, 18 hypokinetic gait disorder, 51 vascular encephalopathy, 38 functional gait disorder) was recorded for two weeks using a wearable inertial sensor system (ActiPAL[®]). Principal component analysis (PCA) with varimax rotation was performed on 14 mobility parameters to derive 5 independent domains of daily mobility. Associations of domains with clinical motor, balance, cognitive, and quality of life scores was evaluated.

Results: 14 mobility parameters were included into PCA, which yielded 5 orthogonal factors accounting for 92.3% of total data variance. We characterized these factors as (I) Ambulatory Volume, (II) Ambulatory Pattern, (III) Sedentary Volume, (IV) Sedentary Pattern, and (V) Transitions. Factors showed differential, significant associations to clinical motor, balance, and cognitive scores.

Conclusion: These results support the approach of reducing the high dimensionality of real-world behavioral data to a small number of clinical meaningful macro-variables. This facilitation of the interpretation of quantitative mobility measures might further promote the application of such measures as clinical meaningful outcome parameters in medical science and clinical routine.

Disclosure: Nothing to disclose

EPR3073

The most impacting factors of Parkinson's disease patients' quality of life

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Background and aims: Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor and non-motor symptoms that collectively contribute to decreased Quality of Life (QoL).

The aim of the study is to identify the most impacting factors of Parkinson's disease patients' quality of life.

Methods: Clinical and neuropsychiatric assessments were studied by the Hoehn&Yahr (H&Y), UPDRS (III), MoCA-test, HADS, Beck depression inventory, Epworth Sleepiness Scale, Apathy Scale, SF-36, PDQ-39.

Results: Clinical assessment were based on 619 PD patients examination results: mean age: 68.13±9.32; mean PD duration: 6.8±4.6; women:men=380:239; H&Y stages 1–4. During the study were identified that most impacting factors of PD patients' QoL are depression, cognitive impairment, moto disfunction and levodopa induced dyskinesia.

Conclusion: Nevertheless, the lack correlations with disease-related variables gives us a suggestion that QoL may be individually impacted by other factors, indicating that an ideal patient-profile with regard to QoL improvement cannot be readily presented.

Disclosure: Nothing to disclose

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EPR3074

Optical coherence tomography is sensitive for detecting asymptomatic optic nerve lesions in clinically isolated syndrome

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Background and aims: To evaluate the ability of inter-eye retinal thickness difference (IETD) measured by optical coherence tomography (OCT) to detect asymptomatic optic nerve involvement in clinically isolated syndrome (CIS).

Methods: We conducted a cross-sectional study of patients who recently presented a CIS (≤ 4.5 months). All patients underwent an OCT and a brain/optic nerve MRI. Optic nerve involvement was defined clinically (episode of optic neuritis[ON] or not) and radiologically (optic nerve hypersignal on 3D-DIR). We evaluated the sensitivity (Se) and specificity (Sp) of IETD thresholds previously published and reported the observed optimal thresholds for identifying symptomatic optic nerve involvement but also for identifying asymptomatic optic nerve involvement (optic nerve hypersignal without ON history). Primary outcomes were ganglion-cells–inner-plexiform-layer (GCIPL) and peripapillary-retinal-nerve-fibers-layer (pRNFL) IETD.

Results: The study group consisted of 130 patients. In the CIS with ON group, 3D-DIR showed a hypersignal in all the 41 symptomatic optic nerves and in 11 asymptomatic optic nerves. In the CIS without ON group, 3D-DIR showed a unilateral optic nerve hypersignal in 22 patients and a bilateral optic nerve hypersignal in 7 patients. For the detection of symptomatic and asymptomatic optic nerve lesion, GCIPL-IETD had better performance. We found an optimal GCIPL-IETD threshold $\geq 2.82\mu\text{m}$ (Se=88.2%, Sp=83.3%) for the detection of symptomatic lesions and an optimal GCIPL-IETD $\geq 1.42\mu\text{m}$ (Se=89.3%, Sp=72.6%) for the detection of asymptomatic lesions.

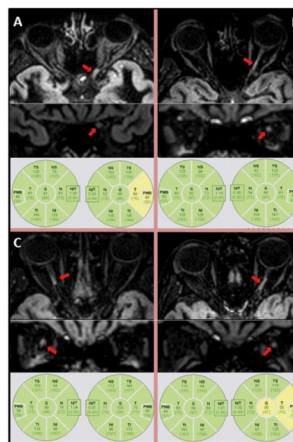


Figure: CIS patients without history of clinical optic neuritis presenting asymptomatic optic nerve lesion (red arrows) detected on 3D-Double-Inversion-Recovery MR sequence (on axial and coronal planes reconstruction) associated with their corresponding pRNFL thicknesses (A-D)

Figure Title: Optic nerve MRI and OCT findings in CIS patients without optic neuritis
 Figure Legend: CIS patients without history of clinical optic neuritis presenting asymptomatic optic nerve lesion (red arrows) detected on 3D-Double-Inversion-Recovery MR sequence associated with their corresponding pRNFL thicknesses (A-D)

Conclusion: Detection of asymptomatic optic nerve lesions at CIS requires lower IETD thresholds than previously reported. GCIPL-IETD represents an alternative biomarker to MRI for the detection of asymptomatic optic nerve lesion.

Disclosure: This work was supported by Bayer and Novartis. Bayer provided research funding for performing MRIs. Novartis provided research funding for the acquisition of the OCT device. Bayer and Novartis had no role in study design, data collection, analysis, interpretation, or writing of the report.

EPR3075

Epilepsy and pediatric multiple sclerosis

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Background and aims: The incidence of epilepsy in multiple sclerosis (MS) is from 1.5 to 7.8%.

Methods: Were analyzed the incidence and features of epilepsy in patients with pediatric MS.

Results: 53 cases of pediatric MS were analyzed. 5 (9.43%) patients had epilepsy, all were girls. The average age of the MS onset was 13.98±2.9 years, of the seizures onset—15.2±2.9 years. In 3 cases, the seizures began after the MS diagnosis and were not during relapse. The EDSS score at the time of the epilepsy onset was: 1.5 (2 cases) and 3.0 (1 case). All children had a relapsing-remitting MS. In 2 cases, epilepsy started before the appearance of neurological symptoms, but the MRI has already revealed demyelinating lesions. At the time of the seizures onset, 3 patients did not receive DMT and 2 were treated by fingolimod. All patients had focal epilepsy: focal sensory attacks were in 3 cases, focal motor attacks—in 2, cognitive—in 1, behavior arrest in—1 and bilateral tonic-clonic—in 4. Epileptic status was not present in any case. EEG in all children recorded focal epileptic activity: in the frontal area in 1 case, frontal-temporal—1, frontal-central—1, frontal-central-temporal—in 1, central-parietal—1. Anticonvulsant therapy was effective in all: in 3 patients—Carbamazepine, in 1—Lamotrigine, in 1—Levetiracetam. In 1 patient, after withdrawal of therapy, seizures did not resume.

Conclusion: As epilepsy started before the MS onset and before DMT using in some patients, so seizures can be one of the clinical disease manifestations. Epilepsy in MS is focal and well treatable.

Disclosure: Nothing to disclose

EPR3076

Population-based comparative studies of the epidemiology of neuromyelitis optica spectrum disorder (NMOSD) in Europe

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Background and aims: Earlier studies suggested differences in prevalence and phenotype of NMOSD in people with different genetic background. No population-based comparative study is available among Caucasian populations. We investigated a potential geographical variation in prevalence and phenotype of NMOSD with aquaporin-4 antibody seropositivity (AQP4-Ab+) among two European populations.

Methods: We performed a large population-based comparative study involving the adult (age≥16) population of Denmark and Hungary. The study focused on AQP4-Ab+ Caucasian NMOSD patients. We utilized the same methodology and corresponding sources (databases, laboratories and neurology departments) to identify cases between 2007 and 2014 in both countries. Overlapping expert groups validated each case. We calculated prevalence based on 2015 IPND criteria. Mann–Whitney U and chi-squared/Fisher exact test were used.

Results: We identified 35 Danish and 99 Hungarian AQP4-Ab+ NMOSD cases. We found significantly higher prevalence in Hungary compared to Denmark on January 1, 2014 (1.39/100,000 [95%CI:1.11-1.71] vs 0.71/100,000 [95%CI:0.48-1.01]; p=0.0019) based on both 2015 IPND criteria. Optic neuritis was the most frequent onset attack in the Hungarian population (n=41 [41%] vs. n=6 [17%]; p=0.013) while transverse myelitis was the most common among Danish patients (n=21 [60%] vs. n=35 [35%]; p=0.009). The Danish cohort was more affected by spinal cord damages such as more frequent use of catheters, more severe EDSS score, more commonly bound to wheelchair/bed, and atrophy in the spinal cord.

Conclusion: These data support differences even among Caucasian populations in Europe and substantiate the need for genetic association studies in NMOSD.

Disclosure: The work was supported by the Economic Development and Innovation Operational Programme (GINOP-2.3.2-15-2016-00039), the Hungarian

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EPR3077

Theory of mind deficits across MS phenotypes

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Background and aims: Theory of Mind deficits (ToM, the ability to decode emotional states) have been described in patients with Multiple Sclerosis (MS). ToM assessment is not included in neuropsychological evaluations of MS, and this is also due to an incomplete understanding of the relationship between general cognition and RMET across the disease stages

Methods: 90 MS patients (age: 44.8±10.7 years, median EDSS 2.0 range 1-6, 62 with relapsing remitting (RRMS) and 28 with progressive MS (PMS)) were assessed with the Symbol Digit Modalities Test (SDMT) to evaluate general cognition and the Reading the Mind in the Eyes Test (RMET) to evaluate ToM

Results: Comparing RRMS and PMS patients, there was a significant difference in SDMT (54.3±12.1 vs 41.3±11.2, p=0.001) and in total RMET (26.4±4.1 vs 23.5±3.2, p=0.03) scores; the difference in RMET performance lost significance after correction for SDMT (p=0.26). There was a significant correlation between SDMT and ToM in the whole sample (p<0.001, r=0.34) and in RRMS (p=0.001, r=0.434), but not in PMS (p=0.83)

Conclusion: The association between SDMT and RMET is modulated by clinical phenotype. RMET seems to probe a cognitive construct not included in the SDMT and thus should be included in the baseline evaluation of MS. The impact of clinical phenotype on the association between RMET and SDMT suggest that these 2 metrics change differently over the disease course and thus provide different vantage points to study cognition in MS.

Disclosure: Nothing to disclose

EPR3078

Gray Matter atrophy is mild in patients with long-term benign MS.

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Background: Whether or not multiple sclerosis (MS) can have a benign course (B-MS) is still controversial, however a small group of patients who are not disabled after many years of disease can be identified.

Aims: To identify whether brain damage is less pronounced in patients with long-term benign disease course.

Methods: We compared 13 patients defined as long-term B-MS (age >55 years, Expanded Disability Status Scale [EDSS] ≤ 3.0, after at least 30 years from disease onset) and 27 non-benign MS (age >55 years, EDSS >3.0). MRI scans (n= 116, on average 3 scans per patient) of both groups were assessed retrospectively (mean follow-up: 11 years, range: 8-13 years and similar between the 2 groups). Brain volumes (BV) and total T2-lesion volume (LV) changes over time were compared between the 2 groups using a mixed effect regression model.

Results: Over 11 years, patients with long-term B-MS showed less global BV and grey matter (GM) decreases (p for slope difference 0.02 and <0.001, respectively) than those with non-benign MS course. By contrast, there was no difference between the 2 groups in the accumulation of T2-LV (p= 0.76; see Table and Fig.1).

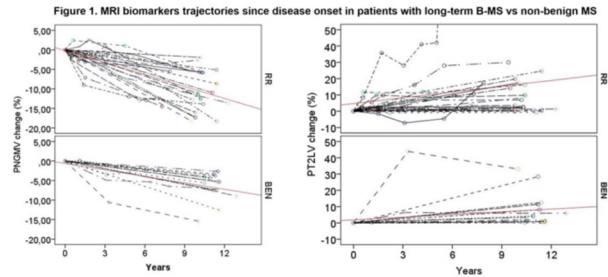


Figure 1

Conclusion: Our findings suggest that global and GM atrophy are less pronounced in MS patients who were not yet disabled after more than 30 years of disease. Changes in GM volume show to be crucial in distinguishing subjects who are less prone to disability accumulation and may be important in characterizing MS patients with benign evolution.

Disclosure: Nothing to disclose

Table 1

Annualized rate of change mean (SE)	B-MS	MS	P value
Brain volumes	0.35 ± 0.04	0.49 ± 0.04	p=0.02
Grey matter volume	0.57 ± 0.08	1.09 ± 0.08	p<0.001
Total T2-lesion volume	0.69 ± 0.29	0.78 ± 0.14	p=0.76

Table 1

EPR3079

Disease modifying therapies discontinuation in relapsing-remitting Multiple Sclerosis: a monocentric cohort study

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Background and aims: Discontinuation of a Disease Modifying treatment (DMT) not followed by switch to other DMTs, is a frequent event in relapsing-remitting multiple sclerosis (RR-MS), but in these cases data on disease reactivation are lacking. To investigate disease course and predictive factors of disease activity occurrence in RR-MS patients after DMT discontinuation.

Methods: RR-MS patients under treatment with a DMT (n=1107), were screened. Those, age 18-65, who discontinued a DMT without switching to a new one were included, excluding who interrupted for SP-MS conversion or for pregnancy. Disease course was evaluated in term of relapse rate and disability worsening. Baseline characteristics potentially associated to disease reactivation after DMTs discontinuation were analysed.

Results: Patients (n=62) were included, age 47.8 (22.1–64.3) years, treatment duration 7.3 (0.3-18.1) years. DMT administered were: azathioprine, beta-interferons, glatiramer-acetate; dimethyl-fumarate. Follow-up duration after discontinuation was 4.4 (0.5-16.6) years. Patients with disease activity after discontinuation were 11/62 (17.7%): 8/62 relapsed, 2/62 developed confirmed disability worsening, 1/62 both. Time to 1st relapse was 1.3 (0.1-5.2) years. Among the baseline demographic, clinical and MRI characteristics, a NEDA-3 (No Evidence of Disease Activity) period length before DMT discontinuation inversely correlated with the frequency of patients with disease activity following discontinuation, with cut-off at >5.5, that was associated to a longer disease-free period after discontinuation (aHR=0.2, p=0.04).

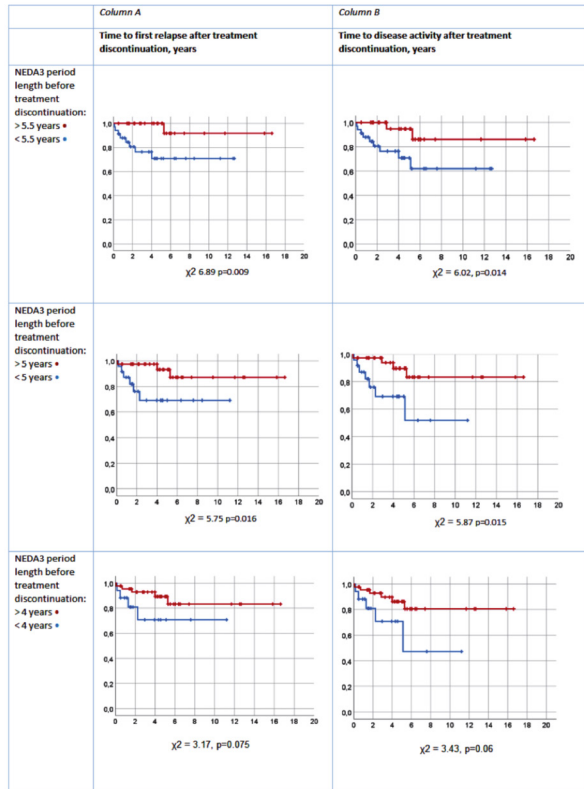
Observation period	Treatment (n=62)		Post treatment N=62		Post treatment, Follow up vs baseline
	baseline	baseline	baseline	Follow-up	
Women n (%)	42 (67.7)	42 (67.7)	42 (67.7)	42 (67.7)	
Previous follow up duration, years	2.7 (0.1-34.3) median (range)	7.3 (0.5-18) 7.7 (0.5)	4.4 (0.5-17) 5.06 (0.5)		
Age, years	38.11 (19.7–57.5) median (range) mean (ES)	47.79 (22.1–64.3) 46.48 (1.3)	53.94 (29.3-77.9) 51 (1.39)		
Number of treated patients (%):					
Azathioprine	36 (58)	36 (58.1)	36 (58.1)		
Beta IFN	15 (24)	15 (24.2)	15 (24.2)		
Glatiramer acetate	6 (9.7)	6 (9.7)	6 (9.7)		
Dimethyl-fumarate	1 (1.6)	1 (1.6)	1 (1.6)		
Azathioprine+beta IFN	4 (6.4)	4 (6.4)	4 (6.4)		
EDSS, score	1.5 (0–5.5)	1.5 (0–6.5)	1.5 (0–6.5)		
Patients with a relapse, n (%)	62 (100)	31 (50)	9 (14)		p=0.0002 (McNemar test)
Annualized relapse rate*	median (range) mean (ES)	0.61 (0.0–16.6) 1.9 (0.4)	0.0 (0.0–3.9) 1.5 (0.06)	0.0 (0.0–2.6) 0.09 (0.05)	p=0.005 (Wilcoxon test)
Patients with MRI activity†, n (%)	62 (100)	24 (38.7)	Not detected		
Patients with disability worsening, n (%)	52 (82)	8 (13)	3 (5)		p=0.33 (McNemar test)
Patients with clinical or MRI activity, n (%)	62 (100)	36 (58.1)	Not detected		
Patients with disease activity (relapse or disability worsening), n (%)	62 (100)	31 (50)	11 (17.7)		p=0.0008 (McNemar test)
Annualized disease activity†	median (range) mean (ES)	0.61 (0.0–16.6) 1.9 (0.4)	0.0 (0.0–3.9) 1.5 (0.06)	0.0 (0.0–2.6) 0.11 (0.05)	p=0.005 (Wilcoxon test)
Relapse free period duration, years	median (range) mean (ES)		5.72 (0.1–14.7) 5.84 (0.39)		
MRI activity† free period duration on treatment, years	median (range) mean (ES)		5.57 (0.1–14.6) 5.78 (0.4)		
NEDA 3‡ period duration on treatment, years	median (range) mean (ES)		5.33 (0.1-12.8) 5.21 (0.36)		

Patient demographic, clinical and MRI characteristics at baseline of the observation periods included and at end of the follow-up.

Observation period median year number (range)	Treatment baseline 2.7 (0.06–34.31)		Post treatment	
	Baseline 7.29 (0.3–18.1)	Follow-up 4.43 (0.5–16.62)	Baseline 7.29 (0.3–18.1)	Follow-up 4.43 (0.5–16.62)
Patient characteristics				
Relapsing (n %)	6 (9.7)	HR: 0.07 (0.24-1.88)	6 (9.7)	HR: 0.07 (0.24-1.88)
Non relapsing (n %)	36 (57.9)	p=0.967	36 (57.9)	p=0.967
Median of the observation period, median years (range)				
Relapsing	1.3 (0.08–16.59)	HR: 0.03 (0.75-1.08)	5.39 (0.5–17.6)	HR: 0.96 (0.80-11.7)
Non relapsing	3.42 (0.08–34.32)	p=0.307	7.36 (1.54–38.1)	p=0.704
Age, median years (range)				
Relapsing patients	26.87 (19.38–44.14)	HR: 0.98 (0.91-1.05)	31.38 (19.07–47.84)	HR: 0.96 (0.89-1.02)
Non relapsing	30.53 (15.54–55.97)	p=0.904	38.59 (20.6–57.50)	p=0.176
EDSS, median score (range)				
Relapsing patients	1 (0–3)	HR: 0.77 (0.43-1.38)	2 (0–3)	HR: 0.74 (0.39-1.41)
Non relapsing	1 (0–5)	p=0.375	1 (0–6)	p=0.360
Patients with a relapse, n (%)				
Relapsing patients	9 (100)		5 (55.6)	HR: 0.91 (0.25-4.41)
Non relapsing	53 (100)		26 (49.1)	p=0.894
Time period AHR*, median (range)				Not applicable
Relapsing patients	0.52 (0.00–12.16)	HR: 1.12 (0.98-1.27)	0.08 (0.0–0.36)	HR: 0.73 (0.14-4.72)
Non relapsing	0.64 (0.03–16.59)	p=0.008	0.0 (0.0–3.8)	p=0.744
Patients with MRI activity†, n (%)				
Relapsing patients	9 (100%)		5 (55.6%)	HR: 1.05 (0.28-3.92)
Non relapsing	53 (100%)		22 (41%)	p=0.487
Clinical and radiological activity†, n (%)				
Relapsing patients	9 (100%)		31 (58.5%)	HR: 0.81 (0.22-3.03)
Non relapsing	53 (100%)		5 (5.6%)	p=0.756
Patients with disease activity†, n (%)				
Relapsing patients	9 (100%)		5 (55.6%)	HR: 0.95 (0.26-3.54)
Non relapsing	53 (100%)		26 (49.1%)	p=0.94
Annualized disease activity†, median (range)				
Relapsing patients	0.52 (0.00–12.16)	HR: 1.12 (0.98-1.27)	0.08 (0.0–0.36)	HR: 0.73 (0.14-4.72)
Non relapsing	0.64 (0.03–16.59)	p=0.008	0.0 (0.0–3.8)	p=0.744
Relapse free period before treatment discontinuation, median years (range)				
Relapsing patients	Not applicable		4.25 (0.33–9.22)	HR: 0.73 (0.58-0.92)
Non relapsing	Not applicable		6.00 (0.09–14.7)	p=0.008
MRI activity† free period before treatment discontinuation, median years (range)				
Relapsing patients	Not applicable		4.2 (0.3–11.1)	HR: 0.83 (0.67-1.04)
Non relapsing	Not applicable		5.75 (0.08–14.63)	p=0.097
NEDA 3‡ period before treatment discontinuation, median years (range)				
Relapsing patients	Not applicable		4.2 (0.33–9.22)	HR: 0.77 (0.60-0.98)
Non relapsing	Not applicable		5.6 (0.08–12.76)	p=0.096

* Annualized relapse rate: relapse number/patient/year. † MRI activity: presence of new T2 lesion or of gadolinium-enhancing lesions. ‡ Clinical and radiological activity: occurrence of relapse or radiological activity. † disease activity: occurrence of relapses or disability progression. § Annualized disease activity: total number of relapses or of disability worsening/patient/years. @NEDA 3: absence of relapse, radiological activity and disability progression.

Patient demographic, clinical and MRI characteristics, at baseline of the observation periods included, stratified according to relapse status at follow up post treatment discontinuation and univariate analysis of their association.



Survival analysis of time to 1st relapse (column A) or time to 1st disease activity (column B) after treatment discontinuation in 2 groups of patients stratified according to different NEDA-3 period length before treatment discontinuation (Kaplan Maier analysis; Breslow's rank-order test).

Conclusion: Discontinuation of a DMT in patients with NEDA-3 period before discontinuation >5.5 years seems safe as associated with very low frequency of disease reactivations.

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EPR3080

How Multiple Sclerosis Disease Characteristics Correspond to Cognitive Impairment Status at Baseline: A Post Hoc Analysis of the Ozanimod RADIANCE and SUNBEAM Phase 3 Trials Using PASAT and SDMT Assessments

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Background and aims: Cognitive impairment occurs early in relapsing multiple sclerosis (RMS) patients, and reliable identification depends on assessment tool(s) used. The Paced Auditory Serial Addition Test (PASAT) assesses several cognitive domains, including processing speed, working memory, calculation ability, divided attention, and mental flexibility. The more sensitive Symbol Digit Modalities Test (SDMT) assesses processing speed and working memory. We compared disease characteristics in RMS participants with/without baseline cognitive impairment assessed by PASAT or SDMT in the phase 3 RADIANCE and SUNBEAM trials of ozanimod, respectively.

Methods: Participants (aged 18–55y) received oral ozanimod HCl 1 or 0.5mg/d or intramuscular interferon beta-1a 30µg/wk in RADIANCE (NCT02047734) and SUNBEAM (NCT02294058). This post hoc analysis compared baseline characteristics between cognitively impaired versus preserved participants within each study. Impairment was defined as baseline PASAT or SDMT score ≥ 1.5 standard deviations below the mean of healthy population norms.

Results: At baseline, most RADIANCE participants were cognitively preserved as assessed by PASAT (preserved 1164/1312 [89%]; impaired 148/1312 [11%]); while SUNBEAM participants were equally distributed regarding their cognitive status assessed by SDMT (preserved 689/1345 [51%]; impaired 656/1345 [49%]). In both trials, cognitively preserved participants were nominally significantly younger, with shorter disease duration, less physical disability and T2 brain lesion burden, and greater QOL and baseline brain volume than impaired participants (Table).

Table. Baseline disease characteristics in phase 3 RADIANCE and SUNBEAM participants by baseline cognitive status (impaired versus preserved)^a

Characteristic, mean (SD)	RADIANCE (PASAT)		SUNBEAM (SDMT)	
	Impaired (n=148)	Preserved (n=1164)	Impaired (n=656)	Preserved (n=689)
Age, years	38.5 (8.33) ^b	35.1 (8.80)	37.9 (9.05)	33.3 (8.93)
No. of relapses in last 12 mo	1.2 (0.52) ^c	1.3 (0.60)	1.3 (0.56)	1.3 (0.57)
No. of relapses in last 24 mo	1.7 (0.86)	1.8 (0.87)	1.7 (0.87)	1.7 (0.83)
Years since diagnosis	4.9 (5.59) ^c	3.5 (4.48)	4.3 (4.55) ^c	3.0 (4.06)
Years since onset	7.7 (6.37) ^c	6.3 (5.85)	8.1 (6.35) ^c	5.9 (5.86)
EDSS score	3.2 (1.19) ^c	2.4 (1.12)	3.0 (1.14) ^c	2.3 (1.01)
MSFC score	-1.1 (0.73) ^c	0.1 (0.60)	-0.4 (0.66) ^c	0.4 (0.46)
PASAT/SDMT score	23.7 (6.42) ^c	50.4 (7.98)	36.2 (6.62) ^c	57.5 (7.98)
Mean 25-foot walk test (sec)	7.9 (4.50) ^c	5.8 (2.74)	6.9 (3.67) ^c	5.6 (2.10)
Mean 9-hole peg test (sec)	27.0 (7.59) ^c	21.5 (5.61)	25.1 (7.66) ^c	20.9 (3.94)
MSQOL-54 score	65.5 (16.92) ^{d,e}	70.0 (15.66) ^d	65.2 (17.52) ^{d,e}	72.3 (15.95) ^d
Mental health composite score	65.6 (18.95) ^d	73.6 (17.49) ^d	65.6 (19.72) ^d	75.8 (17.01) ^d
Physical health composite score	62.4 (18.80) ^{d,e}	70.5 (17.51) ^d	62.9 (18.47) ^{d,e}	74.3 (16.51) ^d
Physical function score	62.7 (27.67) ^d	76.0 (23.56) ^d	65.9 (26.19) ^d	80.0 (22.41) ^d
Cognition function score	69.9 (24.47) ^d	77.6 (21.02) ^d	73.7 (22.07) ^d	80.6 (20.37) ^d
No. of GdE lesions	2.0 (3.77) ^f	1.7 (3.63) ^f	1.9 (3.45) ^{f,g}	1.5 (2.93)
Volume of T2 lesions, cm ³	17.4 (16.97) ^{f,g}	10.7 (12.74) ^f	18.2 (18.46) ^{f,g}	8.1 (9.05)
Whole brain volume, cm ³	1417.0 (82.69) ^f	1452.1 (74.55)	1422.6 (76.33) ^{f,g}	1473.6 (70.93)
Cortical GM volume, cm ³	512.2 (45.50) ^f	531.4 (42.39) ^f	507.8 (47.82) ^{f,g}	539.2 (39.94)
Thalamic volume, cm ³	14.8 (2.18) ^f	15.6 (1.84) ^f	14.5 (2.07) ^f	15.9 (1.64)

^aImpaired was defined as baseline PASAT or SDMT ≥ 1.5 standard deviations below the mean of healthy population norms. ^bnominal P-value <0.0001 for the standard mean difference (preserved - impaired/pooled standard deviation). ^cnominal P-value <0.01 for the standard mean difference (preserved - impaired/pooled standard deviation). ^dnominal P-value <0.05 for the standard mean difference (preserved - impaired/pooled standard deviation). ^en=148, n=1155, n=654, n=686, n=145, n=652, n=685, n=142, n=1131, n=640, n=673, n=1156, n=655, n=147, n=1164, n=1160, n=1181, n=651, n=1162.

BL, baseline; EDSS, Expanded Disability Status Scale; GdE, gadolinium-enhancing; GM, grey matter; MSFC, Multiple Sclerosis Functional Composite; MSQOL-54, 54-item Multiple Sclerosis Quality of Life; PASAT, Paced Auditory Serial Addition Test; SD, standard deviation; SDMT, Symbol Digit Modalities Test.

Table

Conclusion: Our analysis revealed that cognitive impairment at baseline is associated with older age, longer disease duration, and greater disease burden. Although these studies used different cognitive assessments and had dissimilar proportions of cognitively impaired participants, overall findings were consistent across studies.

Disclosure: Study funded by Celgene, a wholly-owned subsidiary of Bristol-Myers Squibb.

EPR3081

Transcriptomic analysis of reactive human iPSC-derived astrocytes induced by neuroinflammatory cytokines

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Background and aims: Astrocytes occupy a central place in neuroinflammatory diseases, such as multiple sclerosis (MS). Recent studies in mice have identified 2 states of astrocyte reactivity, A1 and A2, respectively induced by neuroinflammation and ischemia. However, due to the difficulty in obtaining human astrocytes, validity of these data in a human context remains to be established. Here, we aimed at better characterizing human astrocyte reactivity in different neuroinflammatory conditions. We took advantage of our recently published technique to obtain resting astrocytes from human iPSCs.

Methods: We generated hiPSC-derived astrocytes from healthy donors and MS patients and stimulated them with major neuroinflammatory cytokines (IL-6, IL-1 β and/or TNF α) to assess their transcriptomic profile in response to these stimuli.

Results: Transcriptomic analysis of reactive astrocytes showed 1st that each of these 3 cytokines leads to the modulation of a specific set of genes. 2nd, gene ontology analysis revealed that IL-6 triggered the upregulation of genes mainly involved in cell adhesion, CNS development and ion transport while IL-1 β and TNF α led to the upregulation of genes mainly involved in the inflammatory response, interferon signaling and defense against viruses.

Conclusion: In conclusion, our study reveals specific activation states of astrocytes in response to neuroinflammatory cues, suggesting distinct functionalities in different inflammatory contexts. Our data thus call for a more precise characterization of reactive astrocytes in a given disease to decipher their role in such conditions. Better understanding of these reactive states would lead to a better understanding of astrocyte roles in neuroinflammatory diseases and may allow identifying new therapeutic targets.

Disclosure: Nothing to disclose

EPR3082

Anterior optic pathway pathology in demyelinating CNS diseases

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Background and aims: To characterise pathologic features of pre-geniculate optic pathway involvement in CNS inflammatory demyelinating disorders.

Methods: Post-mortem samples of optic nerves, chiasm, and tracts from 46 cases (MS, n=30; NMOSD, n=6; ADEM, n=5; controls, n=5) were immunolabelled for myelin (PLP), inflammation (CD3, CD20, CD138, C9neo), acute axonal injury (B-APP), astrocytes (GFAP) and AQP-4.

Results: Demyelinated plaques were found in 83% of MS cases, with 76% of cases having active plaques. 43.4% of MS cases had B-APP positivity even in areas without demyelination. An association between plaque activity and B-APP positivity was found ($p < 0.001$). In MS, optic involvement followed an antero-posterior gradient: optic nerves had the largest demyelination area (65.2%; chiasm 45.2%; tract 33.7%; $p = 0.009$), percentage of active plaques (68.2%, 53.8%, 33.3%; $p = 0.053$), and axonal injury (38.2%, 31.6%, 9.5%; $p = 0.027$). In NMOSD, 2 cases with a history of optic neuritis had extensive demyelination, with the remaining cases - without optic neuritis history or demyelination - showed intense infiltration of CD3+ and CD68+ cells in the normal appearing white matter (NAWM) as seen in MS; the 33.3% of samples presented acute axonal injury. Meningeal inflammation was more frequent in NMOSD vs MS and ADEM, both considering CD3+/CD68+ cells (100%, 60%, 60.7%, $p = 0.006$) and B-cells (88.9%, 36%, 0%; $p < 0.001$).

Conclusion: Inflammation and axonal injury along the pre-geniculate pathway are frequent in MS and follow an antero-posterior gradient. Meningeal and NAWM involvement – generally considered typical of MS pathology – are also common in NMOSD without prior optic neuritis.

Disclosure: Nothing to disclose

EPR3083

Effects of Fingolimod and Natalizumab on Slowly Expanding Lesion Occurrence Over Two Years of Treatment in Relapsing-Remitting Multiple Sclerosis

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Background and aims: Fingolimod and natalizumab are highly effective treatments for relapsing-remitting multiple sclerosis (RRMS). We compared their effects on white matter lesions showing a 2-year progressive linear enlargement, a putative biomarker of smoldering inflammation.

Methods: RRMS patients starting fingolimod (n=25) or natalizumab (n=30) underwent 3T brain MRI scans at baseline, month 6, 12 and 24. We identified slowly expanding lesions (SELs) among baseline lesions, by linearly fitting the Jacobian of the non-linear deformation field between timepoints, obtained using T1- and T2-weighted scans. A threshold of annual increase $\geq 12.5\%$ was applied and neighbour voxels were grouped in clusters (≥ 10 voxels). Number, percentage, volume of lesions defined as SELs, and their average magnetization transfer ratio (MTR) and T1 intensity were calculated.

Results: Treatment-groups were matched for baseline variables. The proportion of patients showing ≥ 1 SEL was similar between the 2 treatments (fingolimod=76%; natalizumab=60%, $p = 0.21$). In the 2 groups, similar number (median [interquartile range]) (fingolimod=2 [0-6]; natalizumab=1 [0-5], $p = 0.27$) and volume (fingolimod=7.3 [3.2-14.6]; natalizumab=5.7 [2.7-15.1] ml, $p = 0.31$) of SELs, and percentages of lesions (fingolimod=4.2% [0.3-7.5]; natalizumab=1.8% [0.0-10.6], $p = 0.80$) and of lesional volume (fingolimod=0.4% [0.0-2.9]; natalizumab=0.1% [0.0-1.7], $p = 0.28$) defined as SELs were found. In both groups, compared to not-SELs, SELs showed significantly lower baseline MTR and T1 intensity ($p \leq 0.005$), without significant between-group differences and longitudinal changes.

Conclusion: T1-, T2-weighted and MTR sequences could identify chronic active lesions characterized by smoldering inflammation, ongoing demyelination and axonal loss. Natalizumab and fingolimod similarly influence SEL burden and prevent microstructural tissue damage accumulation both in SELs and not-SELs.

Disclosure: Nothing to disclose

EPR3084

Long-term Disease Stability Assessed by the Expanded Disability Status Scale in Patients Treated with Cladribine Tablets in the CLARITY and CLARITY Extension Studies

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Background and aims: Treatment with cladribine tablets 10mg (cumulative dose 3.5mg/kg [CT3.5] over 2 years) in CLARITY and CLARITY Extension reduced relapse rate and slowed disability progression versus placebo in patients with relapsing remitting multiple sclerosis (RRMS). This study aimed to evaluate long-term disease stability assessed by the Expanded Disability Status Scale (EDSS) in RRMS patients after treatment with CT3.5 in CLARITY and CLARITY Extension.

Methods: Patients randomised to CT3.5 in CLARITY, then placebo in CLARITY Extension (CP3.5, n=98), with ≥1 post-baseline EDSS measurement were included. EDSS score over time (CLARITY randomisation to end of follow-up in CLARITY Extension, including bridging interval between studies) was assessed at 6-monthly intervals, separate 3- and 6-month time intervals confirmed EDSS score progression from CLARITY baseline. EDSS score worsening/improvement in each year defined as any increase/decrease in minimum EDSS score at 6-monthly intervals; all other cases classed as stable.

Results: 5 years after CLARITY baseline, median CP3.5 EDSS score remained stable with values between 2.0–3.0 and median change of 0. At 5 years, median CP3.5 EDSS score (95% confidence interval) was 2.5 (2.0–3.5), versus 3.0 (2.5–3.5) at baseline (Figure 1). In each 12-month period, EDSS score stability was observed in >50% patients, and was observed in 53.9% of patients during Year 5 (Figure 2). Less than 30% of patients reached 3- or 6-month confirmed EDSS progression by Year 5.

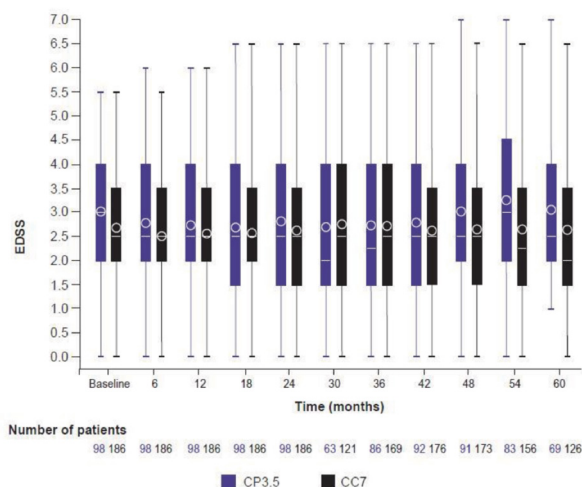


Figure 1: EDSS Score Over Time in Patients Treated with CP3.5 and CC7 (Line = Median. Circles = Mean. Box = Q1, Q3. Error bars reflect the minimum and maximum EDSS score. CC7, CT3.5 CLARITY, CT3.5 CLARITY Extension; CP3.5, CT3.5 CLARITY, placebo Extension; EDSS, Expanded Disability Status Scale)



Worsened: any increase in EDSS score ≥ 1 (baseline EDSS 0.5–4.5) OR ≥ 1.5 (EDSS 0) OR ≥ 0.5 (EDSS ≥ 5.0).

Improved: any decrease in EDSS score ≥ 1 (baseline EDSS 1–4.5) OR ≥ 0.5 (EDSS ≥ 5.0).

Stable: all remaining cases i.e. increase or decrease < 1.0 (baseline EDSS 0.5–4.5) OR < 1.5 (EDSS 0) OR no change (EDSS ≥ 5.0).

Figure 2: Change in EDSS Score in Each 12 Month Period Up to 5 Years in the CP3.5 and CC7 Patient Groups (CC7, CT3.5 CLARITY, CT3.5 CLARITY Extension; CP3.5, CT3.5 CLARITY, placebo Extension; EDSS, Expanded Disability Status Scale.)

Conclusion: EDSS score was stable up to 5 years post-CLARITY baseline for the CP3.5 group. Between 20-30% of patients demonstrated improvement in EDSS score versus baseline each year.

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EPR3085

Efficacy and safety of alemtuzumab in RRMS patients in a real-world experience of a specialized MS centre

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Background and aims: Alemtuzumab is a very high effective treatment for relapsing-remitting multiple sclerosis (RRMS), though a wide range of side effects might be expected. Our aim is to describe its efficacy and safety in a real-world context.

Methods: Prospective collection of clinical, radiological and safety variables in RRMS patients treated with Alemtuzumab from April 2015 to January 2020 in a specialized MS centre.

Results: 50 patients received a 1st infusion and were included. 46 patients had at least 1 year of follow-up and 27 at least 2 years. At baseline, they were mainly young (mean age at first infusion of 34.4 years, SD \pm 8.80) and active (median ARR of 0.86, IQR 0.64-1.76). ARR was decreased by 94.1% ($p < 0.0001$) and 94.8% ($p < 0.0001$) and EDSS remained stable or improved in 95.6% and 89.3% after 1 and 2 years, respectively. After 2 years ($n = 25$), 68% of patients were free of radiological activity. NEDA3 was achieved in 60.9% and 58.3% of patients after 1 and 2 years and 83.3% between years 1 and 2 (mainly due to radiological activity). Treatment-naïve patients with 2 years of follow-up ($n = 12$) remained 100% free of relapses and disability progression after 2 years. Infusion-related reactions and mild-moderate infections were highly incident. Dysthyroidism occurred in 22.0% of patients.

Conclusion: In line with the pivotal trials, Alemtuzumab shows an early high effect, which could be higher in treatment-naïve patients. Similar infusion-related and autoimmunity side effects were observed, but with a higher rate of mild-moderate infections.

Disclosure: Nothing to disclose

EPR3086

The influence of glatiramer acetate on dendritic cells mediated Th17-immune response in multiple sclerosis.

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Background and aims: Glatiramer acetate (GA) can influence on multiple sclerosis (MS) pathogenesis by modulating T-cell function. The effect of GA on Th17-cells which play crucial pathogenic role in MS is not sufficiently investigated. The aim of this study was to clarify the effects of GA on Th17-immune response in MS.

Methods: 25 MS patients and 25 healthy controls were examined. Peripheral blood mononuclear cells (PBMCs) and CD4⁺-T-cells were stimulated with anti-CD3/anti-CD28-antibodies in the absence/presence of GA at concentrations of 50 μ g/ml and 100 μ g/ml whereafter levels of IL-17, IFN-gamma and IL-10 in supernatants were determined by ELISA. Immature DCs were stimulated with lipopolysaccharide in the absence/presence of GA (50 μ g/ml and 100 μ g/ml) whereafter levels of IL-6 and IL-1 beta were determined. CD4⁺-T-cells were also stimulated with GA pretreated DCs whereafter IL-17 and IFN-gamma were assessed.

Results: GA reduced IL-17 production by stimulated PBMCs and CD4⁺-T-cells in both concentrations in all groups ($p < 0.001$) and IFN-gamma production in MS patients ($p < 0.001$). There was no effect of GA at concentration of 50 μ g/ml on IL-10 production in both groups, while at concentration of 100 μ g/ml GA suppressed IL-10 production in healthy subjects ($p < 0.001$). At concentration of 100 μ g/ml GA suppressed IL-1 beta production by DCs in both groups ($p < 0.01$) and IL-6 production in healthy subjects ($p < 0.01$). The treatment of DCs with GA at concentration of 100 μ g/ml suppressed cytokines production by CD4⁺-T-cells in both groups ($p < 0.05$).

Conclusion: These data suggest an inhibitory effect of GA on Th17-immune response in MS.

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EPR3087

Recurrent optic neuritis: 20 years experience in a multiple sclerosis unit.

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Background and aims: Recurrent optic neuritis (ON) can be the first manifestation of multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), chronic relapsing inflammatory optic neuropathy (CRION) or relapsing inflammatory optic neuropathy (RION) among others. Clinical presentation, immunology tests and neuroimaging may help in the differential diagnosis.

Methods: Patients with ≥ 2 ON were retrospectively collected from 1998 to 2018. Clinical, radiological, laboratory, therapeutic and prognostic variables were assessed.

Results: 19 patients with 46 episodes of ON were included, 15/19 (79%) females, with a mean (SD) age at onset of 31 ± 12 years and a median follow-up of 5.5 years (IQR 4-14). 8 patients met criteria of MS, 6 of CRION, 2 of NMOSD, 2 of RION and 1 systemic lupus erythematosus. 2 patients had simultaneous bilateral ON at onset (1 CRION and one NMOSD). Oligoclonal bands were only positive in 5/7 (71%) of MS patients and anti-AQP4 antibodies were positive in 1/2 NMOSD patients. None of the patients had positive anti-MOG antibodies. A normal final visual function was more frequently observed in MS (50%) and CRION (33%) than in NMOSD or RION patients (0%). Immunosuppressor treatment was frequently started in NMOSD (100%), CRION (83%) and MS (62.5%) but not in RION (0%) after a median of 47 months (IQR 11-93), being rituximab (46%) and azathioprine (31%) the most frequently chosen, with only one recurrent ON (NMOSD).

Conclusion: In our experience recurrent ON is a disabling entity with a wide range of possible etiologies. Consequently, the final diagnosis and the start of a specific immunosuppressor treatment may be delayed.

Disclosure: Nothing to disclose

EPR3088

Description of clinical and therapeutic characteristics of Multiple Sclerosis (MS) in elderly patients in our population

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Background and aims: Improvement of global healthcare and life expectancy increase has led to an enhanced number of elderly patients with MS. This raises a lot of questions about the course and therapy in this specific population. We describe the characteristics of MS patients ≥ 55 years old in our population.

Methods: Of a total population (TP) of 248 patients from our database we selected 65 with age ≥ 55 years and studied their characteristics. The average age in this group was 61 (rank 55-76) being 62% women and 32.3% men.

Results: The average age of diagnosis was 44 years (34 in TP). The average time of diagnostic delay was 2.55 years (1.74 in TP), of delay of treatment beginning was 6.10 years (3.65 in TP), and of delay between the diagnosis and the beginning of treatment was 3.5 years (1.95 in the TP). In the group ≥ 55 years, 78.5% were RRMS form (90% in TP), 1.5% PPMS (1.6% in TP) and 20% SPMS (8.5% in TP). Average EDSS in ≥ 55 years patients was 3.77 (2.9 in TP), and 46.15% of this subgroup had a score < 4 (67.7% in TP). Regarding the treatment, 56% received injectable drugs: interferon or glatiramer.

Conclusion: In our MS population, 26.6% are older patients. They have increased disability and more frequent secondary progressive course than our TP. Injectable drugs are the most disease-modifying drugs used. We remark that it's necessary enhance the knowledge about the pathophysiology, the influence of comorbidities, and evolution of MS in aged patients, to optimize the risk/balance of therapies.

Disclosure: Nothing to disclose

EPR3089

Relationships between selected parameters of spectral optical coherence tomography and visual evoked potentials in the natural history of multiple sclerosis.

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Background and aims: Spectral optical coherence tomography (SOCT) and pattern-reversal visual evoked potentials (pVEPs) remain valuable markers of the visual pathway damage in multiple sclerosis (MS). The aim of the study was to assess relationships between selected SOCT and pVEPs parameters in treatment-naïve patients with clinically isolated syndrome (CIS) and various MS types.

Methods: We enrolled 15 CIS patients and 111 MS patients (Table 1). The history of optic neuritis (ON) was confirmed in the case of: 3 eyes from the CIS patients, 35 eyes from the relapsing-remitting MS patients, 12 eyes from the secondary progressive MS patients, 1 eye from the primary progressive patients and 14 eyes from the benign MS patients. All participants underwent SOCT (Copernicus HR-SOCT) with peripapillary retinal nerve fiber layer (pRNFL) thickness and total macular volume (TMV) evaluation as well as pVEPs with P100 wave latency assessment.

Investigated subgroups	No. of patients	The median disease duration (years)	The median EDSS score (points)
CIS	15	1	0
Relapsing-remitting MS (RRMS)	65	3	2.0
Secondary progressive MS (SPMS)	14	9.5	4.3
Primary progressive MS (PPMS)	11	4	5.0
Benign MS (BNMS)	21	16	2.0

Table 1. The clinical characteristics of the investigated patients.

Results: A significant correlation was found between the mean TMV and P100 latency in the eyes of patients with CIS and all assessed MS variants (Figure 1). A significant correlation was found between the the mean pRNFL thickness and P100 latency in the eyes of MS patients. There was no significant correlation between the mean pRNFL thickness and P100 latency in the eyes of CIS

patients (Figure 2).

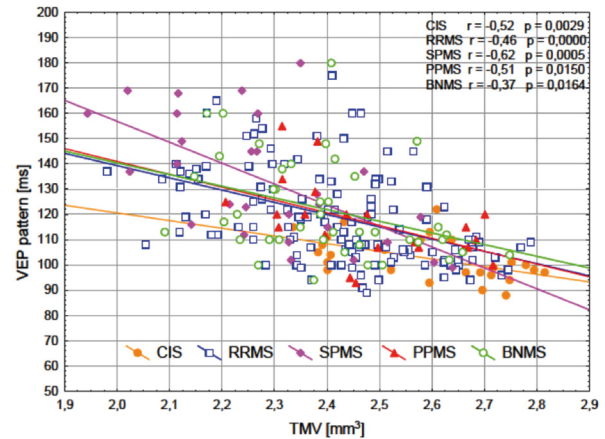


Figure 1. Relationship between TMV and latency of P100 pVEPs in patients with various clinical forms of MS and CIS.

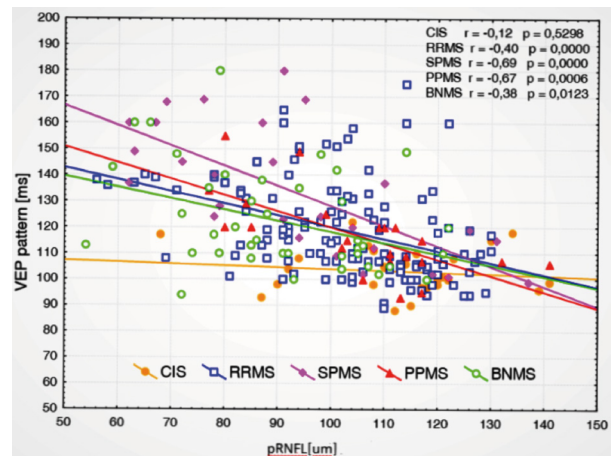


Figure 2. Relationship between pRNFL thickness and latency of P100 pVEPs in patients with various clinical forms of MS and CIS.

Conclusion: In the natural history of multiple sclerosis, the strongest correlation between the analyzed SOCT parameters (pRNFL, TMV) and pVEPs P100 wave latency was found in SPMS patients. In the case of CIS patients, only the mean TMV was significantly correlated with P100 latency.

Disclosure: Nothing to disclose

EPR3090

Long-term natalizumab treatment is related to reduced deep-brain atrophy and increased choline and glutamate levels in relapsing-remitting multiple sclerosis

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Background and aims: Natalizumab (NA) is an effective treatment for relapsing-remitting multiple sclerosis (RRMS). This study evaluated the long-term effects of NA treatment on grey-matter (GM) atrophy, as well as metabolite concentrations in GM, normal-appearing white matter (NAWM), and lesional WM (LWM) in RRMS.

Methods: Patients who switched to NA 4 years prior were matched to patients continuing 1st-line treatment (IFN/GA) and healthy controls (HCs). At baseline (Y4) and after 2 years (Y6) GM volumes and metabolite concentration ratios to total creatine (N-acetylaspartate, choline, myo-inositol, and glutamate and glutamine) were measured for NA (n=18/11; Y4/Y6), IFN/GA (n=20/14) and HCs (n=19/16). Changes over time and between groups were assessed with Bonferroni-corrected linear mixed models.

Results: Over time, IFN/GA patients showed a significant reduction in deep GM volume (p<0.001) and particularly thalamic volume (p<0.001), which were not seen in NA patients. In addition, over time, only NA patients showed an increase of glutamate levels in NAWM (p<0.001), and choline in GM (p=0.004). No significant differences between patient groups were found at Y4, and patients did not show changes in cognitive and neurological performance over time.

Table 1. Demographics and clinical measurements at baseline in controls, first-line and natalizumab treated patients

	HC	IFN/GA patients	NA patients	Pairwise comparisons	
				HC vs MS	IFN/GA vs NA
Age	38.26 (±8.5)	41.50 (±7.0)	37.50 (±8.7)	F=1.3 p=0.270	F=2.5 P=0.126
Gender (F/M)	11/8	10/10	14/4	χ ² =1.6 p=0.446	χ ² =6.2 p=0.045*
Education *	7 (6-7)	6 (4-6)	6 (4-7)	χ ² =14.3 p=0.014*	χ ² =2.6 p=0.635
Handedness (L/R)	4/15	2/18	1/17	χ ² =3.6 p=0.169	χ ² =3.3 p=0.188
Avg. cognition	-0.01(±0.6)	-0.97(±0.8)	-0.71(±0.8)	F=17.299 p<0.001*	F=1.0 P=0.328
EDSS *		2.50 (1.6-3.0)	3.00 (2.4-6.0)		F=2.8 p=0.104

All values per group represent means and standard deviations for continuous variables, the values represent medians and interquartile distance (*) or frequencies for categorical variables. HC=healthy control, NA=natalizumab, IFN/GA=interferon or glatiramer acetate treatment, F is female, M is male, L is left, R is right, EDSS=expanded disability status scale. Education represents the highest level of education attained in the Dutch system (1-7), average cognition represents the average z-score (compared to controls) of the entire expanded Brief Repeatable Battery of Neuropsychological tests (BRB-N).

Demographics and clinical measurements at baseline in controls, 1st-line and natalizumab treated patients

Table 2. MRI measures of atrophy and metabolites in both patient groups over time

	Baseline	Follow-up	F-statistic	p-value
<i>NA patients</i>				
NDGMV	-2.36 (±1.28)	-2.47 (±1.82)	0.0	0.978
NTV	-2.57 (±1.39)	-3.01 (±2.06)	0.6	0.459
GM Glu	-1.59 (±1.07)	0.08 (±1.38)	22.1	0.004*
NAWM Cho	-0.62 (±1.08)	1.12 (±1.60)	42.0	<0.001*
<i>IFN/GA patients</i>				
NDGMV	-2.47 (±1.99)	-3.08 (±2.03)	25.4	<0.001*
NTV	-2.74 (±1.98)	-3.45 (±2.09)	30.4	<0.001*
GM Glu	0.11 (±1.81)	0.51 (±0.89)	0.6	0.445
NAWM Cho	-0.08 (±1.52)	-0.82 (±2.48)	0.9	0.350

All values represent mean z-scores (compared to controls within the time point) and standard deviations; F- and p-values are based on linear mixed models. NA=natalizumab, IFN/GA=interferon or glatiramer acetate treatment, NDGMV=normalized deep grey matter volume, NTV=normalized thalamus volume, GM=grey matter, Glu=glutamate, NAWM=normal-appearing white matter, Cho=choline.

MRI measures of atrophy and metabolites in both patient groups over time

Conclusion: In this study, long-term NA treatment was related to a preservation of deep grey matter volumes and increases in glutamate and choline levels, thought to reflect increased metabolism and membrane turnover. IFN/GA patients, however, showed significant deep-brain atrophy and no metabolite change. These findings could indicate a more neuroprotective profile for NA compared to IFN/GA in RRMS.

Disclosure: This study was funded by a research grant from Biogen.

EPR3091

Long-term Efficacy of Ozanimod in Relapsing Multiple Sclerosis in DAYBREAK: An Open-Label Extension of the Phase 3 SUNBEAM and RADIANCE Trials

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Background and aims: Ozanimod, a sphingosine 1-phosphate receptor 1/5 modulator, significantly reduced annualised relapse rate (ARR) in phase 3 relapsing multiple sclerosis (RMS) trials. We evaluated long-term efficacy of ozanimod in RMS in an open-label extension (OLE) trial. **Methods:** RMS participants who completed a phase 3 double-blind ozanimod trial (SUNBEAM [≥ 12 months], RADIANCE [24 months]) were eligible to enrol in an OLE (DAYBREAK) of ozanimod HCl 1mg/day. In this OLE interim analysis (data cutoff 31/1/2019), ARR, time to 1st relapse, number of new/enlarging T2 and gadolinium-enhancing (GdE) MRI brain lesions, and 3- and 6-month confirmed disability progression (CDP) were analysed descriptively by randomisation to intramuscular interferon β -1a 30 μ g/wk or oral ozanimod HCl 0.5 or 1mg/d in the double-blind trials.

Results: Of 2,666 participants enrolled, 2,394 completed the phase 3 parent trials and 2,257 entered DAYBREAK (interferon: n=741; ozanimod 0.5mg:n=756; ozanimod 1mg:n=760). In DAYBREAK, ARR and numbers of new/enlarging T2 and GdE lesions remained low in the continuous ozanimod 1mg group and were reduced versus

parent trials in those who switched to ozanimod 1mg in DAYBREAK from ozanimod 0.5mg or interferon in the parent trials (Figures 1–3). Median time to 1st relapse in the continuous ozanimod 1mg group was 1,750 days. CDP rates were low and comparable between parent-treatment groups.

Figure 1. Annualised Relapse Rate During Phase 3 Parent and OLE (DAYBREAK) Trials.

Negative binomial regression was used to calculate the annualised relapse rate in the phase 3 (parent) and OLE trials, with adjustments for parent-treatment group, region (Eastern Europe vs rest of world), age at parent baseline and parent-baseline number of gadolinium-enhancing lesions, with time on treatment as an offset term. The phase 3 (parent) treatment period includes parent trial day 1 through the end of treatment during the parent trial; the OLE treatment period is from OLE trial day 1 through the last dose date or the data-cutoff date, whichever occurs first.

CI, confidence interval; IFN, interferon; OLE, open-label extension.

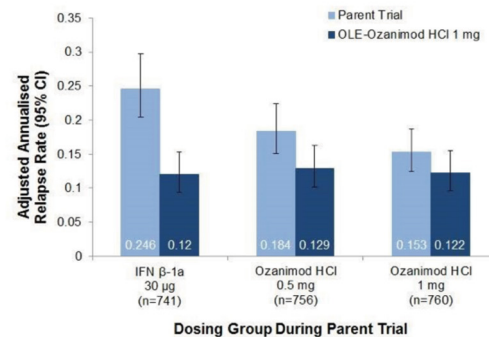


Figure 1

Figure 2. Number of New/Enlarging T2 Lesions Per MRI Scan at Month 12 in the Phase 3 Parent Trials and Months 12 and 24 in the OLE Trial (DAYBREAK).

^aFor the parent trial data, baseline refers to parent trial baseline, and for the OLE trial data, baseline refers to the OLE baseline.

IFN, interferon; MRI, magnetic resonance imaging; OLE, open-label extension; SE, standard error.

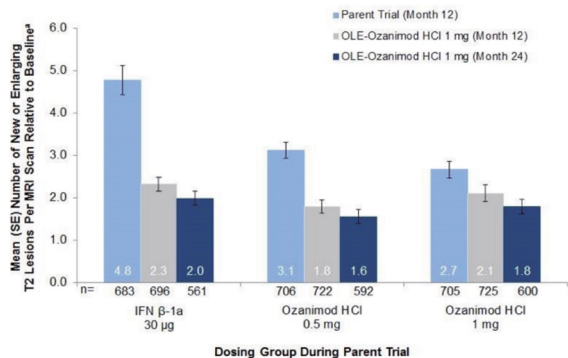


Figure 2

Figure 3. Number of GdE Lesions at Month 12 in the Phase 3 Parent Trials and Months 12 and 24 in the OLE Trial (DAYBREAK).

GdE, gadolinium-enhancing; IFN, interferon; OLE, open-label extension; SE, standard error.

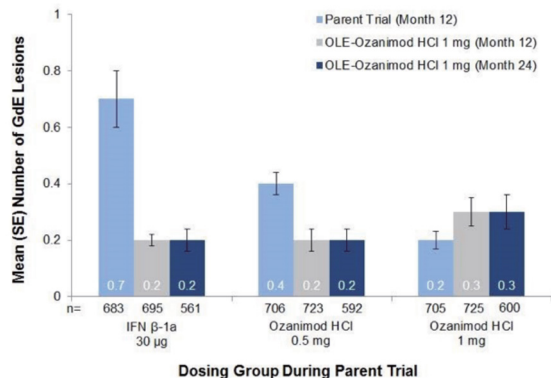


Figure 3

Conclusion: Participants on continuous ozanimod 1mg had sustained low ARR and lesion counts. ARR and lesion counts decreased among those who switched from ozanimod 0.5mg and interferon to ozanimod 1mg in DAYBREAK.

Disclosure: Study funded by Celgene, a wholly-owned subsidiary of Bristol-Myers Squibb.

EPR3092

Assessing the Duration of EDSS improvement After a Therapy Start: A New Statistical Approach Applied to the Long Term Extension of the PRISMS Study

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Background and aims: Incidence of expanded disability status scale (EDSS) improvement in multiple sclerosis (MS) has previously been studied as the incidence of progression, using Kaplan-Meier (KM) curves. However, in a chronic, progressive disease, improvement can be transient. Estimating prevalence of disability improvement over time, accounting also for improvement duration, is of interest.

Methods: In PRISMS-2, patients with relapsing-remitting MS were randomised to subcutaneous interferon-beta-1a (scIFN beta-1a) 22 μ g, 44 μ g, or placebo for 2 years. Only placebo and scIFN beta-1a 44 μ g groups were included in this analysis. At Year-2, placebo patients were re-randomised to scIFN beta-1a 22 μ g or 44 μ g (delayed scIFN beta-1a); scIFN beta-1a 22 μ g or 44 μ g patients continued their initial regimen (early scIFN beta-1a). Disability improvement defined as a 1-point decrease in EDSS from baseline confirmed at 6 months; improvement lost when EDSS score \geq baseline. Prevalence of patients with improved EDSS estimated as the difference between the KM estimators for the probability to experience improvement before time, and probability of returning to baseline before time.

Results: No significant difference in incidence of EDSS improvement estimated by KM curves between delayed and early scIFN beta-1a 44 μ g (Figure 1). Taking duration of improvement into account, the proportion of patients who showed an improved condition after 5 years was significantly different between delayed scIFN beta-1a and early scIFN beta-1a 44 μ g (Figure 2).

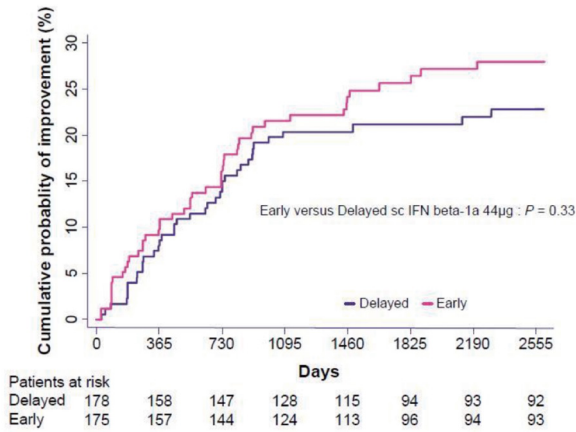


Figure 1: Cumulative Probability of Improvement in Early and Delayed sc IFN beta-1a 44 µg

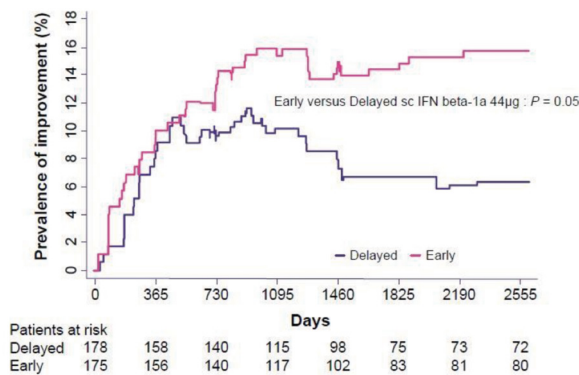


Figure 2: Prevalence of Improvement in Early and Delayed sc IFN beta-1a 44 µg

Conclusion: Early versus delayed scIFN beta-1a 44µg initiation did not significantly affect the number of improvement events from baseline, but did show significant differences in the proportion of patients who maintained disability improvement over 5 years.

Disclosure: The study was sponsored by Merck KGaA, Darmstadt, Germany.

EPR3093

CSF Neurofilament Light Chain for guiding individual treatment decisions in multiple sclerosis

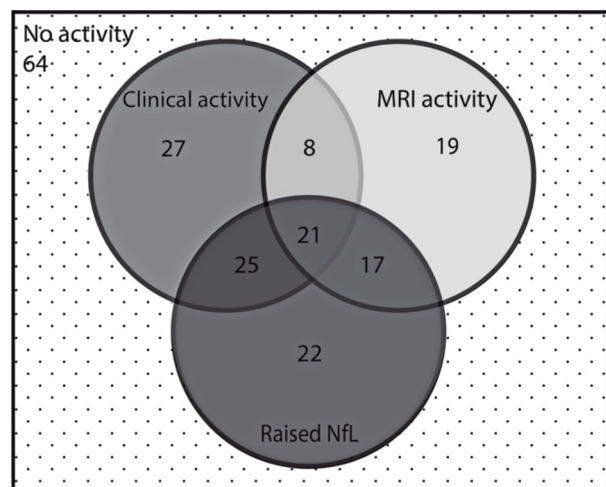
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Background and aims: CSF neurofilament light chain (NfL) levels are a biomarker of axonal damage. The goal of this study is to evaluate the effect of CSF NfL levels on disease-modifying drug (DMT) decisions and outcomes among multiple sclerosis (MS) patients.

Methods: We reviewed a study population of MS patients that had a CSF NfL measurement between December 2015 and July 2018 as a part of their routine clinical follow-up at BartsMS, London. We used NfL levels in parallel with clinical and radiological surrogates of disease activity to guide DMT decisions.

Results: We included 203 MS patients of whom 41.9% had a raised CSF NfL concentration. NfL levels were independently associated with clinical ($P=0.02$) and MRI activity measures ($P=2.78 \times 10^{-5}$). Increased NfL levels ($N=85$) did more frequently influence DMT decisions than clinical activity ($N=81$) or imaging ($N=65$) (Figure 1). In 22 cases, the sole marker of disease activity affecting DMT decisions were NfL levels. In progressive patients, 19.8% had DMT decisions in which NfL levels were the only contributing factor compared to 3.4% in relapsing patients. Higher CSF NfL levels were associated with proactive DMT decisions ($P=7.78 \times 10^{-15}$) and their EDSS change at follow-up was not significantly different from conservatively managed patients ($P=0.78$).



Venn-diagram illustrating how MS patients (N =203) exhibited disease activity.

Conclusion: Our data demonstrate for the 1st time that NfL levels can be integrated in routine clinical practice and complement established markers of disease activity to guide DMT decisions and improve outcome in MS patients.

Disclosure: Nothing to disclose

EPR3094

Withdrawn

EPR3095

Pregnancy outcomes in a French cohort of patients with Multiple Sclerosis: the MUSTANG project

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Background and aims: Since multiple sclerosis (MS) is most common in women of childbearing age, patients and neurologists are frequently confronted with questions regarding family planning and pregnancy. Pregnancy can be considered in all women with MS assuming they are provided counselling, especially to plan the use of Disease-Modifying Therapies (DMTs). Our study aims to increase knowledge about pregnancy-related issues in women with MS in France, and in particular to describe pregnancy outcomes, delivery characteristics and drug exposure.

Methods: A retrospective cohort study was performed on the French national health insurance database over the period 2010-2015 with all the 15-49 year-old, not sterile, women with MS. MS was identified if there was a long-term disease status for MS or at least one DMT reimbursement or at least one hospital admission with a diagnosis of MS. Pregnancies started between January 2010 and March 2015 were identified from their outcomes.

Results: Out of 48273 women with MS, 8466 women (18%) were pregnant at least once over the study period, accounting for 10975 pregnancies. Outcomes were 75% of live births, 17% of elective or therapeutic abortions, 5% of spontaneous abortions, 1% of ectopic pregnancies, 0.5% of stillbirths and 2% of other issues. Incidence rates of pregnancy will be calculated. Pregnancies outcomes according to DMT exposure before and during pregnancies will be described, as well as treatment stops or switches.

Conclusion: This ongoing study will provide detailed data on pregnancy-related issues in MS.

Disclosure: This work is supported by the Foundation for Multiple Sclerosis Research (ARSEP - Fondation pour l'aide à la recherche sur la sclérose en plaques).

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EPR3096

An automated tool for assessment of multiple sclerosis lesions and brain volume - a promising addition to the visual scan inspection

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Background and aims: Magnetic resonance imaging (MRI) is an important tool for the diagnosis and monitoring of multiple sclerosis (MS). We hypothesize that utilizing software designed for evaluating MRI data and providing detailed quantitative measurements in MS will provide added value to the standard neuroradiological evaluation.

Methods: We examined 56 MS patients (mean age 35 years, 70% females and 96% relapsing-remitting MS) both clinically and with brain MRI 1 and 5 years after diagnosis. The T1 and FLAIR brain MRI sequences for all patients were analysed using the LesionQuant[®] (LQ). These data were compared with data from structured visual evaluations of the MRI scans performed by a neuroradiologist, including assessments of the cortical atrophy and lesion count (>0-<10, ≥10-<20 or ≥20).

Results: Lesion count was similarly evaluated by the LQ software and the neuroradiologist in 84% (n=47) of the MS patients at 1 year after diagnosis. LQ detected a reduction in whole brain volume in 51 of 56 patients between the assessment at year 1 and 5 after diagnosis, while the neuroradiologist described 1 patient with increased cortical atrophy in the same period.

Conclusion: For the number of MS lesions we demonstrated good correlation between the assessment done by LQ and the neuroradiologist. LQ-analyses identified reduction in whole brain volume over time far better than when assessed by the neuroradiologist. In conclusion, assessment by LQ seems like a promising addition to the evaluation by the neuroradiologist, providing an automated tool for assessment of MS lesions and brain volume in MS patients.

Disclosure: The project was supported by grants from The Research Council of Norway (NFR, grant number 240102 and 223273) and the South-Eastern Health Authorities of Norway (grant number 257955 and 2019111).

EPR3097

Safety of Alemtuzumab in RRMS Patients During the Peri-infusion Period: Clinical Trial and Postmarketing Experience

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Background and aims: In the CARE-MS trials (NCT00530348, NCT00548405), alemtuzumab significantly improved efficacy outcomes versus subcutaneous interferon beta-1a over 2 years in RRMS patients. Here we present incidences of acute adverse events (AEs) reported during infusion and in the days following in the CARE-MS studies and postmarketing setting.

Methods: In the CARE-MS studies, all AEs and medical events of interest were recorded. Infusion-associated reactions (IARs) in clinical trials were defined as any AE with onset during or ≤24 hours after an alemtuzumab infusion. Safety monitoring continues post marketing using a Risk Management Plan/Risk Evaluation and Mitigation Strategy; acute AEs occurring within 1 week of infusion post marketing are presented.

Results: In the pooled CARE-MS studies (N=811), IARs occurred in 90% of patients; incidence of serious infections was 3%. As of 31 March, 2019, 25,292 patients had received alemtuzumab post marketing; acute AEs within 1 week of infusion post marketing included haemorrhagic stroke/pulmonary alveolar haemorrhage (reporting rate 7.1/10,000 patients treated), other stroke (0.8/10,000), myocardial infarction (MI; 2.0/10,000), and cervicocephalic arterial dissection (1.6/10,000). Reported cases of temporally associated pulmonary alveolar haemorrhage were unrelated to anti-glomerular basement membrane disease. Some patients who experienced MI were aged <40 years and had no risk factors for ischemic heart disease; some cases had temporarily abnormal blood pressure and/or heart rate during infusion.

Conclusion: Notable acute AEs temporally associated with alemtuzumab infusions were predominantly IARs and serious infections in clinical trials. Additional postmarketing events of interest included pulmonary alveolar haemorrhage, MI, stroke, and cervicocephalic arterial dissection.

Disclosure: STUDY SUPPORT: Sanofi and Bayer HealthCare Pharmaceuticals.

EPR3098

Effect of Siponimod on Grey Matter Atrophy in Patients with Secondary Progressive Multiple Sclerosis: Subgroup Analyses from the EXPAND Study

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Background and aims: Several studies suggest that grey matter (GM) atrophy is associated with long-term irreversible disability accumulation and cognitive decline. As reported previously, siponimod significantly reduced GM atrophy in patients with secondary progressive multiple sclerosis (SPMS). Here we investigated the effect of siponimod versus placebo in reducing cortical GM (cGM) and thalamic atrophy in subgroups of SPMS patients from the Phase 3 EXPAND study.

Methods: Percent volume change in cGM and the thalamus relative to baseline at Month (M)12 and M24 was assessed (EXPAND per protocol set, N=1560). The effect of siponimod versus placebo was determined using a mixed-model for repeated measures in patient subgroups defined by age and disease characteristics.

Results: In the placebo group, percentage volume change in cGM from baseline to M24 was similar across all subgroups (-1.17 to -0.94); whereas for thalamus it differed (-3.56 to -1.31) and was more pronounced in subgroups 'with gadolinium-lesion activity' (-3.56), 'active disease' (-2.15), 'age ≤45 years' (-2.12), and 'disease duration ≤15 years' (-2.09). Across the subgroups studied, siponimod reduced cGM atrophy versus placebo by 48% to 116% (p<0.01) and thalamic atrophy by 31% to 68% (p<0.05). Details on select subgroups in Table; further data on all subgroups will be presented.

Parameters	No. of patients ^a (siponimod/ placebo)	cGM		Thalamus	
		siponimod vs placebo (% relative reduction)		siponimod vs placebo (% relative reduction)	
		M12	M24	M12	M24
All patients	692/337	0.01 vs -0.60 (102%)***	-0.39 vs -1.04 (63%)***	-0.47 vs -0.94 (50%)**	-1.02 vs -1.77 (42%)***
Age ≤45 y	246/120	0.10 vs -0.61 (116%)***	-0.30 vs -0.94 (68%)***	-0.38 vs -1.16 (67%)***	-0.82 vs -2.12 (61%)***
Age >45 y	466/217	-0.04 vs -0.60 (93%)**	-0.45 vs -1.08 (58%)***	-0.53 vs -0.82 (35%)*	-1.12 vs -1.63 (31%)*
EDSS score <6	319/165	0.02 vs -0.59 (103%)***	-0.37 vs -1.04 (64%)***	-0.40 vs -0.98 (59%)**	-0.98 vs -1.71 (43%)*
EDSS score >=6	373/172	0.00 vs -0.61 (100%)***	-0.42 vs -1.04 (60%)***	-0.54 vs -0.90 (40%)*	-1.00 vs -1.88 (47%)**
Active disease ^b	347/169	-0.02 vs -0.68 (97%)***	-0.50 vs -1.14 (56%)***	-0.74 vs -1.24 (40%)*	-1.41 vs -2.15 (34%)*
Non-active disease	344/167	0.04 vs -0.53 (108%)***	-0.27 vs -0.94 (71%)***	-0.20 vs -0.63 (68%)*	-0.56 vs -1.34 (58%)**
No prior DMT	152/74	-0.08 vs -0.71 (89%)***	-0.61 vs -1.36 (55%)***	-0.79 vs -1.47 (46%)*	-1.57 vs -2.64 (41%)*
Prior DMT	540/263	0.04 vs -0.57 (100%)***	-0.33 vs -0.94 (65%)***	-0.38 vs -0.78 (51%)**	-0.85 vs -1.53 (44%)**

***p<0.0001; **p<0.001, *p<0.05

^aPer-protocol set, patients with major protocol deviations and data after the treatment switch were excluded from the analysis

^bActive disease defined as the presence of relapses in the 2 years before screening and/or ≥ T1 Gd⁺ lesion at baseline cGM, cortical grey matter; DMT, disease modifying therapy; EDSS, expanded disability status scale; Gd⁺, gadolinium enhancing; M, month

Data for additional subgroups by disease duration, presence or absence of relapses and Gd⁺ lesions will be presented in the poster

Percentage brain volume change from baseline at Month 12 and 24, as assessed by mixed model for repeated measures

Conclusion: Siponimod consistently slowed cGM and thalamic atrophy across all SPMS patient subgroups, including those with less active disease and higher disability. These effects on GM atrophy are in line with the favorable impact of siponimod on long-term clinical outcomes.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

EPR3099

Pregnancy Outcomes in Patients Treated with Ocrelizumab

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Background and aims: Ocrelizumab is approved for the treatment of relapsing forms of and primary progressive multiple sclerosis (MS). As many patients with MS are women of reproductive age, pregnancy outcomes in ocrelizumab-exposed patients are important.

Methods: We report analyses of pregnancies in women who received ocrelizumab in clinical trials/post-marketing sources up to 31/03/2019. Contraceptive requirements for women of childbearing potential were per label (during treatment and for 6 or 12 months after the last infusion) or adapted in clinical trials (2 methods until 6 months or 48 weeks after the last infusion/until B-cell repletion [whichever longer]). In utero exposure was defined as the last infusion occurring within 3 months of conception or during pregnancy if the date was unknown.

Results: As of 31/03/2019, a total of 362 ocrelizumab-exposed pregnancies in women with either MS (N=267), rheumatoid arthritis/systemic lupus erythematosus (N=33; clinical trials only) or an unknown indication (N=62) have been reported. Of the 267 pregnancies in women with MS (mean maternal age of 33.2 years), 118 were considered to have foetal ocrelizumab exposure (no foetal exposure, n=47; foetal exposure unknown, n=102); preliminary outcomes include: 62 live births (57 healthy babies and 5 pre-term births), 86 ongoing pregnancies, 25 elective abortions, 10 spontaneous abortions, 1 stillbirth, 3 ectopic pregnancies, 22 lost to follow-up and 58 unknown/unreported outcomes.

Conclusion: Reviewed cases to date do not suggest an increased risk of adverse pregnancy outcomes, including spontaneous abortions or malformations, with ocrelizumab treatment. The current update remains in line with previous reports.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPR3100

Transactivation of endogenous retroviruses by the Epstein-Barr virus - pathophysiologically relevant key mechanism of multiple sclerosis?

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Background and aims: In Europe, more than 90% of all people are positive for Epstein-Barr virus (EBV) before the age of 30. Even without apparent immunodeficiency, EBV is involved in the pathogenesis of neoplasias, e.g. Hodgkin's and Burkitt's lymphomas. An association of EBV with the pathogenesis of multiple sclerosis (MS) is suggested. Interestingly, EBV seems to be able to transactivate so-called human endogenous retroviruses (HERV). If these integrated virus copies have intact open reading frames, their proteins could possibly contribute to auto-inflammatory and degenerative processes that are observed in the pathogenesis of autoimmune diseases such as MS. The hypothesized mechanism is shown (see figure attached).

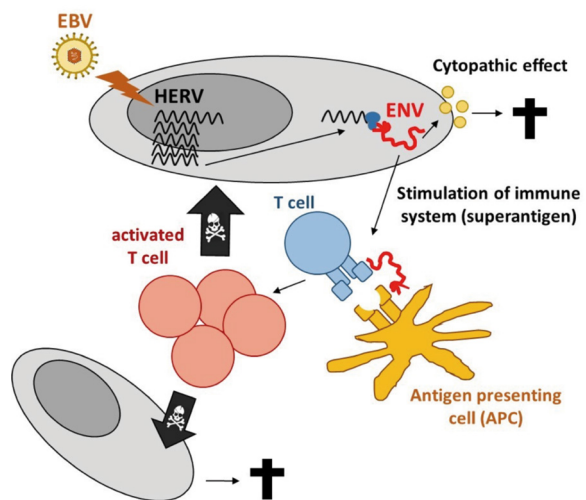


Figure following: Emmer, A., Staege, M.S., Kornhuber, M.E. The retrovirus/superantigen hypothesis of multiple sclerosis. *Cell Mol Neurobiol.* 2014, 34: 1087-1096.111

The retrovirus/superantigen-hypothesis

Methods: The expression of EBV and HERV sequences in EBV-immortalized lymphoblastoid cell lines of healthy donors (coLCL) and MS patients (MSLCL) was investigated by quantitative real-time PCR. In addition, we analyzed overall expression pattern in coLCL and MSLCL by DNA microarrays.

Results: The expression of EBV nuclear antigen 2 (EBNA2) was higher in MSLCL than coLCL. In MSLCL, a stronger correlation of EBNA2 and the lytic EBV life cycle transcripts of EBNA1 with HERV-K, -H and -W transcripts was observed. Furthermore, DNA microarray analyses showed higher transcript amounts of a known MS risk locus (HLA-DRB5, Chr. 6p21.3) in the MSLCL.

Conclusion: The study supports the hypothesis of an EBV-mediated transactivation of HERV in the pathogenesis of MS. The stronger correlation of HERV and EBV transcripts in MSLCL suggests that EBV lytic and latent programs may be regulated differently in B-cells of MS patients and healthy controls.

Disclosure: The authors declare, that the research has been granted by the Novartis Pharma GmbH.

EPR3101

Effect of Ofatumumab on B-cell Depletion and Efficacy Outcomes: Subgroup Analysis from the Pooled Phase 3 ASCLEPIOS I and II Trials

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Background and aims: Ofatumumab, the 1st fully human anti-CD20 monoclonal antibody with a monthly 20mg subcutaneous (s.c.) dosing regimen, demonstrated superior efficacy versus teriflunomide in the Phase 3 ASCLEPIOS I/II relapsing multiple sclerosis trials. We evaluated the effect of ofatumumab on B-cell depletion and efficacy outcomes in subgroups of patients defined by baseline characteristics.

Methods: In the ASCLEPIOS I/II trials, patients were randomised to receive s.c. ofatumumab 20mg (loading dose: Days 1, 7, and 14; maintenance dose: every 4 weeks from Week 4) or oral teriflunomide 14mg once-daily, for up to 30 months. B-cell numbers were determined at baseline and over the course of 96 weeks in all patients and in subgroups by quartiles of baseline body weight (kg): Q1 (<60.1), Q2 (≥60.1≤70.8), Q3 (≥70.8≤84.4), and Q4

(≥84.4). Annualised relapse rate (ARR) and 3-month/6-month confirmed disability worsening (3mCDW/6mCDW) were compared in different subgroups defined by demographics/baseline characteristics.

Results: In both the total population and across body weight subgroups, >90% of ofatumumab-treated patients achieved B-cell counts ≤40 cells/μL at Week 2, >97% at Week 4, and 96–100% over the 96 weeks. Reductions in ARR, 3mCDW and 6mCDW favoured ofatumumab versus teriflunomide across all subgroups. Similar efficacy was achieved between all subgroups; detailed data will be presented at the meeting.

Conclusion: The selected ofatumumab dosing regimen achieved rapid B-cell depletion in all patients, regardless of body weight. Furthermore, ofatumumab demonstrated similar treatment benefits across different subgroups (including body weight) consistent with the effects observed in the overall pooled ASCLEPIOS I/II population.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

EPR3102

Early Effect of Ofatumumab on B-cell Counts and MRI Activity in Relapsing Multiple Sclerosis Patients: Results from the APLIOS Study

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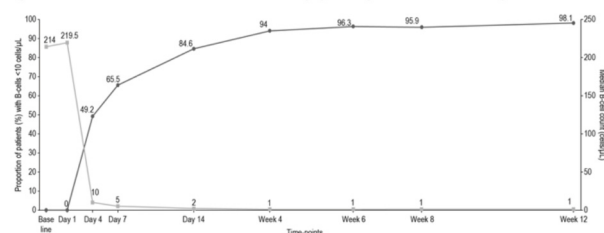
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Background and aims: Ofatumumab, the 1st fully human anti-CD20 monoclonal antibody with a monthly 20mg subcutaneous (s.c.) dosing regimen, of gadolinium-enhancing (Gd⁺) lesions versus teriflunomide in the Phase 3 ASCLEPIOS I/II relapsing multiple sclerosis (RMS) trials. We evaluated the onset of ofatumumab effect on B-cell depletion and magnetic resonance imaging activity in RMS patients in APLIOS.

Methods: APLIOS was a 12-week, open-label, Phase 2 bioequivalence study in 284 patients who received ofatumumab 20mg (0.4mL) s.c. loading doses on Days 1, 7 and 14, and a maintenance dose every 4 weeks (starting at Week 4) via an autoinjector pen (SensoReady) or a prefilled syringe. Suppression of CD19⁺ B-cells and Gd⁺ lesions was serially assessed over 12 weeks.

Results: Ofatumumab rapidly depleted circulating B-cells, from a median B-cell count of 219 cells/ μ L (Day 1) to 10 cells/ μ L (Day 4) and 1 cell/ μ L by the end of the loading regimen (Week 4); the proportion of patients with B-cell counts of <10 cells/ μ L over 12 weeks is presented in Figure. Ofatumumab reduced the mean number of Gd⁺ lesions from 1.5 (baseline) to 0.8, 0.3 and 0.1 by Weeks 4, 8 and 12, respectively; the proportions of patients free from Gd⁺ lesions at the corresponding time points were 66.5%, 86.7% and 94.1%.

Figure. Median B cell counts with ofatumumab treatment and the proportion of patients with B cells <10 cells/ μ L over 12 weeks



Median B-cell counts with ofatumumab treatment and the proportion of patients with B-cells <10 cells/ μ L over 12 weeks

Conclusion: Ofatumumab treatment resulted in a rapid, close-to-complete and sustained B-cell depletion over 12 weeks, leading to a profound reduction of Gd⁺ lesions in

RMS patients, consistent with the effects observed in the pooled Phase 3 ASCLEPIOS I/II population.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

EPR3103

Deep Grey Matter and Thalamic Nuclei Volume Loss Correlation With Whole-Brain Volume Loss in Patients With MS From the TEMSO Study

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Background and aims: Volume loss in deep grey matter (DGM) may correlate with disability progression and cognitive impairment in MS. Here, we examine the correlation of DGM and thalamic nuclei with whole-brain volume (WBV) changes over 2 years in placebo-treated patients from the TEMSO study (NCT00134563).

Methods: Blinded post hoc analysis of a randomly selected subset of placebo-treated patients was carried out by the Medical Image Analysis Center (Basel, Switzerland). The multiple automatically generated templates (MAGeT) algorithm measured nuclei volumes; structural image evaluation using normalisation of atrophy (SIENA) measured WBV. Spearman correlation analysis assessed the relationships between changes in nuclei and WBV over 2 years.

Results: Of 98 placebo-treated patients selected for analysis, 95 (97%) had evaluable data at Year 2; WBV loss was 1.37% over 2 years from baseline. Median volume losses in the nuclei ranged from 0%–5.52%, with the globus pallidus (5.52%) and pulvinar (4.51%) showing the greatest losses. Most nuclei volume losses significantly correlated with WBV loss at Year 2, and were highest for the pulvinar (Spearman coefficient for volume change at Year 2, 0.478; $P < 0.0001$), striatum (0.454; $P < 0.0001$), and central nuclei (0.440; $P < 0.0001$); however, the medial geniculate nucleus (0.173; $P = 0.0937$), anterior nuclei (0.114; $P = 0.2717$), and lateral geniculate nucleus (0.063; $P = 0.5445$) were not correlated with WBV loss.

Conclusion: Over 2 years, WBV loss in placebo-treated patients significantly correlated with nuclei volume losses, most strongly with the pulvinar, striatum, and central nuclei. These findings suggest MS impacts nuclei at variable rates, and potentially identify regions driving disability progression.

Disclosure: STUDY SUPPORT: Sanofi.

EPR3104

Preservation of relapse-free status in Year 2 of treatment with cladribine tablets by relapse-free status in Year 1

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Background and aims: Cladribine tablets (CT) are administered as 2 short courses at the beginning of Year-1 and 2. CT modelling data demonstrated a reduction in efficacy when the dose is < 3.5 mg/kg of body weight; a practical question for physicians is whether to continue treatment in Year-2 if patients experience disease activity in Year-1.

Methods: CLARITY was a 2-year placebo-controlled phase III study of CT in patients with relapsing-remitting multiple sclerosis. Relapse status in Year-2 was stratified by relapse status in Year-1.

Results: Of 433 patients randomised to CT 3.5 mg/kg, 353 (81.5%) did not experience a relapse in Year-1; 60 (13.9%) experienced ≥ 1 relapse; 4.6% unknown. In patients relapse-free in Year-1, 324 (91.8%) were relapse-free in Year-2; 25 (7.1%) experienced ≥ 1 relapse. In patients with ≥ 1 relapse in Year-1, 37 (61.7%) were relapse-free in Year-2; 17 (28.3%) experienced ≥ 1 relapse in Year-2. Of 437 patients receiving placebo, 299 (68.4%) were relapse-free in Year-1; 111 (25.4%) experienced ≥ 1 relapse; 6.2% unknown. In patients relapse-free in Year-1 in the placebo group, 233 (77.9%) were relapse-free in Year-2; 54 (18.1%) experienced ≥ 1 relapse. In patients in the placebo group who experienced a relapse in Year-1, 58 (52.3%) were relapse-free in Year-2; 38 (34.2%) experienced ≥ 1 relapse in Year-2.

Conclusion: Over 60% of patients who experienced a relapse in Year-1 of CT treatment were relapse free in Year-2, supporting the recommended dose of CT 3.5 mg/kg over 2 years for maximum treatment effect.

Disclosure: This study was sponsored by Merck KGaA, Darmstadt, Germany.

EPR3105

Long-term follow up of an Italian cohort of pediatric Multiple Sclerosis patients: real world data from San Raffaele Hospital.

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Background and aims: Multiple Sclerosis (MS) during childhood occurs in 3-10%. Pediatric MS (ped-MS) has a relapsing-remitting course and high relapse rate. Data on disease modifying treatments (DMTs) in ped-MS are scarce. We present baseline characteristics and long-term follow up (FU) of an Italian cohort of ped-MS subjects.

Methods: Data regarding MS onset, annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) score and treatments were collected at San Raffaele Hospital.

Results: 144 patients (101 females) were included, mean age at onset and at last FU were 14.4±2.6 and 24.7±6.1 years. 109 subjects had a monofocal onset. Mean ARR and median EDSS at onset were 4.5±4.9 and 1.5 (0-6). Mean FU was 9.8±6.6 years. Mean age at therapy initiation was 15.1±2.1 years and 59.7% of subjects were initially treated with interferon-beta (IFN). Induction was performed in 4.9%, while second-line treatments as 1st therapy were chosen in 17.4%. 50.5% of subjects were treated with Natalizumab, 13.2% as 1st therapy. 82.6% underwent at least 1 switch, the 1st after a mean of 2.3±3.3 years, predominantly to high-frequency IFN; subsequent switches were to 2nd-line therapy. ARR was reduced during 1st treatment (from 4.4±4.7 to 0.8±1.8) and last FU (0.02±0.1), $p > 0.001$ in both instances. 15.3% of subjects had an EDSS worsening, 76% had no evidence of clinical disease activity at last FU.

Conclusion: Ped-MS patients benefited from 1st-line agents, but the majority had to switch to more powerful DMTs. Our findings highlight the importance of treatment selection and accurate clinical FU in ped-MS population.

Disclosure: Nothing to disclose

EPR3106

Kallikrein 6, an emerging pharmacological target to promote remyelination in Multiple Sclerosis

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Background and aims: In Multiple Sclerosis (MS), treatments promoting remyelination are still an unmet medical need. Remyelination is achieved by oligodendrocyte precursor cells (OPCs) which regenerate myelinating oligodendrocytes. Kallikrein 6 (Klk6), a serine protease mainly secreted by mature oligodendrocytes, is increased in MS lesions, and impairs oligodendrocytes' maturation in vitro. Neutralizing antibodies or loss-of-function of klk6 reduce the severity of mouse models of MS. Therefore, Klk6 could be an interesting target to enhance remyelination in MS.

Methods: We studied Klk6 expression in a mouse model of focal demyelination and assessed the effects of a specific reversible Klk6 inhibitor on remyelination. Focal demyelination was induced by injection of lysophosphatidylcholine (LPC) in the dorsal funiculus of thoracic spinal cord of C57BL6/J mice. Immunohistochemistry targeting Klk6 and glial markers was performed during spontaneous remyelination. Another group was treated with the Klk6 inhibitor (330µg/kg, ip) or a vehicle between 5 and 14 days post injection (dpi), and oligodendroglial cells were quantified.

Results: In normal appearing white matter, Klk6 co-localized mostly with mature oligodendrocytes. In LPC lesions, Klk6 expression increased at 7-21 dpi and co-localized mainly with microglial markers. The density of differentiated oligodendrocytes was lower in the Klk6 inhibitor-treated group (450.8/mm² vs. 802.1/mm², $p = 0.015$), and these cells were mainly at the periphery of the lesions as compared to controls.

Conclusion: Klk6 expression is associated with neuroinflammation in LPC demyelinating lesions. Klk6 inhibitors may impair OPC differentiation and migration following demyelination. Klk6 and related proteolytic pathways could be a new therapeutic target for enhancing remyelination in MS.

Disclosure: Nothing to disclose

EPR3107

Alemtuzumab Outcomes Over 9 Years in RRMS Patients With Highly Active Disease From CARE-MS I and II (TOPAZ)

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Background and aims: Alemtuzumab efficacy and safety over 9 years were evaluated in patients from the CARE-MS and extension studies (NCT00530348, NCT00548405, NCT00930553, NCT02255656) that were previously treated with disease-modifying therapy and fulfilled highly active disease (HAD) criteria.

Methods: Analysis populations: CARE-MS II patients with HAD at core study baseline (9 total years; ≥ 2 relapses in the year prior to study start and ≥ 1 gadolinium [Gd]-enhancing lesion at baseline [definition 1], or ≥ 1 relapse in prior year and ≥ 1 Gd-enhancing lesions [definition 2]), and pooled CARE-MS I/II patients treated with subcutaneous interferon beta-1a (SC IFNB-1a) in the core study with HAD at extension baseline (7 total years; ≥ 1 relapses in prior year and ≥ 1 Gd-enhancing lesions OR ≥ 9 T2 lesions at baseline [definition 3]).

Results: In Years 0-2, annualised relapse rate (ARR) was decreased with alemtuzumab versus SC IFNB-1a (0.33 vs 0.65, $P=0.004$ [definition 1; $n=103$]; 0.28 vs 0.61, $P<0.0001$ [definition 2; $n=180$]). ARR remained low in Years 3-9 (0.16, 0.17, and 0.25, respectively, for patients meeting definitions 1, 2, and 3 [$n=23$]). Through Year 9, 49%-59% of HAD patients achieved 6-month confirmed disability improvement, and 55%-64% remained free of 6-month confirmed disability worsening after alemtuzumab. Median cumulative brain volume loss ranged from -0.64% to -1.80%. Serious adverse events in HAD patients were

similar to those in the overall population (39.8%-47.8% vs 44.8%).

Conclusion: Alemtuzumab improved outcomes versus SC IFNB-1a over 2 years in HAD patients, with maintained efficacy up to 9 years. Safety in HAD patients was similar to that in the overall study population.

Disclosure: STUDY SUPPORT: Sanofi

Muscle and neuromuscular junction disease 3

EPR3108

Development of new biomarkers for Spinal Muscular Atrophy (SMA) type III and IV: a multimodal longitudinal study.

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Background and aims: Aim of this study was the comprehensive characterisation of longitudinal clinical, electrophysiological and neuroimaging measures in type III and IV adult spinal muscular atrophy (SMA) to propose objective monitoring markers for future clinical trials.

Methods: 14 patients with type III or IV SMA underwent standardised assessments including muscle strength testing, dynamometry, functional evaluation (SMAFRS and MFM), MUNIX (abductor pollicis brevis; abductor digiti minimi, ADM; deltoid, tibialis anterior, TA; trapezius) and quantitative cervical spinal cord MRI to appraise segmental grey and white matter atrophy. Patients underwent a follow-up assessment with the same protocol 24 months later. Longitudinal comparisons were conducted using the Wilcoxon-test for matched data. Responsiveness was estimated as standardized response means (SRM) value and a composite score was generated based on the three most significant parameters.

Results: Significant functional decline was observed based on SMAFRS ($p=0.019$), pinch and knee flexion force ($p=0.030$ and 0.027), MUNIX and MUSIX value in the ADM ($p=0.0006$ and 0.043) and in TA muscle ($p=0.025$). No significant differences were observed based on cervical MRI measures. A significant reduction was detected in the composite score ($p=0.0005$, $SRM=-1.52$), which was the most responsive parameter and required a smaller number of patients in the estimation of sample size for clinical trials.

Conclusion: Quantitative force testing, SMAFRS and MUNIX readily capture disease progression in adult SMA patients. Composite multimodal scores increase predictive value and may reduce sample size requirements in clinical trials.

Disclosure: This study was sponsored by the Association française contre les myopathies (AFM-Téléthon).

EPR3109

Safety and Effectiveness of Eculizumab for Patients with Generalized Myasthenia Gravis in Japan: Interim Analysis of Post-Marketing Surveillance

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Background and aims: Eculizumab, a humanised monoclonal antibody targeted to terminal complement protein C5, is approved in Japan for treatment of patients with anti-acetylcholine receptor antibody-positive (AChR+) generalised myasthenia gravis (gMG) whose symptoms are difficult to control with high-dose intravenous immunoglobulin (IVIg) or plasmapheresis.

Methods: In Japan, all patients with gMG receiving eculizumab undergo post-marketing surveillance. This interim analysis assessed safety and effectiveness after 26 weeks of eculizumab treatment (data cut-off, October 2019).

Results: Data are available for 40 adult patients in Japan (female, 62.5%; mean age at eculizumab initiation, 51.0 years). 8 patients discontinued eculizumab during the 26-week follow-up. 1 patient with type 2 diabetes and hypertension died 10 days after the 1st eculizumab infusion due to atrial fibrillation and acute myocardial infarction (causal relationship with treatment unclear). Adverse drug reactions were reported by 7 patients (most frequently headache [n=3]). No meningococcal infections have been reported. The proportion of patients receiving ≥ 1 IVIg treatment/plasmapheresis decreased from 50.0%/35.0%, respectively, in the 6 months before eculizumab initiation to 12.5%/10.0%, respectively, during the 6 months after initiation. Frequency of IVIg use also decreased following eculizumab initiation (Figure 1). Mean (standard deviation) changes from baseline in MG-Activities of Daily Living and Quantitative MG scores were -3.7 (2.61) (n=27) and -5.6 (3.50) (n=26), respectively, at 12 weeks, and -4.3 (2.72) (n=26) and -5.6 (4.02) (n=24), respectively, at 26 weeks.

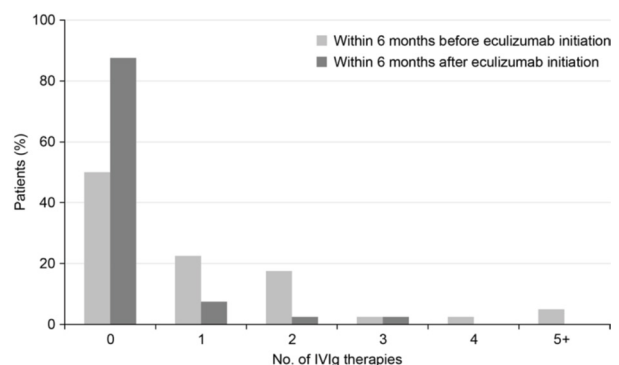


Figure 1. Use of IVIg before and after eculizumab initiation

Conclusion: In a real-world setting, eculizumab was effective and well tolerated for treatment of AChR+ gMG in adult Japanese patients who were refractory to IVIg or plasmapheresis.

Disclosure: This study was conducted by Alexion Pharma GK.

EPR3110

NEO1/NEO-EXT studies: Trends over time in exploratory efficacy of repeat avalglucosidase alfa dosing for up to 5.5 years in late-onset Pompe disease (LOPD) patients

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Background and aims: In NEO-EXT (NCT02032524), an ongoing NEO1 (NCT01898364) extension, long-term avalglucosidase alfa is being assessed in LOPD patients

who at NEO1 enrolment, were either naïve to enzyme replacement therapy (Naïve) or had received ≥ 9 months' avalglucosidase alfa (Switch). Analyses for exploratory efficacy trends over time are reported.

Methods: NEO1 patients received avalglucosidase alfa (5, 10, or 20mg/kg qow) for 6 months. In NEO-EXT, patients initially continued their NEO1 dose; transitioning to 20mg/kg during 2016. Repeated mixed measures model of pooled data (patients ever received 20mg/kg) analysed efficacy trends over up to 5.5 years' avalglucosidase alfa.

Results: 24 patients (age 20–78 years) enrolled in NEO1 (10 Naïve; 14 Switch), 19 continued to NEO-EXT (8 Naïve, 11 Switch), and 17 remained as of July 2019 (7 Naïve, 10 Switch); 2 NEO-EXT withdrawals (personal reasons). After 5.5 years, >2400 avalglucosidase alfa infusions had been received. Table 1 shows slope estimates for efficacy parameters. Upright % predicted FVC remained stable at the group level and in most patients. Upright % predicted MIP and MEP were more variable among individual patients, but remained stable overall. % predicted 6MWT distance remained stable among most patients in both groups. Improvement in 6MWT was observed in patients aged ≤ 50 years at NEO1 enrolment, in both groups. Avalglucosidase alfa was generally well-tolerated, and the safety profile in NEO-EXT consistent with NEO1.

	Slope (years)	
	Naïve patients (N=7)	Switch patients (N=12)
	Estimate (95% CI)	Estimate (95% CI)
FVC, % predicted	0.396 (-0.351, 1.144)	-0.331 (-0.778, 0.115)
MIP, % predicted	0.743 (-0.613, 2.100)	-0.946 (-2.001, 0.110)
MEP, % predicted	0.698 (-0.692, 2.088)	1.192 (-0.148, 2.531)
6MWT, distance walked, % predicted	-0.965 (-1.891, -0.038)	-1.216 (-2.027, -0.405)

6MWT, 6-minute walk test; CI, confidence interval; FVC, forced vital capacity; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure.
Random intercept model assuming an unstructured covariance structure with time (years) as fixed effect and intercept as random effect.

Table 1: Estimates of linear mixed effect model – efficacy analysis set (patients ever received 20 mg/kg avalglucosidase alfa for up to 5.5 years)

Conclusion: After up to 5.5 years' avalglucosidase alfa, efficacy analyses showed that patients had sustained benefit on pulmonary and motor function. Funding: Sanofi Genzyme.

Disclosure: This study was supported by Sanofi Genzyme.

EPR3111

Respiratory Function and Ambulation Status Assessments of Late-onset Pompe Disease Patients with and without the Common IVS1 Variant from the Pompe Registry

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Background and aims: The most common disease-causing variant of late-onset Pompe disease (LOPD) is the c. 32 13T>G (IVS1) splice-site variant, which leads to a reduced acid alpha-glucosidase protein production of about 10-20% residual GAA activity.

Methods: We described patient characteristics by IVS1 status and compared respiratory function and ambulation status at baseline among patients with available data in IVS1 and non-IVS1 patients in the Pompe Registry (NCT00231400; sponsored by Sanofi Genzyme).

Results: Of 980 LOPD patients, 793 (80.9%) had 1 or 2 copies of IVS1: 66.7% came from Europe, 30.9% from North America, and 1.3% from Asia-Pacific. For non-IVS1 patients (n=187), 39.0% were in Europe, 38.5% in North America, and 19.8% in Asia-Pacific. IVS1 vs. non-IVS1 patients were older at symptom onset (median: 34.2 vs. 4.5 years), diagnosis (41.5 vs. 7.9 years), and enzyme replacement therapy (ERT) initiation (45.5 vs. 11.8 years). Non-IVS1 patients were slightly more likely than IVS1 patients to be on respiratory support at ERT initiation (25.0% vs. 17.1%, respectively). Median baseline forced vital capacity (FVC) values were similar (IVS1=72.0%; non-IVS1=66.5%). Most IVS1 (95.6%) and non-IVS1 (85.4%) patients were ambulatory at ERT initiation. Ambulation device use at ERT initiation was similar (IVS1=14.2% vs. non-IVS1=13.2% patients). 23 IVS1 patients were homozygous. For heterozygous IVS1 patients (n=770), the most frequent type of 2nd variant was substitution (missense). At baseline, no significant differences in clinical characteristics were observed in heterozygous IVS1 patients when grouped by second variant type.

Conclusion: Our data provide additional insights into the most common disease mutation variant of LOPD.

Disclosure: This analysis was funded by Sanofi Genzyme.

EPR3112

Clinical characterization of a cohort of 30 BMD patients: stratification of patients towards trial readiness

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Background and aims: Becker muscular dystrophy (BMD) is characterized by a broad phenotypic spectrum. We propose a clinical protocol aimed to describe genetic, muscular and cardiac involvement, to identify different clinical subgroups and stratify patients towards trial readiness.

Methods: We recruited 30 adult BMD patients, for each one we collected medical history and we assess at baseline and after 1-year motor function scales: North Star Ambulatory Assessment, timed function tests, 6-minute walk test, Walton and Gardner-Medwin Scale and MRC scale. Skeletal muscle involvement was studied by standard muscle MRI with qualitative analysis. A comprehensive assessment of cardiac involvement was performed on 10 BMD patients, aged 39±19 years, through cardiac magnetic resonance (CMR) and study of blood biomarkers (troponin T and I, NT-proBNP, norepinephrine, myoglobin and creatine-kinase) of cardiac and muscular damage.

Results: In a 1-year follow-up period, motor functions measures did not show significant evolution of the disease. Muscular MRI was useful to recognize a specific pattern of muscle involvement, related to different mutations. The cardiological characterization allowed to detect that myocardial fibrosis as assessed by late gadolinium enhancement (LGE) was present in 6 patients (60%) with 3 patients demonstrating reduced left ventricular ejection fraction. The same LGE-positive patients showed a trend towards higher values of cardiological blood biomarker.

Conclusion: Genotype-phenotype correlation studies with a detailed clinical characterization are needed to better define prognosis and to identify biomarkers of progression and outcome measures toward trial readiness. In this framework, CMR through LGE can allow early identification of cardiac involvement in BMD.

Disclosure: Nothing to disclose

EPR3113

Myasthenia gravis in Poland – national healthcare database epidemiological study

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disorder of neuromuscular junction. MG epidemiology has not been studied in Poland in a nationwide study before.

Methods: Our epidemiological data was drawn from the National Health Fund (NFZ) database; MG patient was defined as a person who received at least once medical service coded in ICD-10 as myasthenia gravis (G70) and at least 2 reimbursed prescriptions for pyridostigmine bromide (Mestinon[®]) or ambenonium chloride (Mytelase[®]) in 2 consecutive years.

Results: On 1st January 2019, 8702 patients with MG were receiving symptomatic treatment (female:male ratio 1.65:1). MG incidence was 2.36/100,000. Mean age of incident cases in 2018 was 61.05 years, 59.17 years for women, and 64.12 years for men. Incidence of early onset MG (EOMG, <50y) was 0.80/100,000, and 4.98/100,000 for late-onset MG (LOMG), with male predominance in LOMG. Prevalence in patients <50 years old was 9.21/100,000, and 45.34/100,000 in patients ≥50 years old, in total 22.65/100,000. The highest prevalence was observed in the age group of 80-89 years old: 59.65/100,000 in women, 96.25/100,000 in men. In women, there was a constant increase in prevalence of symptomatic MG from the 1st decade of life up to 80-89 years. In men, an increase in prevalence appeared in the 6. decade.

Conclusion: Our findings provide information on epidemiology of symptomatic Myasthenia Gravis in Poland and can serve as a tool to evaluate health care resources needed for MG patients.

Disclosure: Nothing to disclose

EPR3114

The risk factors for developing refractory Myasthenia gravis

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Background and aims: Most patients with Myasthenia gravis (MG) are successfully treated with acetylcholinesterase inhibitors, corticosteroids, and/or steroid sparing agents such as azathioprine and mycophenolate mofetil. We can say about refractory MG when there is insufficient response (e.g. persistent moderate to severe weakness) to maximal safe doses of steroids and at least one immunosuppressive drug at adequate dose and duration.

Methods: We analyzed the history of the disease in 1275 patients with generalized MG, 98 (7.7%) of them had a refractory course. 98 patients with refractory MG were compared with 775 patients with non-refractory MG.

Results: Refractory MG was characterized by: a statistically significant predominance of women (79.6% vs. 69.6%, p=0.039), an earlier age of onset of the disease (40.8 years vs. 47.1 years, p=0.003), the myasthenic crisis developed more often (29.5% of patients vs. 7.1%, p=0.000), there were more common repeated myasthenic crises (in 20.7% of cases vs. 3.6%, p=0.011), the group average level of the titers of antibodies to acetylcholine receptors were higher (27nmol/l vs. 13.2nmol/l, p=0.002). The presence of thymoma and thymectomy were equally often observed in both groups (12.4% vs. 14.3%, p=0.51 and 27.5% vs. 30.3%, p=0.47 respectively). The absence of antibodies to acetylcholine receptors was also equally common in both groups (15.4% vs. 20.4%, p=0.39). 18.3% of patients with refractory MG and 18.9% of patients with non-refractory MG had concomitant autoimmune diseases (p=0.93).

Conclusion: Female patients, early onset of the disease, and myasthenic crisis are the risk factors for developing refractory MG.

Disclosure: Nothing to disclose

EPR3115

Muscle MRI fat fractions correlate with function in Becker muscular dystrophy independent of the unequal proximo-distal fat distribution

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Background and aims: Phenotype variability and slow disease progression in Becker muscular dystrophy (BMD) complicate clinical trial design. Muscle fat fraction (FF) assessed by quantitative MRI is a promising biomarker. We studied the relation between muscle fat replacement and function in BMD.

Methods: 3-point Dixon 3T MRI thigh scan data (23 slices of 1cm, 0.5cm gap) of 24 BMD patients (median age 41.3 years, range 18.8-66.3) were correlated to function. Weighted average FFs (wFF) of the vastus lateralis (VL) and semitendinosus were determined over 2 areas: 3 center slices (3S) landmarked on the biceps femoris short head insertion, and the whole muscle (WM). Statistics with Wilcoxon's Signed-Rank-Test and Spearman's correlation.

Results: Upon visual inspection, VL FF distribution followed an U-shaped curve, while in semitendinosus FF was low near the origo and higher near the insertion (figure 1). wFF of 3S was lower than WM in VL ($50.1 \pm 28.5\%$ and $57.5 \pm 28.8\%$, $p=0.001$), while it was higher in semitendinosus ($57.0 \pm 35.2\%$ in 3S versus $42.0 \pm 30.0\%$ in WM, $p=0.005$). wFF correlations for both the 6-Minute Walk Test and the North Star Ambulatory Assessment were similar for 3S and WM in VL ($\rho=-0.786$ vs $\rho=-0.797$ and $\rho=-0.880$ vs $\rho=-0.887$) and semitendinosus ($\rho=-0.875$ vs $\rho=-0.860$ and $\rho=-0.908$ vs $\rho=-0.924$), see table 1.

Conclusion: FF correlated highly with function in BMD, congruent with findings in other muscular dystrophies, and were not influenced by non-uniform fat replacement. This indicates that muscle MRI may serve as biomarker in BMD trials. Stringent control of year-to-year slice positioning is essential as average 3S versus WM wFF differed significantly.

Figure 1.

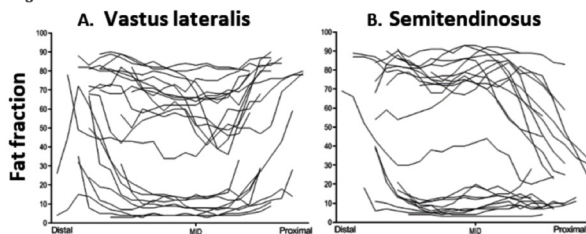


Figure 1. Distribution of FF along the proximodistal axis in Vastus lateralis and Semitendinosus. Mid represents the middle of the thigh based on the biceps femoris short head insertion.

Table 1.

	Vastus lateralis		Semitendinosus	
	3 slices wFF	whole muscle wFF	3 slices wFF	whole muscle wFF
6-Minute Walk Test, rho	-0.786	-0.797	-0.875	-0.908
North Star Ambulatory Assessment, rho	-0.880	-0.887	-0.860	-0.924

Table 1. Correlations between Vastus lateralis and Semitendinosus wFF and function tests

Neurogenetics 2

EPR3116

Exome sequencing results for early onset Parkinson’s disease cases from Kazakhstan

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Background and aims: A number of genes and chromosomal loci for Parkinson’s disease (PD) have been identified for the last decades. The genetic determinants of PD are largely unknown in Central Asia, including Kazakhstan. Here we have genotyped early-onset PD (EOPD) probands from Kazakhstan by exome sequencing. EOPD was defined as the onset before the age of 50 years old (1).

Methods: Genomic deoxyribonucleic acids (DNAs) of 48 EOPD index cases were obtained from the research-ready database of PD cases from Kazakhstan. Whole exome sequencing (WES) was performed at the Institute of Neurology University College London. Variants from WES were filtered such that only novel (or very low frequency <0.1%), coding/splicing, heterozygous, homozygous or compound heterozygous variants in known PD genes that are predicted to be deleterious and damaging or pathogenic were considered as likely causal.

Results: The mean age at PD onset in the cohort was 38.1±7.5 years (range 14-50), mean age of patients was 46.4±7.7, and mean disease duration was 8.3±4.7 (Table 1). The cohort was made of 36 Kazakhs, 11 Russians, and 1 Korean. Only 17 cases were found to be positive for known PD genes (Table 2). 12 cases had variants in LRRK2, and the rest 5 cases had variants in DNAJC13, EIF4G1, UCHL1, VPS13C, and VPS35 genes.

Table 1 Demographic and clinical characteristics of the cohort

Demographic and clinical characteristics	Values
Mean age at onset ± SD(years), (range)	38.1±7.5 (14-50)
Mean age at the last examination ± SD(years), (range)	46.4±7.7 (28-66)
Mean disease duration ± SD(years), (range)	8.3±4.7 (0-24)
Male to female ratio (males:females)	1:0.8 (26M:22F)
Family history, n (%)	10 (21)
Mean Hoehn-Yahr stage	2.4±0.6
Mean motor MDS UPDRS score	40.1 ± 18.3

Table 1

Conclusion: Mostly LRRK2 pathogenic and novel variants were associated with Kazakhstani EOPD cases. WES negative cases warrant further TRIO exome and genome sequencing studies. These studies might reveal candidate genes specific to Kazakhstani PD population.

Disclosure: This research was funded by the Medical research council (MRC) [MR/S01165X/1, MR/S005021/1, G0601943].

Table 2 Positive findings

Gene	Variant	# of cases	allele frequency	Pathogenicity	SB and Pathogenic predictions	Origin	FR	LRN	Ethnic group
LRRK2	NM_130258.4 c.12246C>T p.A4438V	8	0.0000	Deleterious Probably damaging	Pathogenic Start pathogenic (see 33, 39, 42)	East Asian	42.6	1.4	Russian 1 Kazakh 1 Kazakh
LRRK2	NM_130258.4 c.40935A>G p.R1364G	1	0.0000	Deleterious Probably damaging	Not reported	NA	NA	NA	Kazakh
LRRK2	NM_130258.4 c.38137C>T p.Y12712Y	1	Not reported	Deleterious Probably damaging	Not reported	NA	NA	NA	Kazakh
LRRK2	NM_130258.4 c.41232C>A p.R13744I	7	0.0000	Deleterious Probably damaging	Pathogenic Start pathogenic (see 39, 2018)	Both Asian	NA	NA	Both in Kazakh 5
DNAJC13	NM_012288.4 c.42131C>A p.A14011Y	1	0.0000	Deleterious Probably damaging	Not reported	NA	NA	NA	Kazakh
EIF4G1	NM_001159462.2 c.18818C>T p.A62161Y	1	0.0000	Deleterious Probably damaging	Not reported	NA	NA	NA	Kazakh
UCHL1	NM_004481.3 c.1212G>A p.S404N	1	0.0000	Loss of function Deleterious Probably damaging	Not reported	Asian	NA	NA	1 Kazakh
VPS13C	NM_001048151.1 c.7988A>C p.R2662H	1	0.0000	Deleterious Probably damaging	Not reported	NA	NA	NA	1 Kazakh
VPS35	NM_001168415.1 c.20191A>G p.R6730Y	1	Not reported	Deleterious Probably damaging	Not reported	NA	NA	NA	1 Korean

Table 2

EPR3117

Defects in the myogenesis-regulating glycosidase (MYORG) gene in a family with primary brain calcification presenting with stroke-like episodes

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Background and aims: Primary familial brain calcification (PFBC), a traditionally autosomal dominant (AD) disorder, was recently expanded to include an autosomal recessive inheritance associated with defects in the MYORG gene. Until now, only 23 families with MYORG-related PFBC have been reported in the literature.

Methods: Retrospective analyze and MYORG screening of a portuguese family with PFBC.

Results: A 51-year-old female patient with a history of depression, presented with acute onset right hemiparesis. On examination, she had mild cognitive impairment, dysarthria, brisk tendon reflexes, spastic right hemiparesis, slightly symmetrical parkinsonism and dysmetria on finger-nose testing. Brain CT scan revealed symmetric calcifications in basal ganglia and dentate nucleus with cerebellum atrophy. Over the years, the disease followed a progressive course with acute stroke-like episodes. She became wheelchair-bound at the age of 55 years and died at 71 years of age. She had 2 siblings, both sharing a similar phenotype. Genetic testing with a gene panel for AD-PFDC based on whole exome sequencing (WES) was not conclusive. Further reanalysis of WES data for the recently identified MYORG gene, allowed the identification of two likely pathogenic frameshift variants in compound heterozygous state

(NM_020702.4:c[285_310delinsTTC];[535_536insC]).

From the 7 children of the affected cases (all obligate heterozygous carriers), 3 were clinically evaluated. All had brisk reflexes but none presented calcifications on brain CT scan.

Conclusion: A detailed description of stroke-like episodes in PFBC patients is provided. The accumulation of knowledge about the phenotype of MYORG-related PFBC will be useful for early diagnosis and to attain further phenotype-genotype correlations in this clinical entity.

Disclosure: Nothing to disclose

EPR3118

A rare p.R342W TGM6 (SCA35) mutation in a patient with late-onset cerebellar ataxia

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Background and aims: Mutations in TGM6 have been recently implicated in the pathogenesis of spinocerebellar ataxia type 35 (SCA35), a rare autosomal dominant disease, marked by cerebellar degeneration. The associated phenotype includes slow progressive postural instability and incoordination of gait, cerebellar dysarthria, dysmetria, saccadic slowing and pyramidal signs. TGM6, a member of the transglutaminase superfamily specifically expressed in the central nervous system, is involved in proteins cross-linking. Even though it is established that mutations of TGM6 described so far reduce transglutaminase activity, the precise molecular pattern impaired is still unclear. The aim of our study was to report a rare heterozygous missense mutation of TGM6 in a patient with late-onset cerebellar ataxia.

Methods: We performed a neurological evaluation and genetic analysis by whole exome sequencing of a patient with late-onset, progressive cerebellar ataxia and pyramidal tract signs. The identified variant was subsequently confirmed at Sanger sequencing.

Results: A novel TGM6 heterozygous mutation (p.R342W) was detected in a patient with late-onset, progressive cerebellar ataxia, pyramidal tract signs, cerebellar dysarthria and ocular dysmetria. A cerebellar atrophy was confirmed by brain imaging. The mutation, located at a highly conserved position, was rare (MAF 0.02%) and predicted as pathogenic by in-silico tools.

Conclusion: In summary, we described the clinical phenotype of an Italian SCA35 patient, who was confirmed to have a rare heterozygous missense mutation of TGM6. This is the 1st description of an Italian case of SCA35. Despite its rare frequency among general population, we suggest considering SCA35 genetic testing in case of undiagnosed cerebellar ataxia.

Disclosure: This work was supported by ADF's funds, from Intesa San Paolo and Fresco Institute.

EPR3119

Early-infantile onset epilepsy and developmental delay caused by bi-allelic GAD1 variants

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Background and aims: Gamma-aminobutyric acid (GABA) and glutamate are the most abundant amino acid neurotransmitters in the brain. GABA, an inhibitory neurotransmitter, is synthesized by glutamic acid decarboxylase (GAD). Its predominant isoform GAD67, contributes up to ~90% of base-level GABA in the CNS, and is encoded by the GAD1 gene. Disruption of GAD1 results in an imbalance of inhibitory and excitatory neurotransmitters, and as Gad1^{-/-} mice die neonatally of severe cleft palate, it has not been possible to determine any potential neurological dysfunction. Furthermore, little is known about the consequence of GAD1 disruption in humans. We here present four patients from four unrelated families, carrying bi-allelic GAD1 variants, and presenting with distinct phenotypical features.

Methods: Clinical details were collected from patient's charts. Genomic DNA was extracted from peripheral blood from all patients, parents, and unaffected siblings and family-based whole exome sequencing was performed. Variants were annotated with ANNOVAR and analyzed with the use of bioinformatic analytical tools.

Results: All affected individuals carried ultrarare GAD1 variants, which were predicted to result in impaired protein

function. Homozygous variants were identified in three families, whereas heterozygous variants were found in one. Clinical features showed early-infantile onset epilepsy, neurodevelopmental delay independent of successful seizure control, and hypotonia. Whilst cleft palate was not a feature in any of the families we describe, some do show non-CNS manifestations such as skeletal abnormalities and dysmorphic features.

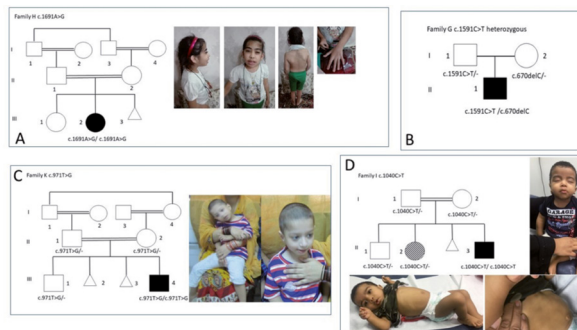


Figure 1: Pedigrees of the reported families and pictures of GAD1 patients

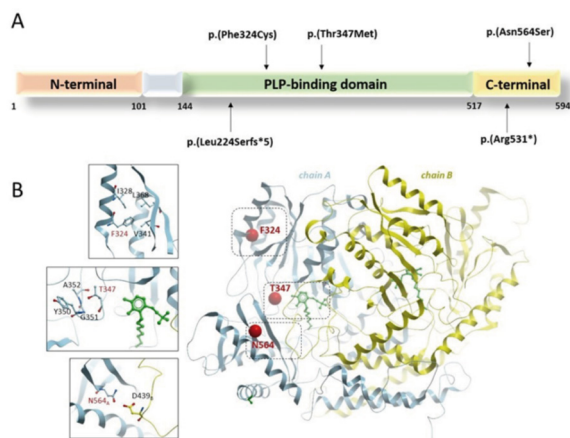


Figure 2: Schematic and cartoon representation of GAD1

Gene	Protein	Enzyme	EC	OMIM
GAD1	glutamic acid decarboxylase	glutamic acid decarboxylase	1.4.1.1	138000
GAD67	glutamic acid decarboxylase	glutamic acid decarboxylase	1.4.1.1	138000
GAD65	glutamic acid decarboxylase	glutamic acid decarboxylase	1.4.1.1	138000

Table 1 Clinical features of GAD1 patients

Conclusion: Our findings highlight an important role for GAD1 in seizure induction, neuronal and extra-neuronal development, and expand the likely impact of GAD1-variant previously assumed.

Disclosure: Nothing to disclose

EPR3120

Mitochondrial trifunctional protein deficiency (MTP-defect) - a metabolic cause of hereditary neuromuscular disorder with a mild course

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Background and aims: MTP-defect is a rare recessive fatty oxidation disorder that might cause several phenotypes including encephalopathy, cardiomyopathy and liver failure. Benign phenotypes including polyneuropathy and recurrent rhabdomyolysis have also been described. We describe three patients with mild symptoms.

Methods: Methods were used as described in results.

Results: Patient 1 was a female around 30-year-old with normal development until 6 years of age when she suffered from decreased energy and was gaining weight. At 9 years old she developed subacute generalized muscular weakness after an infection. Repeated clinical neurophysiology confirmed an axonal neuropathy. Since then she has experienced weekly episodes of weakness lasting several hours. CK and lactic acid have always been normal. An increased concentration of the long hydroxyacylcarnitines was found. Patient 2 and 3 are sisters around 20. They both experienced episodes of weakness after physical activity and more pronounced during infections. Clinical findings were compatible with neuropathy, and neurophysiology confirmed axonal involvement. Muscle biopsy revealed neuropathic changes. After genetic testing, patient 1 was shown to be compound heterozygous for 2 variants of unknown significance (VUS) in the HADHB-gene. The 2 sisters were homozygous for another VUS in HADHB. Low activity of long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) and 3-ketotiolases (Long-chain) confirmed a defect in the MTP metabolism in all patients.

Conclusion: MTP-defects might give rise to mild symptoms mainly causing an axonal neurogenic disorder. However, a correct diagnosis is important since these patients should be instructed in eating a diet low in fat, and they need an SOS-regime during acute illness.

Disclosure: Nothing to disclose

EPR3121

Early structural alterations and longitudinal changes in presymptomatic carriers of the C9orf72 expansion

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Background and aims: The C9orf72 repeat expansion is the main genetic cause of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). Promising therapeutic trials, such as antisense oligonucleotides, are upcoming, and presymptomatic carriers represent the optimal target population. We aimed to assess the earliest MRI alterations and their longitudinal modifications as markers to monitor disease evolution in the presymptomatic stage.

Methods: PrevDemALS is a multicentric, prospective, observational study focused on 1st-degree relatives of C9orf72-associated FTLD/ALS patients. Clinical, cognitive and brain MRI assessments are performed at baseline and every 18 months. 81 participants underwent the 1st 2 evaluations. FreeSurfer cross-sectional and longitudinal pipelines were run through Clinica platform (www.clinica.run) to process T1-weighted sequences. Cortico-subcortical ROIs were defined with Desikan-Killiany and aseg atlases. Baseline ROI volumes and their longitudinal changes were compared between C9orf72 carriers (C9+) and non-carriers (C9-) using generalized linear mixed-effects models.

Results: C9+ (n=42) and C9- (n=39) individuals were comparable for age at inclusion (42.6±11.8 vs 46.1±13.5, p=0.22), well below the average age at onset. Several cortical ROIs in both hemispheres were significantly more atrophic at baseline in C9+, including precentral, orbitofrontal, inferior temporal, fusiform cortex, and precuneus. Both thalami were among the most involved regions. No significant longitudinal progression of atrophy could be detected after 18 months.

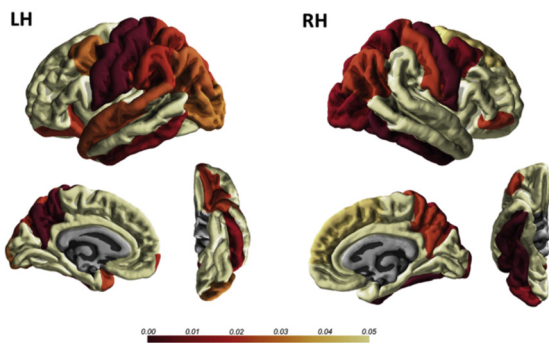


Figure 1. Baseline regional cortical atrophy in C9+ compared to C9-. Several cortical ROIs displayed significant atrophy in presymptomatic carriers. No significant longitudinal progression was detected (data not shown). P-values are corrected for multiple comparisons with Benjamini-Hochberg method. LH: left hemisphere; RH right hemisphere.

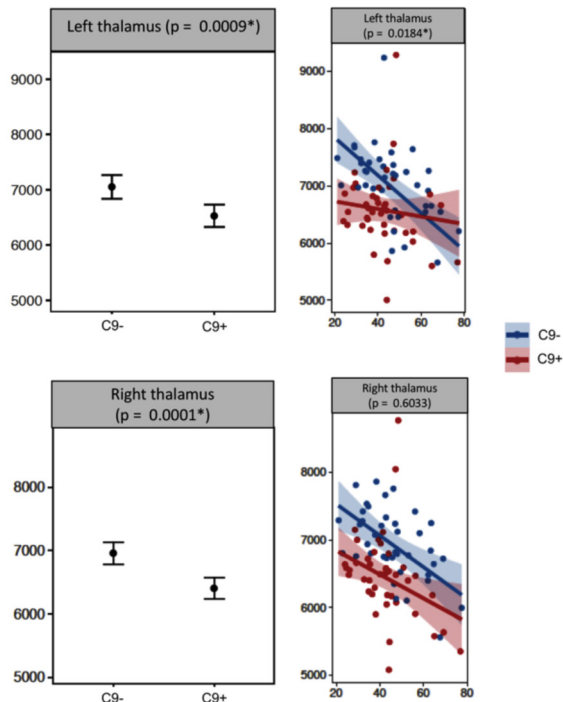


Figure 2. Thalamic volumes in C9+ and C9-. Presymptomatic carriers showed significantly reduced volumes in both thalami at baseline. Thalamic volumes did not show greater decline in the more aged C9+ compared to C9- subjects. Volumes are expressed as mm³. P-values are corrected for multiple comparisons with Benjamini-Hochberg method.

Conclusion: Cortical and subcortical atrophy is detectable several years before clinical onset in C9orf72 disease, but shows little progression over time. Longer follow-up periods and additional neuroimaging techniques will likely help detect slowly progressive alterations in the presymptomatic phase.

Disclosure: Nothing to disclose

EPR3122

Phenotypic expansion of ATP13A2 related disorders

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Background and aims: Pathogenic variants in ATP13A2 gene were 1st described in 2006 as causing Kufor-Rakeb syndrome. Since then the phenotype has been expanded to include developmental delay, epilepsy, dystonia, spastic paraplegia (SPG78), ataxia and peripheral neuropathy. We aim to describe a family with developmental delay who developed spastic paraplegia only in adulthood.

Methods: Descriptive analysis of clinical, imaging, electrophysiological, neuropsychological and genetic findings.

Results: We identified 4 patients in a 9-sibling consanguineous kindred. All had psychomotor delay, with marked intellectual disability and learning difficulties. Gait impairment onset ranged from 20-31 years. Before the age of 40 years all had spastic paraplegia, with additional dystonic signs in 2 and ataxia in 1 patient. MRI disclosed generalized cortical atrophy in all, white matter lesions in 3 and cerebellar atrophy in 2. Electromyography was performed in 2, with normal results. Neuropsychological evaluation of 3 patients revealed multidomain deficits, consistent with abnormal cognitive development. On genetic testing a homozygous missense variant in ATP13A2 (c.1510G>C(p.(Gly504Arg)) was identified.

Conclusion: In this family the dominant phenotype was developmental delay without any additional neurological signs until adulthood. Later in life, all affected siblings developed spastic paraplegia, some including additional dystonia and ataxia, with a mutation previously reported in a patient with juvenile parkinsonism. Besides describing an alternative phenotype for this same mutation, we wish to draw attention into testing for ATP13A2 pathogenic variants in children with “pure” developmental delay.

Disclosure: Nothing to disclose

EPR3123

Frequency of GGGGCC-expansion in C9orf72 gene in Russian cohort of patients with ALS and FTD

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Background and aims: Hexanucleotide repeats expansion in C9orf72 gene is the most frequent genetic cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) in different populations, especially in the combined ALS-FTD phenotype. Our previous work showed that the C9orf72 repeat expansion may occur in Russian patients with ALS. However, the exact frequency of this mutation in ALS and FTD patients in Russian population has never been estimated before.

Methods: We analyzed DNA samples of patients with ALS (n=419), FTD (n=79) and ALS-FTD (n=16). All patients were examined and diagnosed in Research Center of Neurology and I.M. Sechenov First Moscow State medical University (Moscow). The C9orf72 expansion (>50 GGGGCC-repeats) was identified by repeat primed PCR.

Results: The frequency of the C9orf72 repeat expansion in ALS group was 4.3%, including 9% in familial ALS and 4% in sporadic cases. The frequency of this expansion in FTD group was 3.6%, including 3.3% in familial FTD and 4% in sporadic cases. The frequency of the C9orf72 repeat expansion in ALS-FTD group was 38%.

Conclusion: We present the 1st data on the prevalence of C9orf72 expansion in the large group of FTD patients from Russian population. The frequency of this mutation in ALS according to our updated results is higher than the previous estimates, especially in familial cases. In addition, we revealed the high prevalence of C9orf72 gene repeat expansion in ALS-FTD patients that is comparable with data in other populations.

Disclosure: The study was supported by RFBR 19-015-00533

EPR3124

Design of a risk assessment model for Parkinson's disease

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Background and aims: The availability of high-throughput technology and computational facilities enabled a deeper investigation of neurogenetic disorders, paving the way for the development of precision medicine approaches. This study aimed to elucidate the network of genes characterizing Parkinson disease (PD) and identify a set of predictive biomarkers specific for PD.

Methods: 259 patients with idiopathic PD were recruited at the IRCCS Santa Lucia. Genomic DNA was subjected to genotyping analysis by Open Array platform, consisting of the analysis of 120 Single Nucleotide Polymorphisms (SNPs). The obtained results were processed by statistical (Information Theory and Logistic Regression) and bioinformatic (GSEA, IPA, String, Phenolyzer) tools in order to assess the significant association with disease and select a set of SNPs as predictive biomarkers for PD.

Results: The statistical analysis identified 7 SNPs as candidate predictors for PD risk (Table 1). The logistic regression showed that 4 of these SNPs were significantly associated with PD and thereby were utilized to generate a classifier able to discriminate cases and control subjects. This model showed to be accurate, sensitive and specific (AUC:0.95; sensitivity:0.72; specificity:0.88). Concerning bioinformatic analysis, the associated SNPs resulted to be involved in dopamine metabolism, immune-inflammatory processes and endocytosis.

Gene	Informative SNP	p-value
<i>MAOA</i>	rs1137070	0.06
<i>MAOA</i>	rs2072743	0.007
<i>VSIG4</i>	rs1044165	0.0004
<i>MAOB</i>	rs1799836	0.0005
<i>PTGS2</i>	rs20417	0.98
<i>miR-4482</i>	rs45596840	0.07
<i>CLOCK</i>	rs6811520	0.0008

Table 1. Statistical results showing candidate SNPs predictors and the associated SNPs obtained by logistic regression. The cut-off for significant p-value was set at p<0.05. In bold characters are reported the SNPs significantly associated with PD.

Conclusion: This study allowed to set-up an accurate model for assessing the risk of PD based on the patient's genetic profile. Moreover, the bioinformatic analysis highlighted the existence of a network of genes that could elucidate new disease mechanisms and reveal novel therapeutic targets that could be exploited for developing precision medicine protocols for PD treatment.

Disclosure: Nothing to disclose

Neuro-oncology 2

EPR3125

Disparities in Patient Enrollment on Glioblastoma Clinical TrialsN. Mohile¹, Y. Liu², A. Wasilewski¹¹Neurology, University of Rochester, Rochester, USA,²Neurosurgery, University of Rochester, Rochester, USA

Background and aims: To determine if enrollment on glioblastoma (GBM) interventional clinical trials (ICT) in the U.S. is representative of the population, to identify disparities and describe their evolution over time.

Methods: We queried ClinicalTrials.gov for all adult ICT in GBM from 1994 to 2019. Intervention type was assigned based on definitions in the National Cancer Institute (NCI) drug dictionary. Demographics were obtained from ClinicalTrials.gov or the trial publication and compared to corresponding population data from the Central Brain Tumor Registry of the United States (CBTRUS).

Results: 10617 GBM patients enrolled on 118 adult ICT: experimental agents in 99 ICT were systemic therapy (cytotoxic (24), immunotherapy/vaccine (11) and targeted therapy (64)); 19 ICT involved other modalities. Median age was 54.0 (10.05 years younger than CBTRUS, $p < 0.001$). Age was most discrepant in recurrent vs newly diagnosed (11.29 years younger vs. 7.57, $p < 0.001$), non-randomized vs randomized, (10.54 years younger vs 7.65, $p = 0.004$) and NCI consortium vs. other (10.61 years younger vs. 7.83, $p = 0.005$). Median age improved from 52.0 (1994-2002) to 59.5 (2011-2019). Women represented only 37.5% of subjects, 1.23% less than expected from population data ($p < 0.018$). Data on race was unavailable for most trials from any source.

Conclusion: Despite improvement over time, GBM ICTs underrepresent older patients. Fewer women enroll on GBM ICT than men. Reporting of race and ethnicity should be encouraged. ICTs need to be designed and implemented to better represent the population.

Disclosure: Nothing to disclose

EPR3126

Does the location matter?**Characterization of the anatomic locations, molecular profiles, and clinical features of gliomas**C. Mackintosh¹, R. Butterfield², N. Zhang³, J. Lorence⁴,P. Zlomanczuk⁵, B. Bendok⁶, R. Zimmerman⁶,K. Swanson⁷, A. Porter⁸, M. Mrugala⁸¹School of Medicine, Mayo Clinic, Scottsdale, USA,²Department of Biostatistics, Mayo Clinic, Scottsdale, USA,³Mayo, Scottsdale, USA, ⁴Mathematical Neuro-oncologyLab, Mayo Clinic, Scottsdale, USA, ⁵Department of

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Background and aims: Neuroanatomic locations of gliomas may influence clinical presentations, molecular profiles, and patients' prognoses.

Methods: Our institutional cancer registry was queried to include patients with glioma over a 10-year period. Statistical analyses were used to compare demographic, genetic, and clinical characteristics among patients with gliomas in different locations.

Results: 182 gliomas were identified. Of the tumors confined to a single lobe, there were 51 frontal (28.0%), 50 temporal (27.5%), 22 parietal (12.1%), and 7 occipital tumors (3.8%) identified. Tumors affecting temporal lobe were associated with reduced overall survival when compared to all other tumors (11.0 months vs. 13.0 months, log-rank $p = 0.0068$). However, this disparity became insignificant when adjusted for tumor grade, age, and surgical approach [HR(95% CI) 1.26 (0.87, 1.82), $p = 0.212$]. Out of 82 cases tested for IDH-1, 10 were mutated (5.5%). IDH-1 mutation was present in 6 frontal, 2 temporal, 1 thalamic, and 1 multifocal tumor. Out of 21 cases tested for 1p19q deletions, 12 were co-deleted, 9 of which were frontal lobe tumors. MGMT methylation was assessed in 45 cases; 7 of 14 frontal tumors and 6 of 13 temporal tumors were methylated.

Conclusion: Results support the hypothesis that the anatomical locations of gliomas influence patients' clinical courses. Temporal lobe tumors were associated with poorer survival, though this association appeared to be driven by these patients' more aggressive tumor profiles and higher risk baseline demographics. Molecular analysis was limited by low prevalence of genetic testing in the study sample, highlighting the importance of capturing this information for all gliomas.

Disclosure: Nothing to disclose

EPR3127

ABTR-SANO Real-World Pattern of Care Study on Glioblastoma in the Austrian Population.

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Background and aims: The Austrian ABTR-SANO Glioblastoma Registry is the 1st population-based assessment of patterns of care for patients with Glioblastoma across Austrian healthcare institutions. The primary aim is to assess the real world effectiveness of administered therapies. Additionally, characteristics with respect to diagnostics and safety profiles of interventions can be provided on the basis of a surveillance/non-interventional study.

Methods: Clinical data are collected via a common web-based IT platform “ABTR-SANO Net” since 2014. The database and the ongoing evaluation of clinical parameters, as well as interim analysis are provided in cooperation with a review board.

Results: Meanwhile 11 centers across Austria are involved, which collect the information of now over 1500 patients (m/f ratio: 1,3 - median age: 66 years). The proportion of patients with gross total resection increased gradually since 2014 from 36% to 56% in 2019. Almost all patients were MGMT tested in 2019, whereas in 2014 only half of patients underwent MGMT testing. Analysis of median time from clinical presentation to diagnostic scan (overall: 9 days), time from diagnostic scan to surgery (overall: 10 days), and time from surgery to the beginning of first line treatment (overall: 31 days) was stable. First overall survival data show a median survival of 12 months.

Conclusion: 1 defined set of clinical parameters results in phenotypic annotation of the patient cohort from 2014 ongoing. Pattern of care characteristics show a different picture with respect to treatment, as we used to see in RCT. Outcome analysis comparing different Austrian centers will be available in 2020.

Disclosure: Nothing to disclose

EPR3128

Neurological adverse events during immune-checkpoint inhibitors treatment: a report from the Italian Neurological Society (SIN) database.

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Background and aims: Immune-related adverse events (irAEs) due to immune-checkpoint inhibitors (ICI) treatment are increasingly recognized. Although rare, neurological irAEs may be severe and often difficult to diagnose. Their prompt recognition is crucial, as they may be reversed with proper treatment. To better define the clinical spectrum of ICI-related neurological toxicities the Neuro-oncology Study Group of the Italian Neurological Society promoted the creation of a national database.

Methods: A national, web-based database was created. All physicians who manage oncological patients were allowed to spontaneously include cases.

Results: From 01/01/2019 to 15/01/2020, 19 patients (16 males, 3 females; median age 71 years) have been entered in the database. Underlying malignancy and type of ICI treatment are reported in Table 1. The median number of ICI cycles at irAE onset was 3 (range 1-22). 15 patients developed a peripheral nervous system (PNS) toxicity, while four had a central involvement (Figure 1). All but 1 required treatment (n=14: corticosteroids, n=3: IVIg, n=1: corticosteroids+IVIg), with a complete response in 3, partial in 10. 5 required a 2nd-line treatment. Toxicity was severe (CTCAE_≥3) in 17/19, with three fatalities (Figure 2). 3 patients resumed ICI, without neurological relapses.

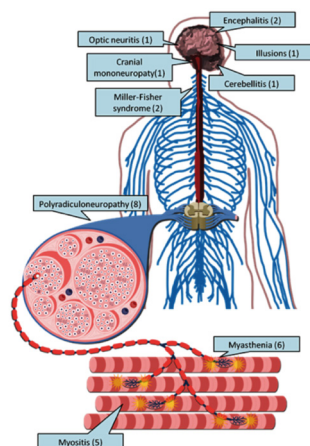


Figure 1. Neurological toxicities during immune-checkpoint inhibitors treatment (19 reported patients, multiple involvement in 7).

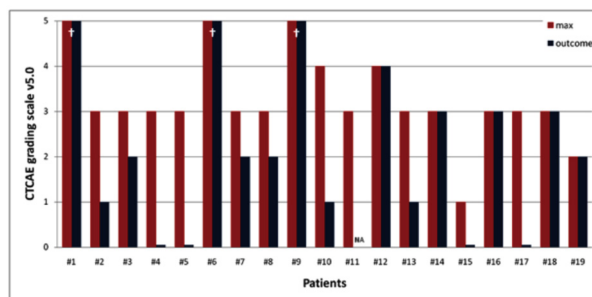


Figure 2. Max toxicity and outcome according to CTCAEv5.0 grading scale. NA = not available. † = deceased.

Conclusion: Neurological irAEs affected most frequently the PNS, and a multiple involvement (“overlap” syndromes) appeared common. Although they frequently improved with immunomodulating treatments (as corticosteroids), irAE progression to death have been reported. In a subset of less severe cases, however, ICI resumption appeared feasible with no neurological irAE relapses. Further inclusions will possibly help us to identify predictors of outcome and response to treatments.

Disclosure: Nothing to disclose

Malignancy (number of patients)	Melanoma (6) Non-small cell lung cancer (5) Urothelial carcinoma (3) Renal-cell carcinoma (2) Other (3)
Type of immune-checkpoint inhibitor (number of patients)	Anti-PD1 (12) Nivolumab (7) Pembrolizumab (5) Anti-PDL1 (3) Atezolizumab (3) Anti-CTLA4 (1) Ipilimumab (1) Combination therapies (3) Ipilimumab + Nivolumab (3)

Table 1. Malignancy and type of immune-checkpoint inhibitor treatment in reported patients (n=19).

EPR3129

Clinical, molecular and radiomic profile of gliomas with FGFR3-TACC3 fusions

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Background and aims: Approximately 3% of gliomas harbor an oncogenic actionable FGFR3-TACC3 (F3T3) fusion. Their characteristics and prognostic remains still poorly defined. We aimed to unravel the clinical, radiological and molecular profile of F3T3-positive diffuse gliomas.

Methods: We screened for F3T3 by RT-PCR 1162 diffuse gliomas (951 unselected, 211 selected for FGFR3 protein immunopositivity). Available clinical and molecular data were collected. We performed a radiological and radiomic case-control study.

Results: We identified 80 F3T3-positive gliomas (Table1). F3T3 fusion was exclusively found in IDH wildtype gliomas (80/843 versus 0/193, p<0.001). F3T3 appeared mutually exclusive with EGFR amplification (0/55 versus 156/558 of F3T3-negative cases, p<0.001), whereas associated with CDK4 amplification (10/46 versus 28/530, p<0.001) and MDM2 amplification (9/46 versus 18/578, p<0.001), creating a defined molecular cluster (Figure1). F3T3-positive gliomas showed a longer overall survival than F3T3-negative gliomas (median OS 29.1 versus 20.5 months, p=0.04), even when analysis was restricted to glioblastomas (31.1 versus 19.9 months, p=0.02), Figure2. Multivariate analysis confirmed F3T3 as an independent predictor of favorable outcome. In radiogenomic analysis, F3T3 associated with poorly defined tumor margins and a trend to spare eloquent areas. Radiomics analysis correctly classified F3T3-positive glioma with AUC of 0.82. We compared different Cox proportional hazards models using Harrel's C-Index: radiomics alone obtained a high C-Index (0.75); the model combining clinical, genetic and radiomic data showed the highest C-index (0.81).

Grade	n of detected FGFR3-TACC3 fusions/n samples tested	
	without prescreening for FGFR3 immunopositivity	prescreened for FGFR3 immunopositivity
II	2/104	4/9
III	1/129	5/27
IV	21/711	46/115
NA	0/7	1/60
	24/951 (2.5%)	56/211 (26.5%)

Table 1. Distribution of the 1162 screened diffuse gliomas according to WHO 2016 classification. Frequency of FGFR3-TACC3 fusions: 2.5% among unselected diffuse gliomas (grade II-IV); 26.5% among FGFR3-immunopositive cases.

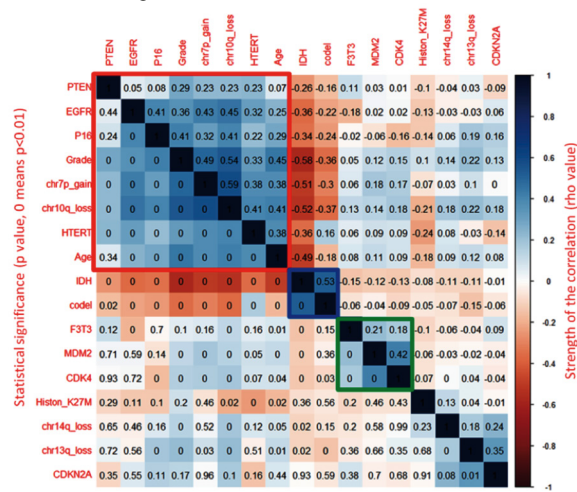


Figure 1. Correlation matrix (blue=positive, red=negative) of the main genetic alterations in 1162 diffuse gliomas. 3 main clusters were identified: EGFR amplification with 7p gain, 10q loss and older age at diagnosis (red), IDH mutation with 1p19q codeletion (blue), and F3T3 fusion with MDM2 and CDK4 amplifications (green).

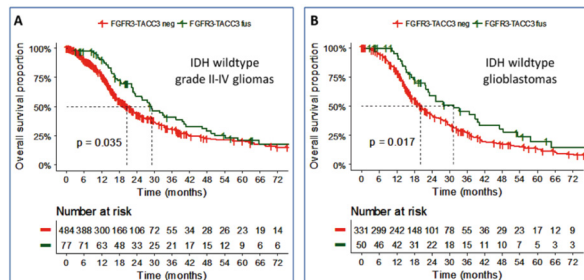


Figure 2. A) survival of IDH-wildtype diffuse glioma patients according to the F3T3 status (median OS 29.1 vs. 20.1 months; p=0.035). B) survival of IDH-wildtype glioblastoma patients according to the F3T3 status (median OS 31.1 vs. 19.9 months, p=0.017).

Conclusion: Diffuse gliomas harboring F3T3 gene fusions show specific molecular and radiological features, along with a less aggressive clinical evolution.

Disclosure: Nothing to disclose

EPR3130

Primary Central Nervous System Lymphoma: Epidemiological Analysis of a Series of Patients of University Hospital Center of Porto

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Background and aims: Primary central nervous system lymphoma (PCNSL) is a subtype of extra-nodal non-Hodgkin lymphoma (NHL), rare but very aggressive with a 5-years survival of just 30% of patients. We intend to describe the epidemiological characteristics and estimate the survival time of patients diagnosed with PCNSL at the University hospital center of Porto (UHCP).

Methods: A retrospective analysis of a cohort of consecutive patients diagnosed with PCNSL between 2002 and 2019 was performed at UHCP. Descriptive statistics were applied for the demographic characterization of the sample and a survival analysis (Log-Rank and Cox Regression) was performed to estimate the mean survival time according to demographic data, clinical manifestations, histological type and imaging characteristics of the tumor.

Results: We identified 109 patients, 56.9% male, with a mean age of 60.5 years (SD 1.3). The median survival time after diagnosis was 34.4 months (SD 5.6). 15.6% of patients were immunocompromised. Histologically, 90% of the tumors correspond to diffuse large B-cell NHL. The most frequent inaugural clinical manifestation was focal neurological deficit. Among the factors analyzed, especially age, histological type, number of lesions, immune status and manifestations, an age greater than 65 years was the only independent prognostic factor ($p < 0.002$, 95% CI). It is noteworthy that the subgroup of immunosuppressed patients showed survival overlapping to the remaining.

Conclusion: These results corroborate the most recent data available in the literature, emphasizing the new epidemiological paradigm of the LPSNC as a tumor that is no longer associated with immunosuppressed young patients.

Disclosure: Nothing to disclose

EPR3131

Real-world experience with pregnancy in patients with glioma: a large retrospective study from the Pitié-Salpêtrière Hospital.

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Background and aims: There is currently limited data on the influence of pregnancy on glioma patients. Specifically, whether the pregnancy might negatively affect the glioma behavior, and vice versa, is not known. The aim of this study was to assess the oncological and gestational outcomes of glioma patients becoming pregnant.

Methods: Patients with a known diagnosis of WHO grade II, III or IV glioma becoming pregnant between 2008 and 2019 were identified from the Pitié-Salpêtrière's hospital database. Retrospective data collection included clinical (age, Karnofsky status, neurological events, concomitant medication), radiological (location, size, contrast-enhancement), and histomolecular characteristics, oncological management (surgical procedure, radiotherapy, chemotherapy), progression-free survival, overall survival, and gestational outcome (preconception counseling, gestational age at diagnosis, obstetrical complications, pregnancy outcomes).

Results: We identified 22 pregnancies in 19 women with a known glioma (7 grade II, 10 grade III and 2 Grade IV). Treatments received before the pregnancy included surgery (n=17), radiotherapy alone (n=5), chemotherapy alone with temozolomide (n=3), and concomitant radiochemotherapy with temozolomide (n=4). 1 patient was treated with radiotherapy during the 2nd trimester of pregnancy. There were 7 terminations of pregnancy (6 of them due to concomitant tumor progression requiring immediate treatment), 15 live births and 3 maternal deaths within 6 months postpartum.

Conclusion: This study provides real-world data on the oncological and gestational outcomes of glioma patients becoming pregnant. In this series, termination of pregnancy was medically necessary for 27.3% of patients. Long-term outcomes of patients and their children will be presented at the conference.

Disclosure: Nothing to disclose

EPR3132

Incidence and characteristics of pseudoprogression in high-grade IDH-mutant gliomas

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Background and aims: Pseudoprogression (PsP) after radiochemotherapy has been well-described in IDH-wildtype glioblastomas but its characteristics in IDH-mutant high-grade gliomas (HGGs mIDH) remain to be fully described. **Methods:** We retrospectively analyzed the characteristics of 212 HGGs mIDH treated with radiotherapy ±chemotherapy in 2 centers (Lyon and Paris) from the POLA network. PsP was defined as the increase or the appearance of a contrast-enhanced lesion after radiotherapy that disappeared or remained stable during follow-up (for at least 6 months) without initiation of a new oncological treatment.

Results: Our series consisted of 105 (50%) anaplastic oligodendrogliomas IDH-mutant and 1p19q-codeleted 60 (28%) anaplastic astrocytomas IDH-mutant n=60 (28%) and 47 (22%) glioblastomas IDH-mutant. After a median follow-up of 4.3 years (range: 1-10 years), 41 patients (19%) developed a PsP, that occurred after a median delay of 10 months after radiotherapy (range: 1-66 months) and lasted a median of 6 months (range: 2-30 months). PsP typically occurred in asymptomatic patients (93%), consisted of nodular (83%) and <1cm (83%) contrast-enhanced lesions that demonstrated no rCBV elevation (76%) on perfusion MRI and no hypermetabolism (90%) on 18FDOPA petscan. PsP was more frequent in patients who received PCV chemotherapy after radiotherapy than in those who did not or received temozolomide (26 vs. 10%, p<0.02).

Conclusion: PsP is frequent in HGGs mIDH, especially in patients treated with radiotherapy and PCV chemotherapy. PsP in this population typically present as small nodular contrast-enhanced lesions in asymptomatic patients. Its timing seems to be delayed compared to PsP in IDH-wildtype glioblastomas.

Disclosure: Nothing to disclose

EPR3133

Paraneoplastic Myeloneuropathies: characterization of a distinguishable phenotype and clinical outcomes

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Background and aims: To describe an identifiable phenotypic presentation, serological and oncological associations of paraneoplastic myeloneuropathies.

Methods: We analyzed patients with co-occurring myelopathy and peripheral neuropathy seropositive for onconeural autoantibodies, and/or a diagnosis of cancer within 3 years of symptom onset and compared to a historical cohort of copper-deficiency metabolic myeloneuropathies.

Results: Among 32 patients presenting with paraneoplastic myeloneuropathy, 26 had detectable onconeural antibodies (Amphiphysin, 8; ANNA1/anti-Hu, 6; CRMP5, 5; PCA1/anti-Yo, 2; PCA2/MAP1B, 1; Kelch-like-Protein-11, 1; combinations thereof: ANNA1 and CRMP5, 1; ANNA1 and Amphiphysin, 1; ANNA3 and CRMP5,1). Among seropositive cases, 19 had underlying malignancy (small-cell lung cancer, 10) and seven had masses suspicious for malignancy but no histopathological cancer diagnosis. All 6 patients without classified onconeural antibodies (unclassified neural-autoantibodies, 3) had malignancies. Asymmetric numbness, with dysesthesias, weight loss, bowel/bladder dysfunction, sensory ataxia and hyperreflexia were common presenting symptoms. Neuropathies were non-length dependent, asymmetric, and painful. Inflammatory CSF was noted in 82%. Tract-specific changes on cervical/thoracic MRI were seen in 12/29(41%) patients. In comparison to copper-deficiency myeloneuropathy (n=11), asymmetric, sensory presentations, subacute progression, weight loss, orthostatic intolerance, inflammatory CSF and gadolinium enhancement of spinal cord or lumbosacral roots were significantly more frequent in paraneoplastic myeloneuropathies (p≤0.05). Median modified-Rankin-Score at last follow-up was 3. 10 of 28 patients (35%) were wheelchair dependent at last follow-up (median duration, 9 months)

Conclusion: A paraneoplastic etiology should be considered in the differential of subacute, progressive presentations of co-occurring myelopathy and neuropathy. Onconeural antibody and malignancy screening may aid in cancer diagnosis and guide management.

Disclosure: to be added

Neurorehabilitation; Spinal cord and root disorders

EPR3134

Aripiprazole Improves Spinal Cord Injury in Rats: Involvement of Inflammatory Pathways

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Background and aims: Neuroinflammation causing central macrophages and microglia imbalance may underlie spinal cord injury (SCI) pathology. There is evidence that aripiprazole (ARP) has anti-inflammatory property. Therefore, the aim of the present study was to assess the therapeutic anti-inflammatory effects of ARP on a rat model of SCI.

Methods: Male Wistar rats underwent T9 vertebra laminectomy. They were divided into 4 groups: a sham-operated and 3 treatment (normal saline as a vehicle control versus ARP 10mg/kg and ARP 20mg/kg) SCI groups. Through a 28-day period, we then assessed locomotor scaling and behavioral tests for neuropathic pain. At the end of the study, tissue samples were evaluated for neuroinflammatory changes using the immunohistochemistry, flow cytometry, and ELISA techniques.

Results: Post-SCI ARP (10 and 20mg/kg) treatment markedly improved locomotors ability (P<0.01) and reduced sensitivity to mechanical (P<0.01) and thermal allodynia (P<0.001). Additionally, ARP treatment significantly decreased tumor necrosis factor (TNF)-α level and increased interleukin (IL)-10 level in spinal cord tissue compared to control groups 28 days post SCI (P<0.01). ARP treatment also markedly reduced expression of M1, increased M2 macrophages, and decreased of M1/M2 ratio in both dorsal root ganglion and spinal cord tissue after SCI compared to controls (P<0.01).

Conclusion: Our data revealed a therapeutic effect of ARP treatment on SCI and showed its potential to reduce neuroinflammation as well as SCI sensory/locomotor complications.

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EPR3135

Combination of non-invasive brain stimulation with standard physical rehabilitation in acute ischemic stroke

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Background and aims: Arm and hand deficits are among the most disabling consequences in the everyday life of people affected by acute ischemic stroke (AIS). Non-invasive brain stimulation techniques (NIBS) showed potential benefits but experiences are limited to small populations in the chronic phase after injury.

Methods: 48 consecutive patients affected by AIS with upper limb impairment within 72 hours were consecutively randomized to receive real or sham bi-hemispheric tDCS for 15 sessions, 3 weeks, 5days/week for 20min/day in a 1:1 ratio. Upon their admission to the stroke unit, they were clinically assessed with NIHSS, ARAT, Fugl-Meyer, Barthel Index. As soon as possible they received a 2-month standard physical rehabilitation program paired with of either real- or sham-tDCS and tested again as baseline after 2 months.

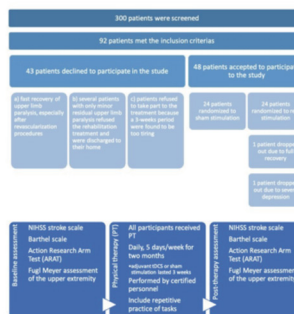


Figure 1: description of precured used for the randomized clinical trial

Results: NIHSS didn't change in both groups. ANOVA analysis revealed in the “real” group a significant improvement in ARAT (tARAT=5.025, p=0.03) and Fugl-Meyer score (tFM=7.441, p=0.01) but Barthel was not significantly improved (tBarthel= 0.531, p=0.600). In the “Real” group, effect was stronger for subtests depending on less fine movements: ARAT sub-tests gross movement (p=0.010) improved more than grasp (p=0.025) and grip (p=0.041) and Fugl Meyer sub-tests of the upper extremity (p=0.006) improved more than hand (p=0.042) and coordination and speed (p=0.022).

Conclusion: A 3 weeks treatment with bi-hemispheric tDCS added to standard physical rehabilitation in the early phases after AIS resulted in a slight improvement of upper limb motor functions with stronger effects on less fine movements.

Disclosure: Nothing to disclose

EPR3136

Eye know about your Neglect: Eyetracking during free visual exploration detects neglect more reliably than paper-pencil tests

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Background and aims: Neglect after stroke is most accurately diagnosed by systematic, ecological observation during everyday behaviour using the Catherine Bergego Scale (CBS). However, CBS is time-consuming and often omitted in clinical settings, especially stroke units. In this study, we aimed to explore if video-oculography during free visual exploration (FVE), which can be performed in few minutes, is sensitive in mirroring neglect in everyday behaviour and whether it is more sensitive than conventional neuropsychological paper-pencil-tests.

Methods: In this retrospective, observational, multicentre study, we identified 78 patients with subacute right-hemispheric stroke, with and without neglect in everyday behaviour, as diagnosed by the CBS, who also performed FVE. 40 age-matched healthy participants served as controls. The sensitivity to detect neglect was compared between FVE and conventional neuropsychological paper-pencil-tests, i.e. Random-Shape-Cancellation, Line-Bisection, 2-Part-Picture, Bells, Star-Cancellation, Letter-Cancellation, Sensitive-Neglect, Five-Point.

Results: FVE (in particular, mean gaze position) correctly identified neglect in 85% of patients, with an AUC value of 0.927 in ROC analysis. Conventional neuropsychological paper-pencil-tests, considered alone or in combination, showed heterogeneous results, and identified neglect significantly less often (21.74%-68.75%). Moreover, there was a significant correlation between mean gaze position and CBS, providing evidence for the relationship between FVE and neglect in everyday behaviour.

Conclusion: FVE has a high sensitivity and specificity to diagnose neglect and it is more sensitive than conventional neuropsychological paper-pencil-tests. It can be performed in short time and has the potential to be used as a fast and accurate screening tool that allows the initiation of comprehensive neuropsychological diagnostics and neurorehabilitative therapy from early on.

Disclosure: Nothing to disclose

EPR3137

Evaluation of serum BDNF in patients with ischemic stroke after motor rehabilitation using augmented reality

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Background and aims: Brain neurotrophic factor (BDNF) is a neuroplasticity factor. BDNF plays a crucial role in motor training and recovery after a stroke. Augmented reality (AR) is a new tool for using sensory stimuli during motor training with biofeedback.

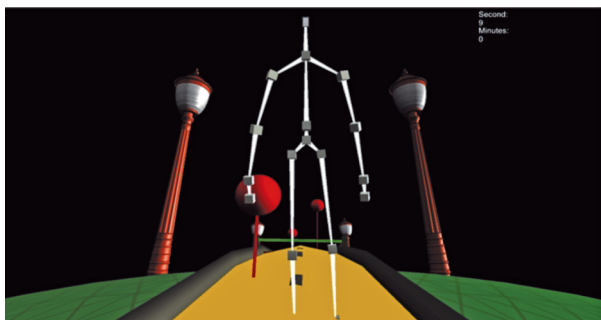
Arm: to identify the correlation between the BDNF content in blood serum and motor neurological symptoms after rehabilitation upper and low extremity by using specialized software Rehab.

Methods: 68 patients in early recovery period of ischemic stroke (average age 63 (57-65) years; Rankin Scale=3 (2-3) points, NIHSS=4 (3-6) points, Asworth=0 - 1 points. The course of motor rehabilitation-10 days, 1 training session-60 minutes. Observation points: I-before, II-after rehabilitation. Neurological examination was completed with Fugl-Meier Assessment scale (FMA). Serum BDNF was determined by MAGPIX multiplex analyzer (Luminex, USA) using xMAP® Technology.

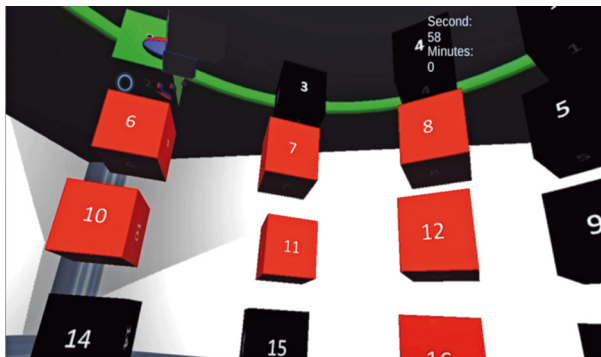
Results: FMA I=199 (190-212) points; FMA II=213 (208-222) points, $p<0.005$. Increment of FMA I-II=12 (9-19) points. FMA sum upper extremity: I=49 (43-57) points; II=61 (56-64) points, $p=0.005$. FMA sum low extremity: I=29 (27-33) points; II=33 (29-34) points, $p=0.046$. BDNF I=1110.0 (679,9–1484.0) pg/ml; BDNF II=2745,0 (1730.0–2739.0) pg/ml, $p=0.022$ - associated with stimulation of the motor cortex as a result of motor training. Strong positive correlation was found between the changes in the level of serum BDNF and quantitative values on FMA ($r=0.610$, $p=0.027$) in patients with ischemic stroke after AR motor rehabilitation.

Conclusion: The results confirm the activation of neuroplasticity processes and the effectiveness of motor rehabilitation with biofeedback based on sensory AR stimuli and the principle of motor learning.

Disclosure: This study was supported by the Russian Science Foundation (RSF), grant No. 18-15-00082 “Laboratory for robotic rehabilitation”



RehabAR for low extremity



RehabAR for upper extremity

EPR3138

Transcranial direct current stimulation add-on to neurorehabilitation of Pisa syndrome in Parkinson's disease

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Background and aims: Pisa Syndrome (PS) is a lateral trunk flexion associated to Parkinson's disease (PD). Transcranial Direct Current Stimulation (t-DCS) is a non-invasive neuromodulation technique, with promising results in focal dystonia. Aim of our study is to evaluate the role of t-DCS as add-on to neurorehabilitation in PS.

Methods: 20 patients affected by PD and PS (15 male, age 72.0±4.9 years, disease duration 8.2±5.6 years, duration of PS 2.8±1.9 years) were managed with neurorehabilitation combined with: 1) t-DCS group (5 daily sessions - 20 minutes - 2mA) with cathode over the M1 cortex contralateral to PS and anode over the M1 cortex ipsilateral to PS; 2) SHAM group. Patients were tested with UPDRS-III, FIM, EMG and cinematic motion analysis at hospital admission (T0) and after 1 month of neurorehabilitation (T1). The study groups were comparable for clinical/demographic and EMG features. At T1 we find a significant reduction of anterior and lateral trunk flexion in both groups (p=0.001 and 0.013 respectively), and an increase of range of motion (ROM) of the trunk bending ipsilateral to trunk deviation (p=0.008).

Results: At T1 the overall improvement in lateral and anterior trunk flexion in upright standing position was higher in the t-DCS group when compared to SHAM group (p=0.032); moreover, the improvement of trunk ROM in the medio-lateral plane was higher in the t-DCS group (p=0.038). The UPDRS-III and FIM scores significantly improved at T1 in both groups.

Conclusion: Our data supports the use of neuromodulation with t-DCS as add on to neurorehabilitation for the treatment of PS.

Disclosure: Nothing to disclose

EPR3139

Rehabilitation of complex arm movement after Ischemic Stroke using haptic device and Virtual Reality (VR)

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Background and aims: rehabilitation in VR enables patients to perform complex arm movement with online feedback. Aim of our study was to evaluate the feasibility of rehabilitation of complex arm movement, using Bimeo.

Methods: 22 patients were included 3 weeks after ischemic stroke. All patients underwent standardised physio-, occupational therapy and rehabilitation in VR using Bimeo. Each patient performed 2 sessions in VR, lasting 4min each. Patients were seated in front of the screen, holding Bimeo in their affected hand. On the screen, a labyrinth appeared, and they have to navigate the cursor to the end of the labyrinth as fast and as accurate as possible.

For each patient, the modified Rankin score (mRS), movement quality index (MQI), smoothness, accuracy, and overall score were measured. All parameters except overall score and mRS were normalised on the scale from 0 to 10, where 10 represents optimum. Differences between sessions were compared with paired t-test.

Results: mean age of patients was 66.7±12.1 years. At the end of rehabilitation mRS significantly improved (1.7±0.7 vs 1.5±0.5 p<0.05). After the 2nd training session, significant improvement in the smoothness (6.7±2.1 vs 7.6±2.0), the accuracy of arm movement (7.2±1.4 vs 7.5±1.0) and overall score were observed (319±173 vs 427±213 points). No improvement was found in MQI.

Conclusion: our study demonstrates that rehabilitation in the VR may improve complex movement already after 2 sessions. In the future, an optimal number of sessions should be determined.

Disclosure: Nothing to disclose

EPR3140

Non traumatic spinal cord injury in Northern Tanzania: burden and etiology

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Background and aims: Acquired non-traumatic spinal cord injury (NT SCI) has a huge burden of disease regardless geography. Few recent studies are available on epidemiology of medical paraplegia on Sub-Saharan Africa (SSA). The purpose of this study is dual: we aim to support the fact that NT SCI causes an important proportion of neurological burden in our settings, and describe the etiologies with the hypothesis that it presents as an end consequence of several medical conditions.

Methods: Retrospective cross-sectional hospital-based study. Patients aged 13 years and above were recorded when presenting with neurological complaints and attended the medical outpatient department or were admitted to a referral and teaching hospital in Kilimanjaro region, during the 6 years study period, April 2007 to March 2013.

Results: Out of 2047 neurological patient records a total of 294 (14.4%) presented with paraplegia/quadriplegia 2ndary to NT SCI. Among NT SCI, malignancy (20%), transverse myelitis (12%) and Pott's disease (6%) were the most common identified etiologies. More than 50% of the cases could not have an etiological diagnosis. HIV infection was present in 20.4% of those patients presenting with PP who were tested (143/294).

Conclusion: NT SCI accounts for a significant proportion of neurological disorders in Northern Tanzania. NT SCI is associated with HIV infection in this study in particular with unexplained paraparesis and Pott's disease. The absence of neuroimaging in particular magnetic resonance imaging made it difficult to reach an etiological diagnosis in many cases.

Disclosure: Nothing to disclose

EPR3141

Validation of the SECONDS: a new short scale to assess disorders of consciousness

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Background and aims: Clinical examination of severely brain-injured patients with disorders of consciousness (DoC) requires repeated standardized assessments to provide an accurate diagnosis. However, the administration time of the current gold-standard Coma Recovery Scale-Revised (CRS-R) limits its use in clinical routine. We here propose and validate a faster tool to assess consciousness.

Methods: The Simplified Evaluation of CONsciousness Disorders (SECONDS) is based on 6 mandatory items (observation, response to command, visual fixation, visual pursuit, oriented behaviours, arousal) and 2 conditional items (localisation to pain, communication) (Figure 1). 57 DoC patients were assessed 4 times on 2 consecutive days: 1 CRS-R and one SECONDS were administered on 1 day, whereas 2 SECONDS were administered on the other day (Figure 2). The 3 examiners remained blind to diagnosis and medical history of patients. Concurrent validity and inter-/intra-rater reliability were computed using weighted kappa coefficients, while administration times for the SECONDS vs. CRS-R were compared with a Mann-Whitney U test.

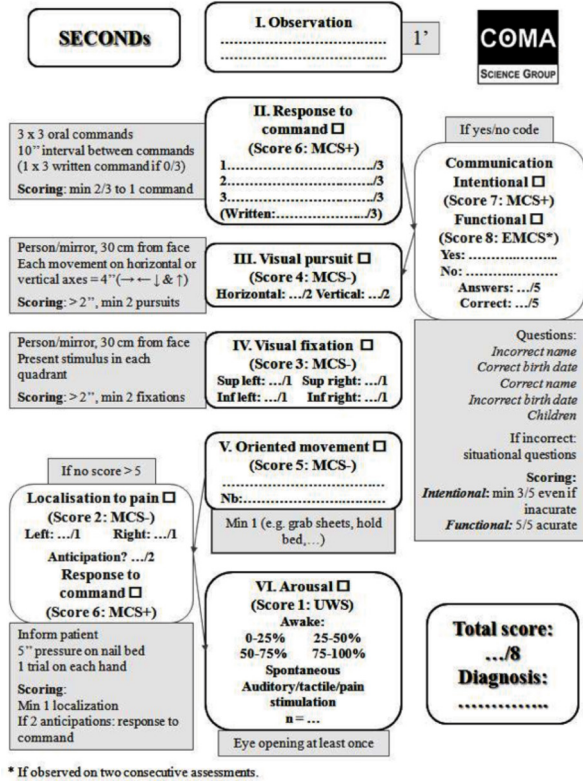


Figure 1. Administration of the Simplified Evaluation of CONsciousness Disorders. We recommend the administration of at least 5 SECONDS in a short time period (e.g., 10 days) to reduce misdiagnosis rates. UWS=unresponsive wakefulness syndrome; MCS-/MCS+=minimally conscious state minus/plus; EMCS=emergence from the minimally conscious state.

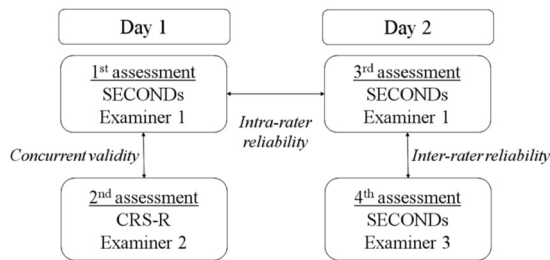


Figure 2. Procedure and validation protocol of the SECONDS. 3 SECONDS and 1 CRS-R were administered by 3 examiners on 2 consecutive days. The 2nd exam was always administered 45-60 minutes after the 1st. The order of the assessments (within a day and between days) and the order of the examiners were pseudo-randomized.

Results: “Substantial” and “almost perfect” agreements (kappas: 0.78-0.85) were found comparing the CRS-R against the same-day SECONDS or against the highest-scoring SECONDS. Intra- and inter-rater reliabilities showed “almost perfect” agreements (kappas: 0.85-0.91 and 0.82-0.85 respectively) (Figure 3). Administration times were significantly shorter for the SECONDS than for the CRS-R (7min vs. 17min).

		Same day SECONDS				Best SECONDS			
		UWS	MCS-	MCS+	EMCS	UWS	MCS-	MCS+	EMCS
CRS-R	UWS	11	1	0	0	10	2	0	0
	MCS-	3	8	3	0	3	8	3	0
	MCS+	0	4	8	2	0	1	11	2
	EMCS	0	0	3	14	0	0	0	17

Figure 3. Comparison of the diagnoses obtained with the CRS-R vs. the SECONDS administered on the same day (left) and the CRS-R vs. the best SECONDS (right). Light grey cells show patients with a better diagnosis using the SECONDS and dark grey cells show patients with a better diagnosis using the CRS-R.

Conclusion: The SECONDS is a fast and valid clinical scale to evaluate patients with DoC. This new tool offers an alternative to existing scales, well-suited for clinicians with major time constraints, and can be easily repeated to provide an accurate diagnosis.

Disclosure: This study was supported by the University and University Hospital of Liège, the Belgian National Funds for Scientific Research (F.R.S-FNRS), the Marie Skłodowska-Curie Actions (H2020-MSCA-IF-2016-ADOC-752686), the European Union’s Horizon 2020 Framework Program for Research and Innovation under the Specific Grant Agreement No. 785907 (HBP SGA2), Luminous project (EU-H2020-fetopen-ga686764), the James McDonnell Foundation, the Public Utility Foundation ‘Université Européenne du Travail’, AstraZeneca Foundation, C.A. and L.S. are research fellows, A.T. is a post-doctoral fellow, and S.L. is research director at the F.R.S-FNRS.

EPR3142

A rationale for a use of non-medication in the patients with the post-stroke spastic muscle pain

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Background and aims: The effect of the non-medication complex on the patients having the pain due to post-stroke muscle spasticity was investigated.

Methods: 98 patients aged from 45 to 65 (41 males and 57 females) having the post-stroke pain due to muscle spasticity were observed. All patients suffered acute cerebrovascular accident in the form of brain stroke. The Ashworth Scale Spasticity: 2–3 points. The patients subjectively rated their spastic muscle pain from 3 to 7 points to the visual analogue scale (VAS). The patients were randomly divided into 2 groups. The 1st group (62 patients) received in addition their basic medication and physiotherapy with combination of ultrasonotherapy – variable sinusoidal high-tension (4-5 kV) high-frequency (22kHz) low-intensive current (power 1-10 Watt), and low-frequency variable magnetic field (frequency to 100 Hertz, magnetic induction 27mTesla) treatment of upper and lower extremities, with taking turn each other, and balneotherapy. Every procedure exposure was 12-15min. The complete course was 10-12 procedures. The 2nd group (control, 36 patients) received only the basic medication.

Results: The spasticity, subjective sensation of constraint extremities and pain due to post-stroke muscle spasticity of the patients in the 1st group was reduced after 25-30 days of treatment (77.4% patients) compared to the control group, where muscle constraint reduced after 32-42 days of treatment (58.3 % patients), $p < 0.05$.

Conclusion: The addition of the complex (ultrasonotherapy, balneotherapy and the low-frequency variable magnetic field) to the treatment resulted in earlier reducing of subjective sensation of constraint extremities and pain due to post-stroke muscle spasticity.

Disclosure: Nothing to disclose

EPR3143

Disturbances of micturition in patients with acute strokeK.I. Tudor¹, D. Petravić¹, M. Botica², S. Nađ Škegro³, M. Bakula³, F. Rajič⁴, F. Mustač⁵, B. Ribarić¹, M. Krbot Skoric¹

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Background and aims: Lower urinary tract symptoms (LUTS) are commonly reported in patients that suffer stroke and the aim of this study was to assess them.

Methods: This was a prospective case-control study performed at tertiary health-care center. LUTS, catheter insertion and diaper administration were monitored and recorded during hospitalisation for each patient.

Results: 49 patients that suffered acute stroke were included (33 women, 16 men; mean age 74.25 ± 10.93 (range 41-95) years), mean Barthel index (BI) 47.80 ± 42.79 (range 0-100). 87.8% (N=43) had ischemic stroke and 12.2% (N=6) hemorrhagic. 51.02% (N=25) had LUTS before the stroke, while 16 (32.65%) developed symptoms now (mean age 72.61 ± 11.99 (range 42-90) years). 28.57% (N=14) of patients had new onset urinary retention, while 2 (4.08%) patients reported new onset urinary incontinence (one mixed and 1 urge urinary incontinence). There were no significant differences between women and men in urinary retention ($\chi^2=1.758$, $df=2$, $p>0.05$) and in urinary incontinence ($\chi^2=3.692$, $df=2$, $p>0.05$). There were significant relationships between catheter and atrial fibrillation ($\chi^2=3.996$, $df=1$, $p=0.046$) and both catheter ($\chi^2=3.864$, $df=1$, $p=0.049$) and diaper use with arterial hypertension ($\chi^2=7.969$, $df=1$, $p=0.005$). Urinary incontinence was found to be significantly more often present with lesion in white matter ($\chi^2=4.622$, $df=1$, $p=0.032$) and insular lesion ($\chi^2=4.622$, $df=1$, $p=0.032$).

Conclusion: In our study majority of patients in the acute phase of stroke experienced urinary retention. Question rises of the proper timing of clean intermittent catheterisation (CIC) in post-stroke rehabilitation.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

EPR3144

The use of forks revisited: which one and how should we use them?

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Background and aims: We use different methods to explore vibratory sensitivity with quantitative or qualitative tuning forks, with little written evidence of their sensitivity (S) and specificity (E), and cut-off values. We propose to analyze the usefulness of these tests.

Methods: We include patients with an ENG request for suspected sensory polyneuropathy (PNP) between 11/11/18-30/03/19. Prior to the diagnostic test, we explore vibratory sensitivity in lateral malleolus (LM) with 2 tuning forks: 1 128Hz conventional fork (CF), recording time in seconds from its activation to patient's sensitive threshold, and the Rydel-Seiffer tuning fork (RSF), noting the scale value in patient's sensitive threshold. Subsequently, ENG was performed for diagnosis of PNP. Data were analyzed using the statistical package SPSS.

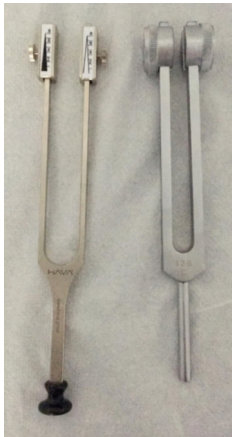
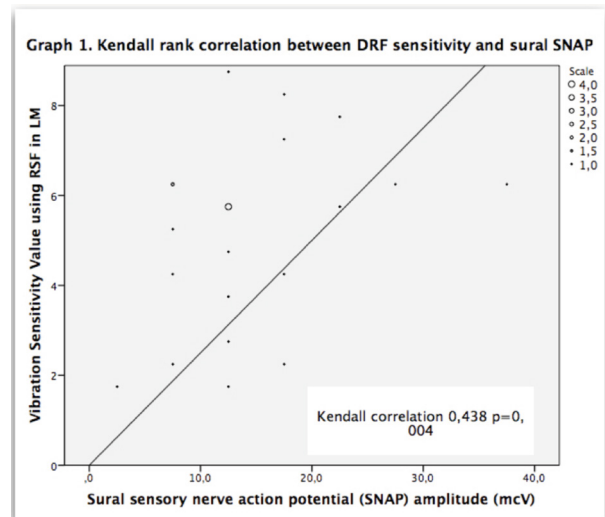


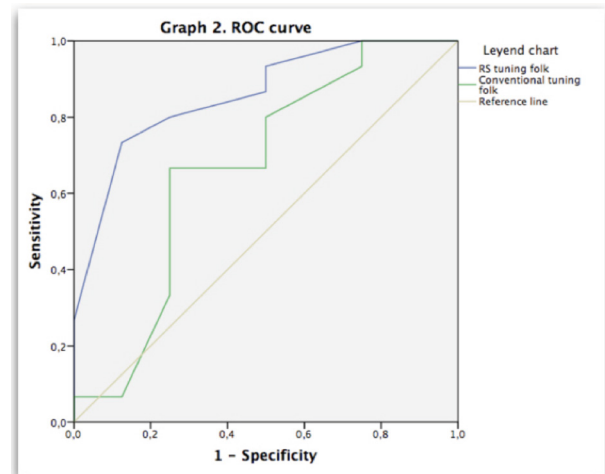
Image 1. The tuning forks used: on the right, the conventional one (CF) and on the left, the Rydel-Seiffer (RSF).

Results: 24 patients (45.8% women; mean age 57 years, average height 1.6m), of which 8 (33%) were diagnosed with PNP in ENG. There were no differences in sex and height between PNP/normal results, although in age, the affected were older. A statistically significant correlation was observed between sural sensory nerve action potential (SNAP) amplitude and the resulting value of the tuning forks (Graph 1). The area under the CF's curve was 0,67 (0.41-0.93) and RSF's was 0.86 (0.70-1) (Graph 2).

Optimum cut-off points for CF: 9s (S75%, E 71%) and for RSF 6Hz (S88%, E71%). Qualitative method (feel/no-feel vibration): S25%, E100%



Graph 1. Linear correlation between sural SNAP amplitude and patient's sensitivity threshold measured with RSF.



Graph 2. Receiver Operating Characteristics (ROC) curve of the 2 tuning forks.

Conclusion: In our experience, given the easy handling and better sensitivity of RSF, this tuning fork is shown as the best option for clinical use. Additionally, the diagnosis of PNP in ENG is quite unlikely if its result is normal.

Disclosure: Nothing to disclose

EPR3145

Variation of Penetrance in hereditary Transthyretin Amyloidosis (hATTR) between European countries: impact on the management of gene carriers

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Background and aims: hATTR is an autosomal dominant peyorative disease characterized by a wide range of age of onset. Early diagnosis is essential to initiate timely the newly available therapies. Hereby, unravel the risk of being affected (penetrance) is essential for the management of asymptomatic gene carriers (AGC). This collaborative study aimed to estimate penetrance in a panel of hATTR kindreds using a Non-parametric Survival Estimation method.

Methods: Genealogical data were collected in 340 families from Sweden, France, Portugal, Majorca, Sicily, Turkey and Brazil; including ATTR-Val30Met (N1=261 families); ATTR-Phe64Leu (N2=20); ATTR-Ser77Tyr (N3=20); ATTR-Ile107Val (N4=14); ATTR-Ser77Phe (N5=10); ATTR-Thr49Ala (N6=9) and ATTR-Glu89Gln (N7=9).

Results: Penetrance ranged broadly between the ATTR-Val30Met families. In the Swedish and French subsets, the risk was below 5% until 30 y-o increasing progressively to 70% at 80 y-o. Penetrance raised dramatically from 11% at age 25 years to 68% at 50 y-o, up to 95% at 80 y-o, in the Portuguese families. The estimates were intermediate in the Majorcan kindred.

Considering the Parent-of-origin, penetrance was significantly higher when maternally inherited in the Swedish and Portuguese ATTR-Val30Met families.

Penetrance varied significantly between the non-V30M ATTR variants, increasing rapidly from 30-35 y-o up to

90% at 80 y-o in ATTR-Glu89Gln and ATTR-Thr49Ala families. In the ATTR-Ser77Phe, ATTR-Ser77Tyr and ATTR-Phe64Leu families, the risk increased after 45 y-o (8%) to 71-94% at 80 y-o. Penetrance estimates were the lowest in the ATTR-Ile107Val families raising after age 50 years.

Conclusion: Our results are important to structure the monitoring for AGC according to their geographical origin and the TTR variant.

Disclosure: Nothing to disclose

EPR3146

Comparative study of patients with an acute-onset chronic inflammatory demyelinating polyneuropathy vs. acute inflammatory demyelinating polyneuropathy in Russian population.

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Background and aims: Up to 16% of CIDP patients may start acutely (A-CIDP) mimicking AIDP. Currently, there are few data to distinguish A-CIDP from AIDP at the onset. We aimed to describe differences in these patients in an acute period.

Methods: We performed a retrospective chart review of 17 A-CIDP and 30 AIDP adult patients from March 2002 to November 2019.

Results: We analysed 47 charts of adult patients consisting of 17 A-CIDP and 30 AIDP. The mean age of patients was lower in A-CIDP group (A-CIDP 34 years vs. AIDP 48 years) with a slight prevalence of women (A-CIDP 57% vs. AIDP 42.3%, $p < 0.05$). No significant differences were found in MRCss between 2 groups (A-CIDP 52.7 vs. AIDP 55.4, $p < 0.05$), but A-CIDP patients were not likely to present pain at the onset and less often required artificial ventilation. 52.9% of patients with A-CIDP showed mainly proximal conduction blocks (CB) on nerve conduction study (NCS) and 17.6% were initially diagnosed as AMAN. No significant differences in protein level in CSF were observed. 47% of A-CIDP patients required repetitive and/or combined courses of immunotherapy. Notably despite of therapy there was a progression of CB and 2ndary axonal involvement on NCS in these patients.

Conclusion: There are still low data to distinguish A-CIDP at the onset. But, according to our study, patients with AIDP with mainly proximal CB on NCS with poor response to the initial therapy need a close follow-up regarding A-CIDP.

Disclosure: Nothing to disclose

EPR3147

Peripheral neuropathy while use different methods of insulin therapy in diabetes mellitus type 1

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Background and aims: Dysmetabolic peripheral neuropathy manifested by polyneuritic symptoms like a feet pain, cramps, numbness, is 1 of most common neurological conditions caused by diabetes mellitus. The aim of the study is a comparative analysis of development of polyneuropathy in patients with type 1 diabetes mellitus (T1DM) who

receive continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDII).

Methods: The study included 100 patients aged 29 ± 11 years with the disease duration 14.25 ± 9.25 , the level of HbA1c 9.5 ± 1.5 %. The 1st group (N=50) consisted of patients were on MDII for 11.3 ± 5.4 , last 4.5 ± 1.5 with CSII. The 2nd group (N=50) of patients with MDII for 12.7 ± 7.7 . The assessment was performed using Neuropathy Symptoms Scores (NSS), Neuropathy Disability Score (NDS), Total Symptoms Score (TSS).

Results: CSII-group had lower polyneuritic signs and symptoms in comparison with MDII-group on 29% by NSS, 76% by TSS, 50% by NDS (Table 1, Figure 1) ($p < 0.05$).

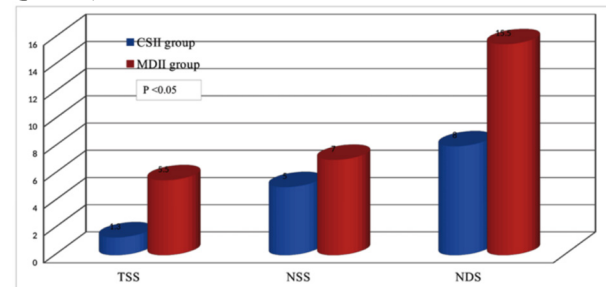


Figure 1. Test results in the study groups

Score	CSII group	MDII group
TSS	1.3 (0; 3.3)*	5.5 (4.7; 7)*
NSS	5 (0; 6)*	7 (6; 8)*
NDS	8 (6; 10)*	15.5 (14; 23)*

($p < 0.05$)

Table 1. Comparative results of neuropathic assessment in the groups.

Conclusion: The comparative analysis of the development peripheral nervous system complications of diabetes mellitus type 1 with use different methods of insulin therapy has revealed significant differences in the presence and severity of signs and symptoms of polyneuritic dysfunction, which indicate the advantages of use CSII in terms of prevents of development of dysmetabolic polyneuropathy in T1DM.

Disclosure: Nothing to disclose

EPR3148

Nerve ultrasound in transthyretin amyloidosis: possible diagnostic red flags.

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Background and aims: The most common neurological manifestations of hereditary transthyretin amyloidosis (ATTR) are axonal symmetric polyneuropathy and carpal tunnel syndrome (CTS). Onset of CTS may occur several years before the diagnosis of amyloidosis. Idiopathic CTS is very common (prevalence of 10%) thus making it difficult an early diagnosis of TTR-related CTS. Also, the accurate monitoring of the asymptomatic ATTR carriers is of great importance in order to detect early signs of disease onset. The 1st aim of our study was to identify possible ultrasound morphological pattern of CTS in ATTR. The 2nd aim was to assess whether extensive nerve ultrasound evaluation would help identify peculiar patterns in ATTR patients and carriers.

Methods: Patients and carriers with TTR mutation were enrolled from several Italian centers. Severity of CTS was assessed with neurophysiology and clinical scales. Median nerve cross-section area (CSA) was measured with ultrasound in ATTR patients and controls (idiopathic CTS). Morphological ultrasound changes were also recorded along whole nerves trunks at four limbs in patients and carriers.

Results: 62 subjects (34 men) with TTR gene mutation were recruited. While in idiopathic CTS a direct correlation between neurophysiological CTS severity and median nerve CSA ($r=0.55$, $p<0.01$) was found, in ATTR subjects median nerve CSA did not correlate with CTS severity. Increased CSA were detected in brachial plexus bilaterally in patients with polyneuropathy but not in carriers ($p<0.001$).

Conclusion: The results of the present study identify and quantify morphological patterns which can be useful in the early diagnosis and in monitoring the carriers in the ATTR.

Disclosure: This study was supported by Pfizer

EPR3149

Compound nerve conduction Z-scores: Sensitivity in polyneuropathy

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Background and aims: Combining several nerve conduction variables into one Z-score can be used to diagnose polyneuropathy (PNP). However, the optimal combination to be selected in clinical practice, from available nerves regarding motor and sensory amplitudes and velocities and F-wave latencies, is not known. Our aim was to compare diagnostic sensitivity for motor and sensory variables and several combinations thereof.

Methods: 92 consecutive patients with confirmed PNP, 21 with diabetes, 13 with cancer, 37 with other diseases and 21 idiopathic, were included. Motor velocities, amplitudes and F-waves were recorded from median, ulnar, tibial and peroneal nerves. Sensory amplitudes and velocities were obtained from median, ulnar, radial, sural, peroneal and medial plantar nerves. Single values and individual age and height-corrected Z-scores were computed for several combinations and compared with 366 control subject data.

Results: Motor nerve sensitivities were rather low. Sensory nerve sensitivities were higher in the leg, ranging from 31 to 73%. The highest sensitivities were found for combined Z scores, ranging from 64-84%. The largest sensitivity was found for a combination of 6 sensory leg parameters (velocity and amplitude), ulnar sensory amplitude, motor peroneal and tibial amplitudes, tibial and ulnar F-wave latencies, and peroneal distal motor latency.

Conclusion: Sensory nerve conduction studies in the legs are generally the most sensitive for the diagnosis of PNP, and amplitude-parameters are more sensitive than conduction velocities. The problems with multiple variable testing can efficiently be solved by the application of combined Z-score variables. Compound Z-scores seem to be the most efficient way to diagnose PNP.

Disclosure: Nothing to disclose

EPR3150

Role of MYD88 L265P mutation in chronic paraproteinemic peripheral neuropathies.

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Background and aims: MYD88 gene (myeloid differentiation factor 88) encodes for a protein involved in the proliferation of memory B-cells. A somatic point mutation of the MYD88 gene, leading to an amino acid change from leucine to proline (L265P), has been reported in 90% of patients with Waldenström disease (MW) and in 50% of patients with IgM MGUS, frequently associated with a peripheral neuropathy. The aim of the study has been to investigate the role of the MYD88-L265P mutation in relation to the clinical features of peripheral neuropathy associated with MW and MGUS IgM.

Methods: 20 patients, with a diagnosis of polyneuropathy associated to an IgM monoclonal peak, carried out at the time of diagnosis genetic test searching for the MYD88 L265P mutation. Total levels of serum IgM, light chains and anti-MAG antibodies were related to neurological and haematological disease signs and electroneurographic parameters. All patients, classified in mild, moderate or severe phenotype according to their deambulation ability and MRC score, underwent a clinical and electrophysiological 12 months follow-up.

Results: Patients with MYD88 gene mutation presented a milder clinical course and a milder involvement of the electrophysiological parameters. A significant difference ($p < 0.05$) was found in the deep peroneal nerve motor conduction velocity between patients with and without MYD88 mutation. No significant difference was found regarding total IgM levels, light chain subtype, and anti-MAG antibodies titer.

Conclusion: Although suggestive, further studies need to clarify the putative protective role of MYD88L265P mutation where associated with a milder clinical course in these forms of paraproteinemic neuropathies.

Disclosure: Nothing to disclose

EPR3151

CMT caused by MORC2 mutations in Spain

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Background and aims: MORC2 mutations are a rare cause of inherited neuropathies that was 1st recognized in 2016.

The aim of this work is to determine the frequency and distribution of these mutations throughout Spain, to provide a comprehensive phenotypical description, and if possible, to establish a genotype-phenotype correlation.

Methods: Retrospectively, we detected all the patients diagnosed with this CMT subtype in the Instituto de Investigación Principe Felipe in Valencia, as well as the patients introduced in a national CMT database. A call for collaboration was also issued in the Neuromuscular Disorder Study Group in the Sociedad Española de Neurología. After informed consent, clinical, electrophysiological, neuroimaging, and pathological data was collected and analysed.

Results: 15 patients with causal MORC2 mutations were detected throughout Spain. 7 belonged to a single kindred, but the rest were sporadic. 60% harboured the most common p.Arg252Trp mutation, while in 4 cases novel mutations were detected. In 2 patients (p.S87L, p.Y394C) the phenotype was an early onset, severe, predominantly motor neuropathy with developmental delay in 1. In the rest, the phenotype was similar, with onset before 30 years, early proximal involvement and asymmetric muscle involvement. Nerve conduction studies revealed an unequivocally axonal neuropathy with patchy denervation. Muscle imaging corroborated the proximal and asymmetric fatty infiltration, and CPK levels were usually increased.

Conclusion: MORC2 mutations are a rare cause of CMT in Spain, but in-depth phenotyping reveals a recognizable pattern that may be clinically relevant for future recognition of this disease.

Disclosure: Nothing to disclose

EPR3152

Rationale and Design of NEURO-TTRansform, a phase 3 study evaluating the efficacy and safety of AKCEA-TTR-LRx in patients with hereditary transthyretin-mediated Amyloid Polyneuropathy (hATTR-PN)

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Background and aims: hATTR-PN is a progressive and fatal polyneuropathy caused by misfolding and aggregation of transthyretin (TTR) systemically. Inotersen (Tegsedi™) is an approved antisense therapeutic that inhibits TTR production. AKCEA-TTR-LRx shares the same oligonucleotide sequence as inotersen but is conjugated to a triantennary N-acetyl galactosamine (GalNAc) moiety for receptor-mediated delivery to hepatocytes, site of TTR production. NEURO-TTRansform (NCT04136184) is a phase 3 global, open-label study that aims to determine safety and efficacy of AKCEA-TTR-LRx compared to a historical placebo-control group for the treatment of hATTR-PN.

Methods: ~140 hATTR-PN patients will be randomized to receive either AKCEA-TTR-LRx or inotersen. Key inclusion criteria include preserved ambulatory status, confirmed TTR mutation, and Neuropathy Impairment Score (NIS) 10-130. Endpoints include changes in: serum TTR concentration, modified NIS+7 and Norfolk Quality of Life-Diabetic Neuropathy at Week 66 with an interim analysis at Week 35. 2ndary endpoints include the change from baseline in the Neuropathy Symptom and Change Score, Physical Component Summary score of 36-Item Short Form Survey, and Modified Body Mass Index.

Results: In a phase 1 study, monthly dosing of AKCEA-TTR-LRx at 45 mg demonstrated a mean reduction of 86% from baseline in serum TTR with no clinically relevant changes in platelet, renal, or hepatic parameters. Based on these results, the phase 3 trial has been initiated.

Conclusion: NEURO-TTRansform evaluates safety and efficacy of AKCEA-TTR-LRx for the treatment of hATTR-PN, a disease for which there is still a need for effective, well-tolerated, and convenient treatments.

Disclosure: This trial is supported by Ionis Pharmaceuticals

EPR3153

The reliability and reproducibility of corneal confocal microscopy

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Background and aims: The aim of the study was to assess the intra- and interobserver reliability of particular parameters of corneal innervation evaluated by corneal confocal microscopy (CCM).

Methods: 30 patients with malignant lymphoma 6 months after the end of anticancer treatment containing neurotoxic vinca-alkaloids (17 men, 13 women, mean age 39 years, range 19-69) were examined using CCM. Corneal nerve fiber density (CNFD) and length (CNFL), the density of corneal nerve branches (CNBD) and nerve fiber tortuosity coefficient (TC), were evaluated by 2 independent observers in 2 different settings: image-level (where the same set of samples was evaluated repeatedly) and patient-level (where each observer chose his/her own set of samples from each patient).

Results: The intraclass correlation coefficients (ICCs) were excellent for intra-observer image-level reliability (0.956 to 0.994) and high for patient-level evaluation (0.583 to 0.852). The inter-observer reliability was slightly lower for image-level setting (ICCs 0.757-0.968), while for patient-level setting, the ICCs were similar to intra-observer reliability (0.618 to 0.910). CNFL was the most reliable parameter (both for intra- and interobserver evaluation). The ICC values in our study were very close to previous studies published mainly in diabetic neuropathy patients. The Bland-Altman plots showed minimal bias between observers.

Conclusion: Corneal confocal microscopy showed very good inter- and intra-observer reliability of most of the parameters evaluated. CNFL is the most reliable CCM parameter. Our findings thus confirmed the results of previous studies in a different group of patients.

Disclosure: Supported by MH_CZ_DRO, FNBr, 65269705.

EPR3154

Incidence, Prevalence, Pattern, and Outcome of AIDP(GBS)and CIDP among Peripheral Neuropathic Libyan Patients at BMC

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Introduction: Peripheral neuropathy, in the broadest sense, refers to a range of clinical syndromes affecting a variety of peripheral nerve cells and fibers.

Objectives: To evaluate the prevalence, incidence, pattern and outcome of AIDP and CIDP with the all PNP patients at BMC

Methods: A retrospective study for 493 peripheral neuropathy patients who presented and followed up in neurology clinic or- being admitted.

Results: The estimated prevalence of PNP patients is 33/100,000 population, M:F ratio PNP 1:2, peak age group is in the middle 2nd, 3rd and 4th decade (25-50 years), the mean age at 37 years. the most common PNP is due to CTS and Diabetic PNP (30.4 and 21.1% respectively), the overall prevalence for GBS/CIDP is 1.8/100.000 (in which GBS 0.3 /100,000 and CIDP 1.5/100,000), the incidence for GBS/CIDP is 0.4/100,000, M:F for GBS/CIDP 1:0.9, the most common pattern is symmetrical weakness (52.2%), The outcome of GBS/CIDP patients using Erasmus and (INCAT) Disability Score shows the predominant outcome range between 3 to 5.

Conclusion(s): The prevalence of PNP and GBS/CIDP is in keeping with various international figures, with incidence for GBS/CIDP of 0.4/100,000. It increases with age, females affected > males in PNP 2:1, while in GBS/CIDP there is slight male predominance 0.9:1, the most common PNP is CTS (30.4%) and diabetic PNP (21.1%), the most common pattern is the symmetrical weakness for GBS/CIDP (52.2%), with disability outcome score from 3 to 5.

Disclosure: Nothing to disclose

Sleep disorders 3

EPR3155

Disrupted Nighttime Sleep (DNS) in Pediatric Narcolepsy

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Background and aims: Disrupted nighttime sleep (DNS) is a core symptom of narcolepsy in adult patients that to date lacks a validated polysomnographic measure and not yet investigated in young patients. Here, we assess the construct validity of various DNS objective measures and evaluate its diagnostic utility for pediatric Narcolepsy Type 1 (NT1) when combined with a nocturnal Sleep Onset REM period (nSOREMP) in a large cohort of pediatric patients with CNS hypersomnias.

Methods: Retrospective, cross-sectional study of consecutive polysomnograms (PSGs) and multiple sleep latency tests (MSLTs) obtained in Boston and Bologna. Participants were drug-free, ages 6-18 years and slept at least 6 hours during the PSG. We analyzed associations between objective DNS measures and outcomes of self-reported sleep disturbance, Epworth Sleepiness Score, MSLT sleep latency, NT1 diagnosis, and CSF hypocretin values when available. We then combined the best performing DNS measure with the presence of a nSOREMP to determine the diagnostic value for NT1 using bootstrap analysis. We included n=151 NT1, n=21 narcolepsy type 2 (NT2), n=27 idiopathic hypersomnia (IH) and n= 117 controls in this analysis.

Results: Across groups, the Wake and NREM 1 bouts index had the most robust associations objective sleepiness, subjective sleep disturbance and CSF hypocretin levels ($p < 0.0001$). From 1000 bootstrap samples, the Wake/N1 index and nSOREMP have greater diagnostic accuracy for NT1 than the nSOREMP alone ($p < 0.0001$).

Conclusion: A Wake and NREM 1 bout index is a good objective measure of DNS. Combined nSOREMP and this DNS measure can improve screening for pediatric NT1 and potentially reduce diagnostic delays.

Disclosure: This study was supported by an investigator initiated grant from Jazz Pharmaceuticals, Inc and National Institutes of Health (NINDS, K23 NS104267-01A1) both awarded to Dr. Maski.

EPR3156

Telemedicine with mobile internet devices for innovative multidisciplinary patient-centred care of patients with narcolepsy. Protocol of the randomized controlled trial TENAR (TElemedicine for NARcolepsy)

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Background and aims: Narcolepsy is a rare chronic sleep disorder. Severe endocrine-metabolic and psychosocial aspects are intrinsic to the disease and require a multidisciplinary approach. Given the scarce number of specialized Sleep Centres worldwide, the disease burden is increased by the need for traveling for medical consultations, with high costs for patients and families. Telemedicine may be an important resource for both patients and clinicians. The TENAR trial is the 1st randomized controlled trial (RCT) designed to evaluate feasibility, efficacy, safety and costs of a Telemedicine multidisciplinary approach for the management of narcolepsy.

Methods: Open RCT assessing the non-inferiority of the multidisciplinary management of narcolepsy via Video Consultation (VC) through Mobile Telemedicine devices compared to usual in-office care. 202 children and adults with narcolepsy will be randomly allocated in 1:1 ratio to VC or to in-office usual care for a 12 months follow-up. At baseline, all patients will undergo a neurologic, metabolic and psychosocial assessment. Primary (i.e., excessive daytime sleepiness according to the Epworth Sleepiness Scale) and secondary endpoints (i.e., other symptoms, metabolic control, quality of life, patient and family satisfaction with care, feasibility, safety and costs) will be measured at 6 and 12 months.

Results: We expect the Telemedicine approach not only to be non-inferior for sleepiness control but also to significantly improve other patient-centred outcomes compared to the usual in-office care.

Conclusion: TENAR will provide 1st evidence of feasibility, efficacy, safety and costs of Telemedicine for the management of patients with narcolepsy.

Disclosure: This study is supported by a grant of the Italian Ministry of Health "Ricerca Finalizzata" (490.000 euro)

EPR3157

Narcolepsy with intermediate hypocretin levels: clinical and polysomnographic phenotype of 52 patients

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Background and aims: Narcolepsy is a chronic disorder currently classified in type 1 and type 2 based on the presence of excessive daytime sleepiness, established Multiple Sleep Latency Test (MSLT) findings, and either on the presence of cataplexy or cerebrospinal-fluid hypocretin deficiency (CSF-hcrt1 < 110pg/mL). We aimed to explore the clinical and polysomnographic features of narcoleptic patients with intermediate hypocretin levels.

Methods: We collected clinical, neurophysiological and biological data of suspected narcoleptic patients referred to French and Italian National Reference Centres for narcolepsy with at least 1 night of polysomnography (PSG) followed by the MSLT, and CSF-hcrt1 comprised between 110 to 200pg/ml. 52 subjects (5 children) were identified. 50% of them fulfilled the MSLT diagnostic criteria for narcolepsy, 78% carried the HLADQB1*06:02 haplotype. The mean delay between the disease onset and CSF-hcrt1 evaluation was 11.3 y.

Results: 7 subjects reported familial narcolepsy (parents affected with either NT1 or NT2), 2 subjects DNMT1 gene mutations and 4 subjects autoimmune/lesional forms. Cataplexy (atypical in 41.4%) was present in 55.8%. Patients with cataplexy displayed worse disturbed nighttime sleep at nocturnal PSG. Subjects without cataplexy frequently reported sleep drunkenness and prolonged nocturnal sleep time. BMI was not different between groups. Patients with cataplexy presented more SOREMPs at nocturnal PSG and at MSLT compared to those without cataplexy.

Conclusion: Narcolepsy patients with intermediate hypocretin levels represent a heterogeneous population. The high rate of cataplexy in patients with CSF-hcrt1 comprised between 110 to 200pg/ml challenges the current classification.

Disclosure: Nothing to disclose

EPR3158

Altered sleep in a group of patients affected by Pediatric acute-onset neuropsychiatric syndrome (PANS)

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Background and aims: Sleep disorders represent 1 of the most frequent manifestations in pediatric acute-onset neuropsychiatric syndrome (PANS), but very few polysomnographic studies have been conducted in this population. The aim of this study is to describe nocturnal sleep and identify any sleep disorders in a cohort of patients affected by PANS.

Methods: 23 PANS patients with a drug-free period of at least 4 weeks were consecutively enrolled. They underwent a comprehensive anamnestic and sleep habits history, a complete laboratory and neuropsychological assessment, and a complete full-night polysomnography recording (PSG).

Results: 74% showed PSG alterations. Specifically, 47% have ineffective sleep, 58.8% fragmented sleep, 47% a Periodic Limb Movement Disorder condition, and 64.7% a REM Sleep Without Atonia. 82.6% of the patients received a diagnosis of Tic Disorder/Tourette's Disorder, which was strongly correlated with the presence of a sleep disorder. Lab analysis showed high prevalence of infectious markers (Anti-Chlamydia Pneumoniae and ASLO titer) and of vitaminD deficiency, with a strong link between vitaminD deficiency, infectious markers and the sleep alterations.

Conclusion: This study confirms that sleep disorders are very frequent in PANS, representing a cardinal symptom. Results of this work lead us to hypothesize an inflammatory/dysimmune pathogenesis of sleep disorders in these patients. Sleep disturbances have been associated with a wide range of cognitive, mood and behavioral impairments, and low school performances. Therefore, evaluation of sleep since the early stages of the disease should be mandatory in these patients in order to improve quality of sleep and daytime performances.

Disclosure: Nothing to disclose

EPR3159

Determinants of excessive daytime sleepiness in restless legs syndrome

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Background and aims: Restless legs syndrome (RLS) is a neurological sensorimotor disorder characterized by uncomfortable sensations in the legs worsening in the evening, often associated with periodic limb movements during sleep (PLMS). RLS may result in sleep disturbances (insomnia and sleep fragmentation), but also excessive daytime sleepiness (EDS). We aimed to determine which factors predict subjective and objective EDS in RLS.

Methods: 97 consecutive untreated RLS patients (58.76% females, mean age 55.49±13.11 years) underwent a polysomnography (PSG) and an evaluation of RLS severity and depressive symptoms (BDI). EDS was assessed via the Epworth sleepiness scale (ESS>10/24=subjective EDS) and via the multiple sleep latency test (MSLT≤8minutes=objective EDS).

Results: The mean ESS score was 11.03±5.58, with half of the patients having subjective EDS (51 patients, 53.13%). The mean MSLT latency was 13.7±4.61min, with objective EDS in 14 subjects (14.43%). Patients with subjective EDS had shorter mean MSLT latency compared to non-sleepy patients (12.7±4.55 vs. 14.22±4.56min, p=0.04). No differences were seen between subjectively sleepy and non-sleepy patients on demographic, PSG parameters and RLS severity scale; however patients with ESS>10 had higher BDI scores.

Objective sleepiness was associated with older age and disease duration. PSG showed shorter sleep duration, reduced sleep efficacy, higher wake after sleep onset, microarousal index and PLMS index in objectively sleepy patients.

Conclusion: The presence of subjective EDS is frequent in RLS patients and associated with depressive symptoms. In contrast, objective sleepiness is less frequent, associated with older age and disease duration, worse sleep quality, higher sleep fragmentation and PLMS.

Disclosure: Nothing to disclose

EPR3160

Childhood onset REM sleep behavior disorder, ocular saccades disorder and facial development abnormalities: a new syndrome?

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Background and aims: Originally described in older patients, REM behavior sleep disorder (RBD) is now recognized as a condition that can affect childhood in association with some conditions, such as narcolepsy type 1, antidepressant medication use, structural brainstem abnormalities (e.g. midline tumors) or neurodevelopmental disorders (e.g. autism spectrum disorder). We report a patient presenting with a childhood onset sleep disturbance suggesting RBD.

Methods: A 26-year-old female was referred for a sleep disturbance characterized by episodes of screaming, vocalization and non-stereotyped movements of limbs occurring during the night, since the age of 5. She is affected from scoliosis and ankyloglossia. She had no family history of neurological or sleep disorder.

Results: Clinical and neurological evaluation revealed nasal voice and ocular flutter aggravated by lateral fixation. Oral cavity examination revealed high-arched palate and ankyloglossia. Brain MRI was unremarkable. A 48h video-PSG revealed a normal night-sleep architecture with loss of physiological REM-sleep muscle atonia and repeated episodes of vocalization and motor behaviors during all REM sleep episodes, typical of RBD. Multiple sleep latency test (MSLT) excluded excessive daytime sleepiness. Skin biopsy searching for p- α syn deposits was negative.



Fig.1: Images showing ankyloglossia (left panel) and high-arched palate (right panel)

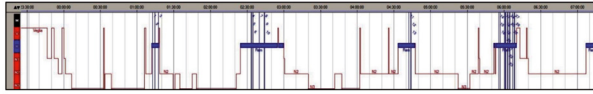


Fig.2: Hypnogram of the patient, showing normal night-sleep architecture. Five REM-sleep episodes were recorded during the night. Vertical bars and numbers indicate major episodes of abnormal motor behavior during REM sleep.

Daytime sleep	
Daytime TST (min)	0
Number of naps	0
REM latency (min)	0
Overnight recording	
Sleep efficacy (%)	95.76%
TST (hours)	7.20
Sleep latency (min)	9
REM latency (min)	85
PLM index	2.32
REM atonia index	0.466 (n.v. ≥ 0.9)
MSLT	
SL	20
SOREMP	0

Tab.1 48h video-PSG and MSLT findings. TST, total sleep time; SE, sleep efficiency; REM, rapid eye movements sleep; PLMI, periodic limb movements index; MSLT, multiple sleep latency test; SL, sleep latency; SOREMPs, sleep onset REM periods.

Conclusion: This case could represent a new syndromic condition in which scoliosis and oral abnormalities coexist with a brainstem dysfunction accountable for congenital RBD and ocular flutter. The association of RBD and saccade disorder strongly suggests a lateral pontine tegmentum dysfunction. An unknown genetic or developmental disorder could underlie a functional or structural, even if not detectable with MRI-scan, abnormality in the dorsal pons responsible for this peculiar phenotype.

Disclosure: Nothing to disclose

EPR3161

Ambient temperature (Ta) manipulation as a novel technique to dissociate REM sleep and cataplexy in narcolepsy

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Background and aims: The lateral hypothalamic melanin-concentrating hormone (MCH) system is critical for maximizing REM sleep during thermoneutral ambient temperature (Ta) warming (Komagata et al. Curr. Biol., 2019). Given the role of the hypocretin (Hcrt) system in MCH inhibition, we hypothesized that Hcrt loss in narcolepsy may enhance REM expression or cataplexy during Ta warming. We thus investigated REM sleep expression as a function of Ta during both light (inactive) and dark (active) phases in wild-type (WT), MCH receptor 1 knock-out (MCHR1-KO) and narcoleptic Hcrt-KO mice.

Methods: Mice were implanted for sleep-wake monitoring with additional video recording for cataplexy and actigraphy analyses. Thermoneutral Ta warming bouts were presented during the light or dark phases as previously described (Curr. Biol., 2019).

Results: WT mice significantly increased REM sleep with Ta warming during the light phase, but not the dark phase. Unexpectedly, we found an opposite circadian responsiveness pattern in Hcrt-KO mice, showing increased REM sleep only during the dark phase. Additionally, narcoleptic mice significantly decreased cataplexy during Ta warming. As expected, MCHR1-KO mice did not respond to Ta warming during either circadian phase.

Conclusion: Narcoleptic mice demonstrate a reversed circadian REM sleep responsiveness pattern to Ta warming compared to WT mice. Moreover, Hcrt-KO mice show a dissociation of REM sleep and cataplexy with Ta manipulation, i.e., increasing REM sleep and decreasing cataplexy during warming. These data suggest unique neural mechanisms for REM sleep and cataplexy and that Ta manipulation is a novel technique to modulate their expression for clinical or research aims.

Disclosure: Nothing to disclose

EPR3162

The value of the pupillary unrest index as a screening tool for assessing fitness to drive

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Background and aims: Sleepiness contributes to around 20% of car crashes in industrialised nations. However, its quantification remains challenging and reliable, cheap, and practical assessment methods are urgently sought. This study aimed to determine the accuracy of the pupillary unrest index (PUI) as a screening measure to assess fitness to drive in sleepy patients.

Methods: We retrospectively (1997-2016) analysed clinical data of untreated patients with narcolepsy-cataplexy and narcolepsy without cataplexy (NC=30, N=28), idiopathic hypersomnia (IH=47), non-organic hypersomnia (NOH=103), fatigue syndromes (FS=94), and insufficient sleep syndromes (ISS=53). The mean sleep latency in the maintenance of wakefulness test (MWT-SL) was used as the gold standard and the PUI as testing variable. We defined a private (PRIV-M) and a professional driver model (PROF-M) according to the following MWT-SL and PUI cut-off values: $\geq 20\text{min}/<9.80$ (PRIV-M), $\geq 34\text{min}/<6.64$ (PROF-M).

Results: The PUI in the PRIV-M or PROF-M reached a sensitivity of 0.52 or 0.63, a specificity of 0.80 or 0.58, a positive predictive value (PPV) of 0.51 or 0.69, and a negative predictive value (NPV) of 0.8 or 0.52. According to ROC-curves, PUI cut-off values (6.64 - 9.8) were within the optimal range.

Conclusion: The PUI was more accurate in the PRIV-M, however, 20% of the patients with an 'acceptable' PUI were not able to stay awake for 20min in the MWT. Therefore, our data suggest that the PUI should not be used as a screening measure to assess fitness to drive in sleepy patients.

Disclosure: Nothing to disclose

EPR3163

The (Mis-)Perception of Sleep: Factors influencing the discrepancy of subjective vs. objective sleep parameters

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Background and aims: Subjective perception of sleep often differs from objective measures derived from sleep studies, but factors predicting the discrepancy between subjective and objective sleep parameters are controversial, and a comparison of inpatient vs. ambulatory polysomnography (PSG) is lacking.

Methods: We retrospectively analysed 347 recordings (49% females, median age 48 years) of inpatient (n=258) and outpatient (n=89) PSG conducted between 2012 and 2016. Linear regression was applied to predict the discrepancy of objective and subjective sleep parameters (total sleep time, sleep efficiency, sleep latency), using age, gender, sleep disorder (hypersomnia, parasomnia, sleep-related movement disorders, sleep-related breathing disorders), and PSG type (inpatient vs. outpatient) as regressors.

Results: Sleep disorder was the best predictor of discrepancy between objective and subjective total sleep time (Beta=0.21, $p=0.003$) and sleep efficiency (Beta=0.25, $p<0.001$), independent of age and PSG type ($p>0.05$). Sleep efficiency showed a contributory effect of female gender (Beta=0.15, $p=0.01$). Patients with insomnia showed higher discrepancy of objective vs. subjective sleep parameters compared to all other patient groups (all $p<0.05$). Insomniac patients underestimated both total sleep time (median discrepancy: 46 minutes, $p<0.001$) and sleep efficiency (median discrepancy: 11%, $p<0.001$). No significant predictor for discrepancy of sleep latency was found.

Conclusion: Misperception of sleep duration and efficiency is common in sleep lab patients, but found to be most prominent in patients suffering from insomnia, independent of age, gender, or inpatient vs. ambulatory recording setting. These findings challenge the concept of sole clinical diagnosis of insomnia, and highlight the significance of performing sleep recordings in insomniac patients.

Disclosure: Nothing to disclose

EPR3164

RLS, Insomnia, and OSA in postmenopausal women: the effect on sleep, emotional profile and cognitive functioning

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Background and aims: Sleep curtailment is linked to cognitive impairment via cerebrovascular alterations or enhanced amyloid deposition, especially in women. Our research aimed to compare the effects of sleep on women's cognitive and emotional profiles in 3 sleep disorders: primary insomnia, obstructive sleep apnea (OSA), and restless leg syndrome (RLS).

Methods: 30 postmenopausal women, 10 per disorder (mean age: 61.00; SD=6.84), completed the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Hamilton Anxiety Rating Scale (HAM-A), Beck Depression Inventory (BDI), cognitive assessment and neuroimaging (CT/MRI). Menopausal onset was comparable among groups (mean age: 48.3; SD=5.05).

Results: ESS was worse in OSA (mean score:12.20) versus insomnia (6) and RLS (9.6). PSQI, BDI, and HAM-A were worse in insomnia versus OSA and RLS. 63.3% of our sample had mild cognitive impairment (MCI): 60% presented vasculopathic changes on MRI/CT, 3.3% brain atrophy. 80% of OSA patients had MCI, of which 70% presented vascular changes, 10% atrophy. 60% of insomniacs and 37.5% of RLS subjects had vascular-related MCI. In all groups, years from menopause-onset positively correlated with PSQI; in OSA also with ESS. ESS correlated with anxiety and depression in RLS and insomnia, only with depression in OSA. MCI correlated with PSQI in RLS and insomnia, and with depression and anxiety in OSA.

Conclusion: Depression, anxiety and poor sleep quality are highly prevalent in all groups. Excessive sleepiness affects only OSA subjects, who also share the highest-burden of MCI. Sleep quality is more altered in insomnia and RLS, correlating with MCI in both groups.

Disclosure: Nothing to disclose

EPR3165

Migraine, Depression, and Sleep-Related Eating Disorder (SRED): gender-related comorbidities of RLS

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Background and aims: Possibly related to a common dopaminergic imbalance, migraine, depression and sleep-related eating disorder (SRED) are often co-morbid to RLS and appear to be more prevalent in women. We aimed to explore the prevalence, features, and impact of these disorders in RLS women versus men.

Methods: 100 consecutive RLS patients, 61 women (mean age: 57.49; SD=12.52) and 39 men (mean age=60.38; SD=9.78), were assessed for RLS family history, comorbidities, RLS severity (IRLS-RS), Beck Depression Inventory (BDI), Eating Disorder Inventory (EDI) on at least two visits: T0 and T1 (6-24 months later).

Results: 44.9% of the female cohort vs. 27.7% men had a positive RLS family history. As far as comorbidities, migraine was present in 30.2% women vs. 5% men, SRED in 25.6% women versus 7.5% men and depression in 43% women versus 38% men. Mere suspension of antidepressants led to full remission of RLS in 44% of our cohort with significant improvement of symptoms. Depression and RLS symptoms were worse in women versus men both at T0 ($p=0.000$, $p=0.003$ respectively) and T1 ($p=0.005$, $p=0.000$ respectively), however, response to therapy (dopaminergic and alfa-2-delta drugs) was better in women (72.8% improvement) versus men (51.8%).

Conclusion: In our cohort, women were prevalent, had more severe RLS with positive family history, a higher burden of comorbidities, but a greater improvement of BDI and RLS symptoms with therapy. RLS proved iatrogenic in 44% of our sample on antidepressants

Disclosure: Nothing to disclose

EPR3166

Circadian phase tailored light therapy in Alzheimer's disease: preliminary findings on sleep and cognition

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Background and aims: Our study aims to investigate the effects of a tailored light therapy protocol on sleep and cognition parameters in patients with Alzheimer's disease (AD) of mild/moderate severity.

Methods: 20-drug-free, AD patients were consecutively investigated for cognitive and behavioral performances, subjective nocturnal sleep quality, circadian phase and actigraphic sleep parameters before and after a single-blind 4-weeks tailored light therapy versus sham protocol (Luminette glasses with light (10000 lux) 20 minute-exposure). We present preliminary data of 8 patients (M/F: 4/4; mean age 72±5.7 years; mean MMSEc 19.02±2.71) who completed the protocol.

Results: Light therapy induced a circadian phase shift in five patients. The circadian phase was delayed of 171 minutes (Dim Light Melatonin Onset (DLMO) 21:30±0:53) in the 2 early circadian phase (ECPpts; DLMO 18:39±0:32) while it was advanced of 66 minutes in 3 late circadian phase (LCPpts; DLMO 22:21±1:05 vs DLMO 21:15±1:07), unchanged in 1 and unexpectedly delayed in 2. Sleep efficiency did not change in both ECPpts and LCPpts; 24-hour total sleep time increased and sleep quality significantly improved ($p<0.05$) in both subgroups of patients. The cognitive performances in the ECPpts improved after light therapy (MMSEc 18.20±5.94 vs 22.55±0.77) while it remained unchanged in the LCPpts (MMSEc 20.30±3.25 vs 21.04±2.79).

Conclusion: The light therapy protocol tailored on the circadian phase proved to be associated to an objective phase shift, an increase in subjective sleep quality, 24-hour total sleep time and a better cognitive performance in patients with mild/moderate forms of AD.

Disclosure: Nothing to disclose

EPR3167

The Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (SPHYNCS)

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Background and aims: Narcolepsy type I (NT1) is a disorder with well established biomarkers and a suspected autoimmune etiology. Conversely, narcolepsy type 2 (NT2) and the narcoleptic borderland (NBL) lack well defined biomarkers and remain controversial in terms of etiology, diagnosis, and management. SPHYNCS is a multicentre cohort study which will study presentation and long-term course, search for new biomarkers and assess the frequency of established biomarkers of NT1, NT2 and NBL.

Methods: 5 swiss sleep centers which belong to the Swiss Narcolepsy Network joined the study (additional 4 may be added soon) will prospectively enroll over 4 years over 300 patients with recent onset of excessive daytime sleepiness (EDS), hypersomnia (H) or a suspected central disorder of hypersomnolence (CDH). Healthy controls (HC) and patients with EDS due to severe sleep related breathing disorder, which is improved after therapy, will represent a control group of over 50 patients.

Results: Clinical, electrophysiological (polysomnography, actigraphy, vigilance tests, longterm monitoring with wearables) and questionnaire information will be collected at baseline and after 6, 12, 24 and 36 months. Potential biomarkers will be searched for in blood, cerebrospinal fluid, and stool. Analyses will include hypocretin measurements, proteomics and peptidomics, immunological, genetic and microbiota studies.

Conclusion: SPHYNCS, which in the near future plans to include also pediatric patients, will increase our understanding of CDH and the relationship between NT1, NT2 and NBL. The identification of new (clinical, neurophysiological, laboratory) biomarkers is expected to lead to better and earlier diagnosis and personalized management of CDH.

Disclosure: Nothing to disclose

ePoster Sessions

Saturday, May 23 2020

Ageing and dementia 1

EPO1001

Brain functional connectivity disruption in a large cohort of patients with primary progressive aphasia

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Background and aims: To assess resting state (RS) functional connectivity patterns associated with each variant of primary progressive aphasia (PPA) in a large cohort of patients recruited from two clinical centres.

Methods: 40 nonfluent (nfvPPA), 28 semantic (svPPA), and 22 logopenic (lvPPA) patients and 62 healthy controls (HC) underwent neuropsychological/clinical assessments, and a MRI scan with T1-weighted and RS-fMRI sequences. Brain networks of interest were compared between groups accounting for gray matter atrophy.

Results: Compared to HC, all PPA patients showed reduced connectivity in the left posterior cingulum and inferior parietal cortex within the default mode network (DMN). Compared to HC and lvPPA, nfvPPA and svPPA patients showed: reduced connectivity in the left superior frontal and parietal gyri, and increased connectivity in the right lateral parietal cortex within the left frontoparietal network, in the bilateral insular cortices and anterior cingulum within the salience network, in the left cerebellar subregion VIII within the cerebellar network, and in the left anterior cingulate cortex within the frontostriatal network. Compared to HC, lvPPA patients showed increased connectivity in the right insula and thalamus within the salience network.

Conclusion: In all PPA variants, the DMN is affected

regardless the underlying pathology. NfvPPA and svPPA cases showed common alterations reflecting their common frontotemporal degeneration. Compared to the other 2 variants, lvPPA showed increased connectivity in anterior regions, as observed in patients with typical Alzheimer's disease.

Disclosure: Supported by: Italian Ministry of Health (GR-2010-2303035; GR-2011-02351217; GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK); Ministry of Education and Science, Republic of Serbia (Grant#175090).

EPO1002

Clinical comparison of FTD cases carrying intermediate C9ORF72 expansions (16 to 25 repeats) versus cases carrying the full (>30 repeats) expansion

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Background and aims: Full C9ORF72 hexanucleotide expansions (>30 repeats) are associated with frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS).

There is evidence supporting that intermediate expansions (16-29 repeats) may also have pathogenic impact.

Methods: Retrospective study of a cohort with FTD recruited at a Dementia Unit.

Results: There were 18 probands carrying full expansions (plus 2 siblings n=20, 40% men, mean age at onset 62,6 years) and 17 with intermediate expansions (16 to 25 repeats, 29% men, mean age at onset 65,6 years). Each group corresponded to around 5% of the cohort. None of 216 controls had alleles with more than 14 repetitions.

All cases with the full expansion had a family history of dementia or ALS, while 7 of the cases with intermediate expansion had no family history. Behavioral variant was the most common phenotype in both groups, as well as symmetric frontotemporal atrophy on neuroimaging. ALS was more frequent in cases with full (3 probands plus another 4 proband having a sibling with ALS) versus intermediate expansions (1 proband plus another 2 probands with a sibling). Parkinsonism was present in around 14% of cases in both groups.

Conclusion: Intermediate C9ORF72 expansions are as prevalent as full expansions in our FTD cohort. Patients carrying intermediate expansions have a similar dementia phenotype but association with ALS is less frequent and they are less likely to have a positive family history.

Disclosure: Nothing to disclose

EPO1003

Nonsense mutation in ADAM10 (p.tyr167*) associated with familial Alzheimer's disease: a clinical correlate of alpha-secretase haploinsufficiency

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Background and aims: The disintegrin metalloproteinase 10 (ADAM10) is the main α -secretase acting in the non-amyloidogenic processing of the amyloid precursor protein. Some ADAM10 gene variants have been associated with higher susceptibility to develop late-onset disease, though a clear clinical-genetic correlate has not been reported yet. We present a family in whom development of AD was associated with a nonsense ADAM10 prodomain mutation (p.Tyr167*) causing haploinsufficiency.

Methods: Clinical-genetic and CSF biomarker study of a family with AD.

Results: The p.Tyr167* mutation was absent from public databases and segregated with the disease. Age at onset for 3 affected siblings ranged from 58 to 68 years, and their clinical phenotypes have been noteworthy for the slow disease evolution. CSF Ab42, total tau, and phosphorylated tau biomarkers were consistent with AD. Haploinsufficiency was demonstrated by: a) ADAM10 isoforms in CSF decreased around 50%, and b) 70% reduction of CSF sAPP α peptide, both compared to controls. Sporadic AD cases had a similar decrease in CSF ADAM10 levels to that of mutants, though their sAPP α levels resembled those of controls.

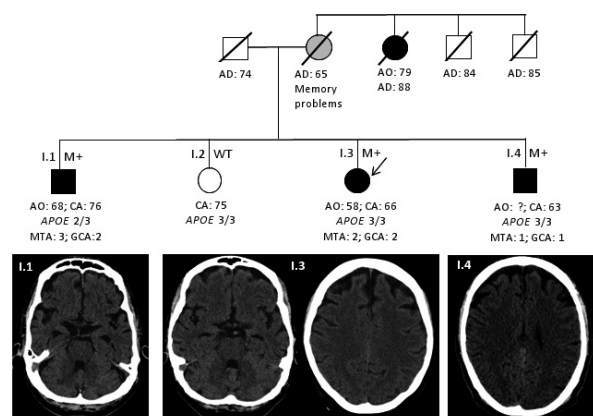


Figure 1 Family tree including ADAM10 Tyr167* mutation and clinical status

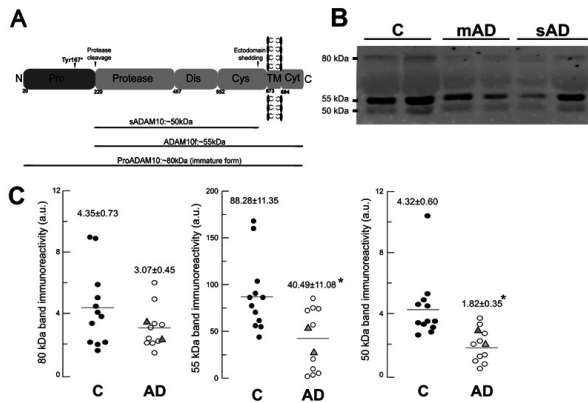


Figure 2 Levels of ADAM10 in AD CSF samples

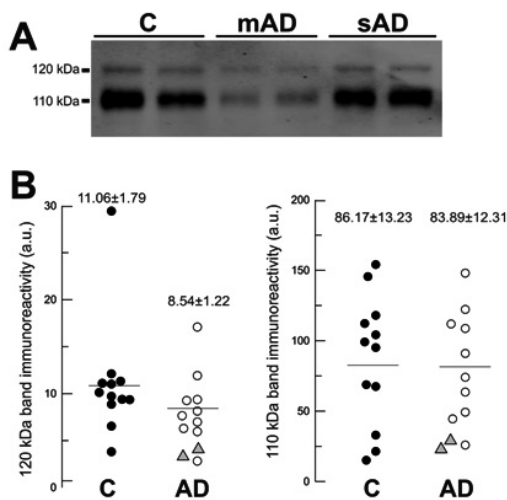


Figure 3 Levels of sAPPα peptide in CSF samples

Conclusion: This family provides the first example of a deleterious coding variant in ADAM10 associated with familial AD, and further implicates the amyloidogenic process in the development of the disease. Similarities between clinical and biomarker findings suggest that this family could represent a genetic model of sporadic late-onset AD due to an age-related down-regulation of α-secretase activity.

Disclosure: Nothing to disclose

EPO1004

Blood-brain barrier dysfunction in Alzheimer’s disease is different in female and male patients

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Background and aims: Blood-brain barrier (BBB) breakdown, measured by CSF/serum albumin ratio(Qalb), can be linked to Alzheimer’s disease (AD). Recent studies report that BBB impairment may be associated with sex-related differences and brain microvascular damage but doesn’t relate to amyloid pathology or APOE genotype. We assessed if the disruption of BBB was associated with demographic and clinical data, AD biomarkers and the APOE genotype. We also investigated possible risk factors for BBB damage.

Methods: We included 206 AD patients and compared demographic variables, cognitive and laboratorial measures, namely CSF protein electrophoresis, CSF amyloid β, total tau, and p-tau, and APOE4 genotype. BBB impairment was defined a priori as a CSF albumin index>9. Descriptive and comparative statistical analysis was performed, defining p<0.05 as statistically significant.

Results: BBB breakdown was more apparent in men (p=0.001). Patients with BBB impairment were more likely to be older (p=0.061) and have later onset (p=0.075), but didn’t have a higher prevalence of diabetes, hypertension or hypercholesterolemia. We didn’t find any associations between the Qalb and APOE genotype (p=0.306). Qalb was associated with coexisting obesity (p=0.003) and smoking (p=0.029). When adjusted for other variables, Qalb was only independently associated with sex (β=-0.001, -CI=[-0.002,-0.001], p=0.003).

Conclusion: BBB integrity isn’t directly associated with Aβ pathology or the APOE ε4 genotype. BBB impairment may be associated with obesity and smoking. The lower BBB integrity in males suggests a sex-specific difference, possibly related to different prevalence. Sex-specific BBB integrity may be important in therapeutic interventions, as it may modulate the drug SNC penetrance.

Disclosure: Nothing to disclose

EPO1005

A novel machine learning algorithm to predict the lewy body dementias using clinical and neuropsychological scores

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Background and aims: Parkinson's disease dementia (PDD) and Dementia with lewy bodies (DLB) are dementia syndromes that overlap in many clinical and neurocognitive features, making their diagnosis difficult in clinical practice, particularly in advanced stages. We propose a highly predictive machine learning algorithm, based only on non-invasively and easily in-the-clinic collectable predictors, to identify these disorders.

Methods: The algorithm was developed using dataset from 2 general hospitals, employing a sample of 58 PDD and 28 DLB subjects whose diagnosis was confirmed by 2 chief physicians. A restricted set of information regarding clinico-demographic characteristics, 7 neuropsychological tests (mini mental, PD Cognitive Rating Scale, Brief Visuospatial Memory test, Symbol digit written, Wechsler adult intelligence scale, trail making A and B) was used as predictors. 2 classification algorithms, logistic regression and K-Nearest Neighbors (K-NNs), were investigated for their ability to predict successfully whether patients suffered from PDD or DLB.

Results: The K-NN classification model classified with accuracy 91.2% of overall cases based on 15 best clinical and cognitive features achieving 96.42% sensitivity and 67% specificity on discriminating between the 2 conditions. Regarding the binomial logistic regression classification model, it achieved an accuracy of 87.5% on average based on 15 best features, showing 93.93% sensitivity and 57% specificity.

Conclusion: This algorithm has a high prognostic performance to predict these disorders with high accuracy using easy -to calculate- neuropsychological scores. Furthermore, it improves the recruitment in clinical trials, which could potentially be used as additional decision-making tools in the clinical practice.

Disclosure: Nothing to disclose

EPO1006

Progression of brain functional connectivity changes associated with altered cognition in amyotrophic lateral sclerosis

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Background and aims: To investigate the progression of brain functional connectivity alterations in patients with amyotrophic lateral sclerosis (ALS) and to define the relationship between ALS cognitive alterations and Resting State-Functional Connectivity (RS-FC) changes over time.

Methods: At baseline and after 6 months, 23 newly diagnosed ALS patients underwent 3D T1-weighted MRI, RS-fMRI and a computer-based battery (Test of Attentional Performance-TAP). To assess RS-FC over time, an independent component analysis was performed. For each network of interest, general linear models accounting for grey matter atrophy assessed RS-FC changes over time and the relationship between RS-FC and cognitive changes.

Results: Longitudinally, ALS patients showed an increased FC in the left anterior cingulate cortex, left middle frontal gyrus and bilateral superior frontal gyrus within the frontostriatal network, and in the left middle frontal gyrus, right inferior frontal gyrus and bilateral inferior parietal gyri within the left frontoparietal network. We observed that a worse performance at baseline TAP divided attention subtest was related with increased FC over time in the left middle frontal gyrus within the frontostriatal network. No association emerged between RS-fMRI and cognitive changes over time.

Conclusion: Over 6 months, FC progressed beyond the brain motor network. Increased connectivity in frontal regions in relation with greater frontal-executive deficits at baseline suggests that it is likely not a mechanism of compensation but rather a sign of disease progression as observed in the frontotemporal lobar degeneration. These findings offer new potential markers for monitoring the ALS progression.

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EPO1007

Brain functional connectivity associated with the right temporal degeneration

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Background and aims: The aim of the present study was to assess functional connectivity (FC) patterns associated with the right temporal variant of frontotemporal dementia (rtvFTD) in comparison with normal aging.

Methods: We enrolled 6 patients with a recent clinical and imaging-based diagnosis of rtvFTD and 20 age- and sex-matched healthy controls (HC). A comprehensive neuropsychological assessment targeting all cognitive domains and resting state functional MRI (RS-fMRI) were obtained from all participants. RS FC networks were identified using an independent component analysis (GIFT toolbox, SPM12). For each network of interest, comparisons between groups were performed. Differences in cognitive scores were also measured between groups.

Results: At the neuropsychological assessment, all patients presented with behavioural changes, difficulties in naming and language comprehension, abstract reasoning, and emotion and famous faces identification. Compared to HC, rtvFTD patients showed increased connectivity in the right fusiform gyrus within the anterior-temporal network, and in the right inferior temporal cortex (Brodmann area 20) within the right FPN.

Conclusion: This study showed that rtvFTD patients are characterized by altered FC in networks beyond the pure frontal and language circuits, mostly targeting pivotal regions involved in high-level visual processing. Whether the observed increased FC is a compensatory mechanism or rather reflects the underneath pathological process still needs to be determined. RS-fMRI is a fundamental tool which permits to improve the distinction between this rare and still poorly investigated condition and other variants of FTD.

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EPO1008

Behavioural and psychological symptoms in mild cognitive impairment: could they differentiate Alzheimer dementia vs other dementia in very early stages?

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Background and aims: Neuropsychiatric symptoms (NPS) are core features of Alzheimer's dementia (AD) and related dementias. These symptoms are currently to manifest in early disease such as Mild Cognitive Impairment (MCI). Depression, anxiety, apathy, sleep disorders have been hypothesized to represent a prodromal stage of dementia increasing the risk for conversion from minor to major neurocognitive disorder. We assessed frequency and severity of NPS in MCI patients evaluating their relationship with presence of amyloid biomarker assessment (PET or CSF).

Methods: 423 subjects affected by MCI were enrolled. Of those, 177 with unclear clinical diagnosis, were evaluated for amyloid biomarkers. Geriatric Depression Scale and Neuropsychiatric Inventory were administered to understand prevalence and severity of NPS.

Results: Female gender was prevalent (58.2%) in a sample with a mean age of 69.5 (5.8 SD). Of the amyloid positive patients, the 49.2% was positive for depressive symptoms, while only the 33.3% of the amyloid negative reported depressive symptoms. Total burden of NPS was higher in amyloid positive patients (26.4 SD 4.4) than negative ones (18.9 SD 3.7). Neurodegenerative dementia due to AD showed a rate of depression, anxiety and apathy are the prevalent NPS in amyloid positive patients while hallucinations, and sleep and appetite behaviour disorders are prevalent in amyloid negative patients.

Conclusion: AD prevalent NPS, (depression and apathy) were significantly more present in amyloid positive MCI patients. Those findings confirmed that NPS in prodromal phases could help physicians in defining diagnosis of dementia since prodromal phases.

Disclosure: Nothing to disclose

EPO1009

Preliminary data from a study on clinical and neuroradiological correlations between cerebral microbleeds and different subtypes of mild cognitive impairment

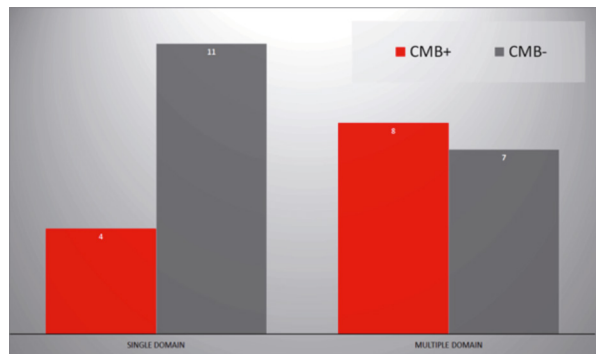
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Background and aims: Mild cognitive impairment (MCI) is a cognitive decline greater than expected for an individual's age and education level but that does not interfere with activities of daily life. Cerebral Microbleeds (CMBs) are small hypointense lesions seen in specific MRI sequences, expression of impaired small vessel integrity, due to either hypertensive vasculopathy or cerebral amyloid angiopathy. Our aim is to explore correlations between the presence and location of CMBs and different subtypes of MCI.

Methods: Our cohort consisted of 30 patients with MCI who underwent an extensive neuropsychological assessment defining the subtype. We then performed a brain MRI-scan including T2*Gradient-Recalled Echo and Susceptibility-Weighted Imaging sequences. Microbleed Anatomical Rating Scale was used to assess CMBs burden and location.

Results: Neuropsychological evaluation showed 15 multiple-domain and 15 single-domain MCI; 15 subjects were amnesic (aMCI) and 15 non-amnesic (naMCI). CMBs were present in 12 patients and absent in 18 patients. In the CMB+ group, 8/12 patients were MD (66.6%); in the CMBs- group only 7/18 patients were MD (38.8%). All CMBs+ patients had lobar-CMBs, with deep CMBs in 3 cases.



Comparison between CMB+ and CMB- groups in relation to the clinical subtype of MCI, showing a higher prevalence of CMBs in multiple domain MCI.

Conclusion: Although the number of patients is too small to outline definitive conclusions, the lobar location of all CMBs+ cases may indicate that amyloid deposition in the wall of vessels has probably a greater role than cardiovascular risk factors in determining CMBs formation. Another more interesting observation, never reported, is that CMBs seems to have a higher prevalence in MD subtypes, thus suggesting that the presence of CMBs may extend the cognitive spectrum of MCI.

Disclosure: Nothing to disclose

EPO1010

Approximating dementia prevalence in population-based surveys of aging worldwide: an unsupervised machine learning approach

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Background and aims: Estimating dementia prevalence in low and middle-income countries (LMIC) remains challenging. We sought to calculate dementia prevalence in high income countries (HIC) and LMIC using unsupervised machine-learning in population-based surveys of aging.

Methods: We applied hierarchical clustering after principal component analysis to participants' data from 10 studies: HRS (USA, 2014, N=18,290), SHARE (Europe and Israel, 2015, N=67,226) MHAS (Mexico, 2015, N=14,645), ELSI (Brazil, 2016, N=9412), CHARLS (China, 2015, N=16,262), IFLS (Indonesia, 2014-2015, N=7999), LASI (India, 2016, N=1083), SAGE-Ghana (2007, N=4294), SAGE-South Africa (2007, N=3840), SAGE-Russia (2007-2010, N=3643). We used demographics, health factors, functional status, cognition and neuropsychiatric symptoms (NPS) to identify individuals with high likelihood of dementia. We approximated dementia prevalence using weighting methods.

Results: Our classification identified individuals with high likelihood of dementia based on impaired functional status, mobility, cognition and higher NPS. Estimated number of dementia cases (standardized prevalence over age 50) was in China: 40.2 million (15.5%), India: 18.0 million (13.7%), Russia: 5.2 million (14.9%), European countries and Israel from SHARE: 5.0 million (4.6%), United States: 4.4 million (4.0%), Brazil: 2.2 million (8.0%), Mexico: 1.6 million (8.5%), Indonesia: 1.3 million (5.2%), South Africa: 1.0 million (19.2%), Ghana: 319 thousand (19.2%). Our estimations were similar to prior dementia estimates for HIC but much higher than previous ones in LMIC.

Conclusion: Unsupervised machine-learning can approximate dementia prevalence in population-based surveys. This approach suggests dementia affected almost 130 million people worldwide in 2015. It may be helpful to inform public policy and interventions.

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EPO1011

Amyloid PET imaging: potential applications to white matter pathology in neurodegenerative disorders

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Background and aims: White matter (WM) pathology in dementia has been broadly attributed to cerebral microangiopathy. Previous studies speculated a role of β -amyloid ($A\beta$) in this process accounting for the higher WM lesion load (LL) described in Alzheimer disease (AD). Recently, positron emission tomography (PET) with $A\beta$ tracers (amy-PET) has been regarded as an emerging tool for the assessment of microstructural WM damage.

Methods: 45 cognitively impaired patients underwent brain magnetic resonance imaging (MRI), amy-PET and $A\beta$ 1-42 determination from CSF samples. 24 subjects exhibiting concordant results between amy-PET (evaluating also cortical amyloid deposition) and CSF analysis were recruited and splitted according to their amyloid positivity (Ab^+ vs Ab^-). LL quantification and brain volumes segmentation were performed. Standardized uptake values ratio (SUVR) were calculated in grey matter (GM), NAWM and in DWM after MRI coregistration.

Results: Ab^+ showed a higher WMLL ($p=0.05$) as well as higher SUVR in all brain tissues compared to Ab^- ($p<0.001$). No correlation between CSF $A\beta$ levels and DMW and NAWM SUVR was found in Ab^+ , whereas in Ab^- CSF $A\beta$ levels showed direct correlation with DMW ($p=0.006$) and NAWM SUVR ($p=0.05$). CSF $A\beta$ concentration was the best predictor of DWM ($p=0.003$) and NAWM SUVR ($p=0.049$) in Ab^- . In Ab^+ only direct correlations among WM and GM SUVR were found.

Conclusion: Our data support that amyloid pathology may be involved in microstructural myelin damage in non-AD dementia, whereas amy-PET seems unsuitable to assess WM damage in AD patients as a consequence of amyloid accrual therein.

Disclosure: Nothing to disclose

EPO1012

Transcranial magnetic stimulation evaluation in patients with cognitive impairment: a three-year follow up study

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Background and aims: Alzheimer's disease (AD) is characterized by loss of synaptic connections, cell death and disruption of structural and functional networks. One of the most consistent findings is the impairment of cortical plasticity, especially Long Term Potentiation (LTP) mechanisms. Recently, the use of new diagnostic criteria allowed to consider AD as a clinico-biological entity identifiable in vivo on the presence of biomarkers. In light of these new criteria, aim of the current work is to investigate cortical plasticity in patients with hippocampal type memory impairment admitted for the first time in the memory clinic and stratified according to CSF biomarker profile; moreover we followed patients up to a period of three years to explore the relationship between neurophysiological, neuropsychological and CSF biomarker and clinical progression.

Methods: 73 patients were recruited and followed up for 36 months. They underwent CSF sampling and Transcranial Magnetic Stimulation to investigate LTP and intracortical circuits. According to the new AD criteria we divided patients in 3 groups: 1) Mild Cognitive Impaired (MCI) patients (n=21); Prodromal AD (PROAD) patients (n=24); AD Dementia (ADD) patients (n=28).

Results: ADD and PROAD showed a paradoxical reversal of LTP, while no difference was observed for intracortical circuits. Kaplan-Meier analyses showed that patients expressing the worst LTP were the ones to progress faster.

Conclusion: LTP impairment drives the clinical progression to dementia in patients at prodromal stages identifiable with the new criteria based on biomarkers' presence. These results pave the way for the identification of new therapeutic targets such as synaptic plasticity modulators.

Disclosure: Nothing to disclose

EPO1013

Altered cerebellar cortical plasticity in Alzheimer's disease patients

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Background and aims: Recent evidence suggested that cerebellum undergoes degenerative changes in Alzheimer's disease (AD): the posterior cerebellar lobes are significantly smaller in AD patients compared to healthy subjects, and atrophy of the posterior cerebellar regions is associated with poorer cognitive performance. Transcranial Magnetic Stimulation (TMS) of the cerebellum is able to activate underlying cerebello-thalamo-cortical pathways that are linked with distinct intracortical M1 circuits.

In AD patients it is already been described an altered cortical plasticity following M1 theta burst stimulation (TBS), but mechanisms of cerebellar plasticity have not been investigated yet. Thus we aimed at examining the effect of continuous and intermittent cerebellar TBS (respectively cTBS and iTBS) over M1 excitability in a sample of AD patients.

Methods: We recruited 15 newly diagnosed AD patients and 10 age-matched Healthy Control (HC). All subjects underwent in 2 different sessions cTBS and iTBS. 20 consecutive Motor evoked Potentials (MEPs) were collected before and after TBS.

Results: AD patients showed an impairment of cortical plasticity mechanisms, as detected by after effects of iTBS. Indeed, while HC showed the expected increase of amplitude of the MEPs after iTBS,

AD patients did not have any increase of MEPs, that instead seemed to decrease showing an impairment of Long Term Potentiation (LTP) mechanisms even after stimulating the cerebellum. No difference was observed for cTBS protocols, in which both populations exhibited the expected decrease of MEP amplitude

Conclusion: Cerebellum is affected by AD pathology and neuroimaging and neurophysiological studies showed alterations in morphometry and functions. Given its role in high order cognitive functions, new potential therapeutic strategies could be built up in the future to modulate cerebellum activity.

Disclosure: Nothing to disclose

EPO1014

Dyrk1a Inhibition as a treatment for AD

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Background and aims: The Dyrk1a kinase phosphorylates APP and tau, contributing to amyloid and tau pathologies of Alzheimer's disease. We previously demonstrated that inhibition of Dyrk1a in the 3xTg-AD mouse model improves memory, reduces amyloid plaques, and reduces insoluble and hyperphosphorylated forms of tau protein if inhibition occurs after pathology onset. However, overt neurofibrillary pathology was unaffected, a result not unexpected for an inhibitor of tau phosphorylation. Here we initiated treatment prior to pathology onset and tested for delay of amyloid and tau pathology in the 3xTg-AD mouse to determine if reducing tau phosphorylation can delay neurofibrillary pathology onset.

Methods: 3xTg-AD mice were dosed once daily with a Dyrk1a inhibitor (Dyr219) via IP injection starting at 6 months of age. At ages 9 and 12 months, amyloid and tau pathologies were assessed.

Results: Dyr219 significantly delayed the onset of amyloid and tau pathologies. No mice had either pathology at 9 months of age. At 12 months of age, mice had minimal plaque pathology and 25% of the cohort had no tau pathology. In contrast, vehicle treated mice had robust amyloid and tau pathology.

Conclusion: Dyrk1a inhibition significantly delays the onset of amyloid and tau pathology in the 3xTg-AD mouse model of AD. These results suggest that Dyrk1a inhibition may be a reasonable approach for the treatment of AD.

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EPO1015

Dementia in patients with psychiatric disorders: neurodegenerative syndrome or pseudo-dementia?

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Background and aims: The term pseudo-dementia (PDEM) refers to cases that closely mimic dementia, and has been especially used to describe the cognitive impairment occurring in patients with psychiatric disorders. However, neurodegenerative dementia syndromes (NDS) may also independently occur in these patients, therefore distinguishing between PDEM and NDS remains challenging. We studied baseline clinical, demographic and biomarkers differences between patients with psychiatric disorders subsequently diagnosed with PDEM or NDS.

Methods: We retrospectively recruited all patients with a diagnosis of psychiatric disorders and cognitive complaint referred to the Cognitive Neurology Clinic of Modena. They had undergone neuropsychological assessment, structural MRI and FDG-PET imaging, and measurement of CSF biomarkers for AD when indicated. We stratified them in PDEM and NDS according to the diagnosis received at clinical follow-up based on the presence/absence of progression of cognitive impairment and/or development of symptoms suggestive of dementia syndromes, then compared the two groups.

Results: We identified 46 eligible patients, of whom 15 were diagnosed with NDS (13 bvFTD, 1 AD, 1 VaD) and 31 with PDEM at clinical follow-up. There were no baseline significant differences in demographical and CSF biomarkers data. There were no baseline differences in tests of verbal and visuospatial memory, WAIS-IV test, Trial Making Test, Raven's progressive Matrices, and Frontal Assessment Battery. At baseline NDS patients had worse performance in the Stroop Test than PDEM patients ($p=0.049$).

Conclusion: Our study highlights the limited usefulness of neuropsychological test and CSF biomarkers in this context. Neuroimaging and clinical follow-up are essential for a correct differential diagnosis.

Disclosure: Nothing to disclose

EPO1016

Epidemiology of early onset dementia in Northern Italy

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Background and aims: Early onset dementia (EOD), defined as onset of dementia <65 years, frequently present with atypical, fast-progressing clinical syndromes, and has a significant impact on families and society. EOD epidemiologic data in Italy are scarce, and international estimates of prevalence are variable. We aimed at establishing EOD epidemiology in a defined population of 700.000 inhabitants in the Modena province, Northern Italy. **Methods:** We identified patients diagnosed with EOD residing in Modena province retrospectively from January 2006 to December 2016, and prospectively from January 2017 to June 2019. We collected clinical data such as age at onset, time delay from onset to diagnosis, and data on residence and occupational status.

Results: At the census date 30 June 2019 there were 258 patients with EOD. Prevalence was 74.3/100000 (71.2/100000 in males, 77.4/100000 in females) in the population aged 30-64, and 119.9/100000 (117.1/100000 in males, 122.6/100000 in females) in the population aged 45-64. Overall prevalence was 36.4/100000 inhabitants. Alzheimer's disease (AD) was the most frequent clinical diagnosis (113 patients, 43,8%) followed by the frontotemporal dementia spectrum (FTD) (78 patients, 30.23%), vascular dementia (24 patients, 9.3%), and Lewy bodies dementia (9 patents, 3,49%). Incidence was estimated in 46 new cases per year in the period 2016-2019, corresponding to approximately 13.17/100000 inhabitants.

Conclusion: We provide the first epidemiological data on EOD in Italy. These are consistent with the estimates calculated by transposing European data to the population of Modena province (estimated prevalence=200 patients, detected prevalence=258 patients).

Disclosure: Nothing to disclose

EPO1017

Biomarkers in saliva for Alzheimer's disease and other neurodegenerative diseases

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Background and aims: The pathological changes of a plethora of neurodegenerative diseases begin decades prior to their clinical expression, and therefore there is a need for an early, inexpensive and noninvasive diagnostic biomarker that can detect the changes in the pre-symptomatic phase. Currently neuroimaging biomarkers and analysis of cerebrospinal fluid (CSF) biomarkers are used to aid the diagnosis of AD and other neurodegenerative diseases. However, neuroimaging is expensive and causes radiation, while lumbar puncture is an invasive procedure. Saliva is an easily obtained source of biomarkers, and therefore saliva could be a valid alternative to CSF, neuroimaging or even blood.

Methods: A systematic review investigating biomarkers in saliva for the diagnosis of AD, was conducted in order to identify potential biomarkers. Following the systematic review, a total of 222 saliva samples from patients and healthy controls were collected. The patients were diagnosed with AD, dementia with Lewy bodies (DLB), vascular dementia (VaD), mixed dementia, frontotemporal dementia (FTD) or normal pressure hydrocephalus (NPH).

Results: In the systematic review 16 studies were included, and 10 out of the 16 studies identified biomarkers with statistical significance between patients with AD and healthy controls. It was concluded that amyloid beta 1-42 (A42β), tau, lactoferrin and selected metabolites have potential as future salivary biomarkers for AD. Results from the cross-sectional study will be presented.

Conclusion: In conclusion, non-invasive biomarkers for AD are needed, and saliva is a viable source of AD biomarkers. Potential salivary biomarkers are currently being verified in our cross-sectional study.

Disclosure: Funding obtained from: Lundbeckfonden, Absalonfonden, Frimodt Heineke Fonden, Augustinus Fonden, Fonden for Neurologisk Forskning, Grosserer L. F. Foghts Fond

EPO1018

Identification of subtypes for the behavioral variant of frontotemporal dementia based on the assessment of disinhibition and compulsion

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Background and aims: The behavioral variant of frontotemporal dementia (bvFTD) is characterized by cognitive and behavioral decline due to the progressive brain damage of frontal and temporal regions. We aimed to: 1. identify bvFTD subtypes through the behavioral assessment of social disinhibition and perseveration/compulsion; 2. disentangle the underlying functional and anatomical correlates.

Methods: We assessed occurrences of 19 behaviors (derived from current clinical criteria of bvFTD) linked to disinhibition and perseveration/compulsion in a quasi-ecological setting in 17 bvFTD patients and 16 healthy controls (HC). Subjects also underwent neurocognitive tests and a structural MRI examination. Dimensions extracted through Principal Component Analysis from the behavior variables were compared between patients and HC. A clustering approach applied to behavioral scores allowed to isolate subgroups within the patients. Voxel based morphometry (VBM) was performed to identify specific grey matter atrophy patterns in each subgroup.

Results: We identified 2 principal behavioral dimensions significantly different between bvFTD and HC. Using scores on these 2 components (labelled as Compulsion and Disinhibition), we identified 2 different subgroups of bvFTD patients (bvFTD-G1 and bvFTD-G2). BvFTD-G1, characterized by high Disinhibition, had a small pattern of atrophy, centered on left medial anterior and posterior temporal cortices. BvFTD-G2, characterized by high Compulsion and cognitive impulsivity, presented a more diffuse and bilateral atrophy pattern largely involving frontotemporal and subcortical regions.

Conclusion: The assessment of disinhibition and compulsion symptoms in bvFTD patients allows the clinical stratification of bvFTD patients from less to more severe stages or forms, and the identification of specific brain circuits associated with disinhibition and compulsion.

Disclosure: Nothing to disclose

Autonomic nervous system disorders

EPO1019

Cognitive performances in a cohort of pure autonomic failure patients

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Background and aims: Some patients with autonomic failure onset maintain a Pure Autonomic Failure (PAF) presentation for many years, others develop motor and/or cognitive deficits. While motor changes were exhaustively evaluated in previous cohorts, cognitive functions had been marginally examined with screening tests, like MMSE, to detect the presence or not of a dementia stage. To find out whether mild cognitive impairment is associated to phenotype conversion as well, we extensively assessed cognitive performances in a prospective cohort of PAF patients.

Methods: From the well-characterized IAF-BO cohort, we selected patients who meet PAF criteria and underwent a comprehensive neuropsychological evaluation (NPS).

Results: 24 patients performed NPS (mean age 59.75±8.66 years; disease duration 11.76±5.43 years). Although nobody had subjective complains, 10 out of 24 patients (41.7%) were cognitively impaired (CI), 9 on attentive-executive tests and 1 on short-term verbal memory. 5 out of 10 patients meet criteria for mild cognitive impairment (MCI). No differences in clinical variables, cardiovascular autonomic function parameters or sleep disturbances were found between cognitive normal, CI and MCI patients. After 2-8 years of observation, 3 patients converted to overt synucleinopathies. Nobody was cognitive impaired at NPS before conversion-time. None of PAF patients with CI patients converted during follow-up.

Conclusion: A comprehensive neuropsychological evaluation disclosed an attentive-executive dysfunction in 37.5% of PAF patients. Cognitive deficits are not strictly associated with phenotype conversion over 5 years. Further evaluations are mandatory to disclose the cause of cognitive impairment in PAF.

Disclosure: Nothing to disclose

EPO1020

Autonomic dysfunctions in males with Parkinson's disease: case control study

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Background and aims: Autonomic symptoms are frequent non-motor complains in Parkinson's disease (PD). The aim of this study is to assess the prevalence of autonomic symptoms in male PD patients and their impact on quality of life.

Methods: A case-control study including 63 male PD patients and 63 controls. The assessment of patients included the following instruments: Non-Motor Symptoms Questionnaire and Scale, Parkinson's Disease Questionnaire (PDQ-39) and SCOPA-AUT scale.

Results: In the study group, mean age was 66.8±14.3 years, mean duration of PD 6.2±4.7 years. PD patients disclosed a higher prevalence for all autonomic domains, compared to control group (p<0.05). The prevalence is higher for drug-naïve PD patients and increases with age and disease severity. The most affected domains were the urinary, gastrointestinal and sexual ones. There was a higher prevalence of autonomic symptoms in PD group vs control group: i.) erectile dysfunction in 63 (73.01%) vs 17 (26.98%) patients; ii.) constipation 38 (60.31%) vs 9 (9.52%); iii.) urgency 28 (44.44%) vs 4 (6.34%).

In the PD group there was at least one autonomic symptom described by 57 patients comparing with 12 in the control group. PD patients scored higher than controls in the total SCOPA-AUT score. Mean total SCOPA-AUT score was correlated with disease duration, disease severity and PDQ-39 scores.

Conclusion: Autonomic symptoms in PD have a high prevalence compared to control group. The actively assessment of these symptoms is needed in clinical practice.

Disclosure: Nothing to disclose

EPO1021

The autonomic innervation of hairy skin in humans: an in vivo confocal study

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Background and aims: The chemical code skin autonomic innervation is complex and often difficult to ascertain and a detailed description of skin autonomic fiber subtypes is lacking in man. This study aimed to characterize subtypes of autonomic fibers in relationship to their target organs by means of an immunofluorescent technique and confocal microscopy

Methods: We studied 7 healthy subjects (5 males and 3 females) with mean age of 45±2 years. A combination of autonomic (i.e. tyrosine-hydroxylase- TH, and DbH and VACHT) and neuropeptidic (i.e. Calcitonin Gene Related Peptide-CGRP, substance P-SP, and vasoactive intestinal peptide-VIP) markers. Skin autonomic structures analysed included: 58 sweat glands (SG), 91 skin vessels mainly arterioles (SV) and 47 arrector pili muscle (APM)

Results: All skin structures presented sympathetic adrenergic and cholinergic innervations but with a different proportion. Sympathetic adrenergic fibers were particularly abundant around SV and APM whereas cholinergic fibers were mainly found around SG. Neuropeptides were differently expressed in sympathetic fibers: CGRP, SP and VIP were expressed in sympathetic cholinergic fibers but they were not found in adrenergic fibers. Pure cholinergic fibers expressing CGRP, SP or VIP were found in SV and APM and they likely represent parasympathetic fibers. Neuropeptidic fibers devoid of adrenergic and cholinergic markers were found in a small subset of fibers in all skin structures analyses with a likely sensory function.

Conclusion: Hairy skin contains sympathetic adrenergic and cholinergic fibers differently distributed around skin structures with different distribution of neuropeptides. The autonomic skin innervation also contains a small amount of likely parasympathetic and sensory fibers

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EPO1022

The interplay between psychological distress and autonomic nervous system symptom burden

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Background and aims: Psychological distress in the form of anxiety or depression is a common comorbidity in patients with disorders of the autonomic nervous system (ANS). Therefore, we aimed to evaluate the influence of depression, anxiety and stress on ANS symptom burden.

Methods: Consecutive patients referred to the Laboratory for testing of the ANS, Zagreb, Croatia for the evaluation of dysautonomia (N=524, mean age 43.98, 371 females) and healthy controls (N=88, mean age 41.15, 57 females) completed validated Croatian versions of the Depression Anxiety Stress Scales 21 (DASS-21) and Composite Autonomic Symptom Score 31 (COMPASS-31). There was no difference in age and sex between groups ($p \geq 0.05$).

Results: Significantly more patients had severe or extremely severe depression, anxiety and stress compared to healthy controls (50 vs 2, $p=0.036$; 143 vs 4, $p=0.001$ and 63 vs 2, $p=0.008$; respectively). All 3 subscales of DASS-21 and COMPASS-31 were significantly higher in patients compared to healthy controls (all $p=0.001$). There was a significant correlation between depression, anxiety and stress subscales of DASS-21 and COMPASS-31 in both patients ($r_s=0.444$, $p=0.001$, $r_s=0.501$, $p=0.001$ and $r_s=0.413$, $p=0.001$, respectively) and healthy controls ($r_s=0.382$, $p=0.001$, $r_s=0.423$, $p=0.001$ and $r_s=0.461$, $p=0.001$, respectively). COMPASS-31 values were significantly higher in patients with DASS depression score ≥ 9 , anxiety score ≥ 7 and stress score ≥ 14 (all $p=0.001$).

Conclusion: Reported psychological distress is common in patients referred to autonomic laboratory, and our study demonstrates that they are interwoven in the complex pathophysiological and clinical picture of ANS disorders.

Disclosure: Nothing to disclose

EPO1023

Psychiatric symptom burden in patients referred to the tilt-table test

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Background and aims: To evaluate the difference in autonomic symptom burden and psychiatric symptom burden depending on the tilt-table test results.

Methods: Consecutive patients referred for testing of the ANS, Zagreb, Croatia, for the evaluation of dysautonomia (N=524, mean age 43.98, 371 females) and healthy controls (N=88, mean age 41.15, 57 females) completed validated Croatian versions of the Depression Anxiety Stress Scales 21 (DASS-21) and Composite Autonomic Symptom Score 31 (COMPASS-31). Furthermore, in all patients tilt-table test was performed. It was defined as abnormal if syncope, postural orthostatic tachycardia or orthostatic hypotension were diagnosed.

Results: In 168 (27.5%) patients the tilt-table test was abnormal. There was a significant difference in COMPASS-31 between patients with abnormal tilt-table test (group 1), patients with normal tilt-table test (group 2) and healthy controls (group 3), it was significantly lower in group 3 compared to groups 1 and 2 ($p < 0.001$). Similarly, there was a significant difference in all 3 subscores of the DASS-21 between groups where healthy controls (group 3) had lower values in comparison with both groups of patients. We found an association between the results of the tilt-table test and pathological results of all 3 subscores of the DASS-21, where group 3 had the lowest and group 2 the highest percentage of people with depression score > 9 , anxiety score > 7 and stress score > 14 (all $p < 0.001$).

Conclusion: Psychiatric symptom burden is most prevalent in patients referred for evaluation of suspected ANS disorder with normal tilt-table test.

Disclosure: Nothing to disclose

EPO1025

Dysautonomia in children with inflammatory bowel disease and irritable bowel syndrome

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Background and aims: To evaluate the presence of autonomic nervous system (ANS) abnormalities in children with inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS).

Methods: In consecutive children with IBD (N=24, mean age 15.7, 16 females), IBS (N=18, mean age 14.8, 9 females) and aged and sex matched healthy controls (HC) (N=18, mean age 14.2, 9 females) we evaluated ANS symptoms with the Composite Autonomic Symptom Score (COMPASS-31). Heart rate (HR) and blood pressure (BP) responses to the Valsalva maneuver, HR response to deep breathing (RSA), BP response to passive tilt, heart rate variability (HRV) analysis and quantitative sudomotor axon reflex test (QSART) were performed.

Results: Children with IBS scored highest on COMPASS-31, followed by patients with IBD and HC (median 15.6, 8.7 and 2.3, respectively). No differences between groups were observed in HR and BP responses to the Valsalva maneuver, RSA and BP response to passive tilt. Children with IBS had higher sweat volumes on proximal lower leg on QSART ($p = 0.039$). There was no difference in the HRV parameters between groups. However, children with IBS had significantly higher drop in total power of low frequency domain ($p = 0.01$) and standard deviation of normal-to-normal intervals ($p = 0.03$) and lowest drop in percentage of successive RR intervals that differ by more than 50ms ($p = 0.01$) during tilt test compared to children with IBD and HC.

Conclusion: We found significant subjective and objective ANS abnormalities in children with IBS compared to children with IBD and HC.

Disclosure: Nothing to disclose

EPO1026

The relationship between autonomic regulation of cardiovascular function and body composition

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Background and aims: The aim of this study was to investigate if there is a correlation between autonomic function tests and the body composition and shape in healthy young people.

Methods: In 32 healthy subjects (19 males and 13 females, mean age 22.1±1.9 years) cardiovascular reflex tests (heart rate (HR) and blood pressure (BP) responses to Valsalva maneuver and HR response to deep breathing) and the tilt table test were performed. Participants completed the Composite Autonomic System Score-31 (COMPASS-31), anthropometric measurement sequence (weight, height, upper arm, hips and waist circumference, triceps and subscapular skinfold), bioelectric impedance testing and hand grip strength measurement.

Results: Markers of obesity, other anthropometric measures, functional measures and basal metabolic rate (BMR) were significantly positively correlated with sBP and dBP in both supine and tilted positions. There was a positive correlation of Δ HR with markers of obesity, functional marker of dominant handgrip strength (dHGS) and BMR. We have also found the correlation of HRV during rest and tilt with anthropometric measurements. Participants with body mass index (BMI) <25 had statistically significantly lower median values of HR, dBP in tilt-test, sBP at rest and sBP at tilt-test compared to participants who had BMI>25.

Conclusion: The results of this study have shown the relationship between higher sympathetic activity, evaluated by cardiovascular regulation, and higher share of adipose tissue in young healthy persons.

Disclosure: Nothing to disclose

EPO1027

Fibromyalgia and generalized anxiety disorder; common neurophysiological findings may be related to common clinical signs

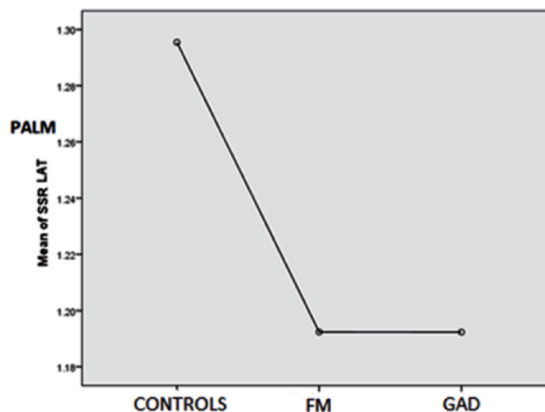
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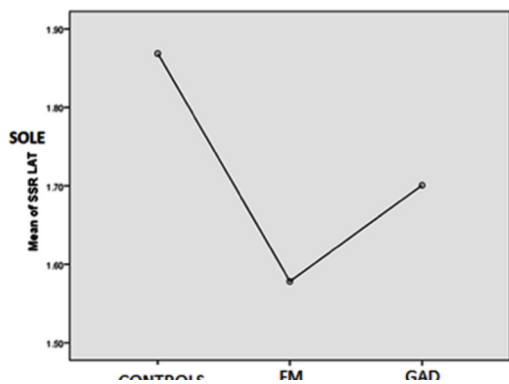
Background and aims: Fibromyalgia (FM) is characterized by widespread pain and is accompanied by fatigue, sleep and cognitive dysfunction, anxiety and depression. Generalized Anxiety Disorder (GAD) is characterized by excessive and persistent worry about everyday matters. Patients may also present with restlessness, fatigue, sleep disorders, irritability, difficulty in concentrating, muscle tension, aches and pain. Both diseases are of unknown aetiology, affect mainly young women, share common clinical features and worsen quality of life. Dysregulation of autonomic nervous system could be considered responsible for the overlapping symptoms.

Methods: We investigated 13 patients with GAD and 17 with FM. Demographic, biochemical, psychometric and neurophysiological (Sympathetic Skin Response (SSR), Cross Sectional Area of mid cervical vagus) data were collected and compared to each other and to healthy controls, matched for age and sex.

Results: Patients of the 2 groups did not differ in any biochemical, psychometric nor in neurophysiological parameter. When they were compared to controls, they differed in regard to the latency of SSR (Table 1) in both palm (standardized effect size: -0.5, CI 95%: -1.01 - 0.00), and the sole (standardized effect size: -0.70 CI 95%: -1.32 -0.07) (Figure 1,2).



SSR mean latencies recorded from the palm in controls and patients suffering from FM and GAD.



SSR mean latencies recorded from the sole in controls and patients suffering from FM and GAD.

Table 1

	CONTROLS	FM	GAD
Mean SSR latency palm (SD)	1,29 (0,21)	1,19 (0,19)	1,19 (0,18)
Mean SSR latency sole (SD)	1,86 (0,19)	1,57 (0,46)	1,70 (0,26)

Mean Values and Standard Deviations of SSR latency in palm and sole

Conclusion: Our study suggests that both conditions share not only common clinical features, but also common findings in autonomic nervous system tests (SSR latency) that can distinguish them from healthy controls. These findings might help further investigate the neurophysiological substrate in both conditions.

Disclosure: Nothing to disclose

EPO1028

Autonomic nervous system symptoms in relation to the social status

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Background and aims: It has been shown that social status can influence the autonomic nervous system function. Therefore, we aimed to evaluate whether we can quantify the influence of social conditions on symptoms of autonomic nervous system (ANS) involvement.

Methods: Consecutive patients referred to the Laboratory for testing of the ANS, Zagreb, Croatia for the evaluation of dysautonomia (N=526, mean age 44.07, 371 females) completed validated Croatian version of the Composite Autonomic Symptom Score 31 (COMPASS-31). Following social parameters were collected: marriage status, education level, working status, number of children, smoking status and body mass index (BMI).

Results: Educational level, working status and smoking had a significant influence on COMPASS-31 results. COMPASS-31 was higher in participants with 12 years of education compared to those with ≥14 years of education (p=0.048), in participants who were unemployed compared to employed (p=0.032) and in participants who smoked compared to those who did not smoke (p=0.013). For further analysis, smoking, 12 years of education and unemployment were defined as risk factors, and summed in the social risk score (value 0 to 3). According to linear regression model, the social risk factor was a statistically significant predictor of COMPASS-31 results (B=2.845, 95% CI 1.162-4.529, p=0.001).

Conclusion: Parameters related to social status (education level, working status and smoking) play a significant role on the autonomic symptom burden.

Disclosure: Nothing to disclose

EPO1029

The influence of the social status on the objective testing of the autonomic nervous system

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Background and aims: It has been shown that social status can influence autonomic nervous system function. Therefore, we aimed to define the influence of parameters related to the social status on the results of the objective testing of the autonomic nervous system (ANS).

Methods: In consecutive patients referred to the Laboratory for testing of the ANS, Zagreb, Croatia for the evaluation of dysautonomia (N=526, mean age 44.07, 371 females) heart rate and blood pressure response to deep breathing, Valsalva manoeuvre and tilt-table test were performed. Results were interpreted in the form of adrenergic index (AI) and cardiovagal index (CI) of the Composite Autonomic Scoring Scale (CASS). Following social parameters were collected: marriage status, education level, working status, number of children, smoking status and body mass index (BMI).

Results: People with BMI >25 had significantly higher involvement of sympathetic and parasympathetic nervous system measured with AI (p=0.003) and CI (p=0.006), respectively. CI was also influenced by marriage status, working status and number of children. Participants who were single had lower CI in comparison with participants who were in relationship (p<0.001) and widowed participants (p=0.025). People who were retired had higher CI compared to employed and unemployed participants and students (all p values <0.001). Participants without children had lower CI in comparison with participants with children (p=0.001).

Conclusion: Social status expressed through marriage status, working status, number of children and BMI has a statistically significant influence on the results of the parasympathetic nervous system function.

Disclosure: Nothing to disclose

EPO1030

Levodopa treatment and orthostatic hypotension: which effect on cognitive functions in a patient with Parkinson's disease and mild cognitive impairment?

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Introduction: Patients with Parkinson's disease (PD) present concomitant non-motor symptoms including cognitive impairment (CI) and orthostatic hypotension (OH). Frequently CI and OH take place together. It is unclear whether OH cause or worse cognition in PD. Similarly, effect of Levodopa on cognition in patients with PD and OH is debated. Dopaminergic stimulation could improve executive dysfunctions related to dorsal striatum pathways impairment. Otherwise hypotensive effect of Levodopa could transitionally worsen attentive functions.

Methods: We report a case of a 71-year-old man with 4 years history of PD, who developed episodes of drowsiness and confusion 45 minutes after Levodopa assumption. To characterize episodes and their correlation with Levodopa assumption, we evaluate patient's cognitive performances in 4 conditions: supine without Levodopa (1, baseline), supine 60 minutes after Levodopa (2), tilt test without Levodopa (3) and tilt test 60 minutes after Levodopa (4).

Results: Baseline neuropsychological evaluation (1) showed multidomain CI (memory, attentive-executive, visuospatial). Levodopa assumption (2) gets worse cognition with a decrease of global efficiency. Notably the patient showed a slowing down on attentive-executive tasks (Barrage, Stroop tests, Digit span), functions that are usually improved by Levodopa assumption. Tilt test showed OH, slightly worsen after Levodopa assumption but asymptomatic for the patient. During tilt test (3), cognitive performances get worse in short-term verbal memory and verbal analogies, while Barrage test improved. Detrimental effects of Levodopa are even more enhanced in standing condition (4).

Comparing conditions 2 and 3, detrimental effect of Levodopa is greater than orthostatic hypotension.

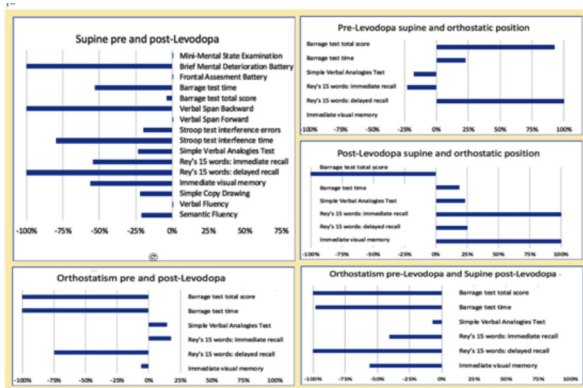


Figure 1: Rate of change of cognitive performances in the different conditions

	1 (baseline)	2	3	4
Position testing	Supine	Supine	Standing	Standing
Levodopa assumption	Pre	60' after	Pre	60' after
Blood pressure (mmHg)	154/84	166/85	113/65	120/62
Mini-Mental State Examination	28	28		
Rey's 15 words: immediate recall	22	10	17	20
Rey's 15 words: delayed recall	2	0	4	1
Immediate visual memory	16	7	16	15
Barrage test time (seconds)	132	202	102	240
Barrage test point	10	8	8	2
Barrage test errors	1	1	0	5
Barrage test total score	1,08	1,04	0,08	5,01
Simple Verbal Analogies Test	17	13	14	16
Brief Mental Deterioration Battery	0,28	-2,09		
Verbal Span Forward	5	5		
Verbal Span Backward	3	0		
Frontal Assesment Battery	12	12		
Stroop test interference time	62	111,5		
Stroop test interference errors	5	6		
Simple Copy Drawing	9	7		
Verbal Fluency	18	18		
Semantic Fluency	38	30		

Table 1: Neuropsychological evaluation in four conditions.

Conclusion: Levodopa could have a detrimental effect on cognitive functions independently to the hypotensive one.

Disclosure: Nothing to disclose

EPO1031

Improvement and stabilization of cardiovascular autonomic modulation three months after acute ischemic stroke

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Background and aims: Previous studies showed that patients with acute ischemic stroke have reduced cardiovascular autonomic modulation (CAM) with too little parasympathetic but augmented sympathetic modulation. It is unclear whether CAM improves several months after stroke. Therefore, this study compared CAM of ischemic stroke patients assessed during the acute phase and three months after stroke.

Methods: In 52 patients with ischemic stroke [20 women and 32 men, mean age 64.6±9.1, median NIHSS 2 (interquartile range 1-5)], we recorded RR-intervals (RRI), systolic, diastolic blood pressure (BPsys, BPdia), and respiration (RESP) at rest, within the first 72 hours and 3 months after the acute stroke. We calculated parameters of total cardiac autonomic modulation [RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), RRI-total-powers], sympathetic [RRI-low-frequency-powers (RRI-LF), BPsys-LF-powers] and parasympathetic cardiovascular modulation [Root-Mean-Square-of-Successive-RRI-Differences (RMSSD), RRI-high-frequency powers (RRI-HF-powers)], sympathetic-parasympathetic balance (RRI-LF/HF-ratios), and baroreflex sensitivity (BRS). We compared acute and 3 months values using paired-t-tests for normally distributed values and Wilcoxon-tests for non-normally distributed values. Significance was set at p<0.05.

Results: After 3 months, RRIs were slightly higher (886.4±16.2 vs. 843.0±18.9 ms, p=0.032), i.e. heart rate was lower than in the acute phase. Three months BPsys-LF-powers were lower (10.1±1.2 vs. 16.0±2.3 mmHg², p=0.017) and BRS was higher (5.2±3.0 vs. 3.9±3.1 ms/mmHg, p=0.001) than respective acute phase values. Otherwise, parameters remained unchanged.

Conclusion: Heart rate slowing, decreased sympathetic modulation, and enhanced BRS indicate significant improvement and stabilization of CAM within 3 months after acute ischemic stroke.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EPO1032

Characteristics of the main types of stroke in Uzbekistan in the first half of 2019 according to the Register of StrokeZ. Abdullaev¹, Y. Madjidova²¹Tashkent city, Uzbekistan, ²Tashkent, Uzbekistan

Background and aims: Cerebrovascular disease is one of the urgent problems and the main cause of mortality in Uzbekistan. To determine the clinical and epidemiological data of cerebral stroke, the “Stroke Register” (RI) program is the optimal method, in which diagnostic criteria and research methods are standardized.

Objective: To determine the features of the course of cerebral stroke in patients with cerebrovascular accident in the first half of 2019 according to (RI) data.

Methods: (RI) was carried out by the population-territorial method in patients older than 18 years. More and more cases of cerebral stroke have been registered with permanent residents of the Republic. Information about cases of stroke has been received from doctors at ambulance stations, clinics and hospitals, as well as from the Republican Cardiology Center, the Republican Scientific Center for Emergency Medical Aid, and the Republican Centralized Anatomical Laboratory.

Results: During the study period, 28536 stroke patients were identified. Distribution by types of stroke: 69.4% of patients were diagnosed with ischemic stroke, 13.6% had cerebral hemorrhage, unspecified stroke was diagnosed in 14.8%, and 2.2% of patients developed subarachnoid hemorrhage.

Neuroimaging was performed in 15.9% of patients.

Conclusion: The true distribution of types of cerebral stroke in the first half of 2019 was revealed. A large share in the structure of the incidence of stroke is an unspecified stroke, which is probably due to the inaccessibility of neuroimaging methods.

Disclosure: Nothing to disclose

EPO1033

The epidemiological characteristics of stroke in Uzbekistan in the first half of 2019 according to the register of strokeZ. Abdullaev¹, P. Y. Majidova²¹Tashkent city, Uzbekistan, ²Neurology, pediatric neurology and medical genetic, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Background and aims: Brain stroke (MI) is one of the most common causes of death in Uzbekistan. According to various sources, the frequency of cerebral strokes varies from 1.5 to 3 per 1000 people, and in our Republic there are no official epidemiological statistics on the register of stroke (RI).

Objective: To obtain reliable data on the main epidemiological indicator (RI) in the first half of 2019.

Methods: (RI) was carried out by the population-territorial method according to the questionnaire of the national stroke register for patients over the age of 18 years. All new and repeated cases and all deaths from (MI) have been recorded.

Results: During the 6 months of the program (RI) in the Republic of Uzbekistan, 28536 patients with stroke were identified. The average incidence of stroke was 1,73 per 1000 population. The maximum incidence of stroke was detected in the age group older than 50 years of age 81.1% and only 18.9% of patients in the age group under 50 years old. Mortality was -0.4 per 1000 population and the percentage of cases of stroke ending fatally, relative to all cases of stroke in percent- about 20%.

Conclusion: The true incidence, mortality and mortality from stroke in the first half of 2019 were revealed. The necessity of implementing preventive measures on the basis of (RI), which showed a high prevalence of the disease, low public awareness of stroke, and untimely seeking medical help, is substantiated.

Disclosure: Nothing to disclose

EPO1034

Analysis of data on the medical care system for patients with acute cerebrovascular accident according to the register of stroke

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Background and aims: Currently, vascular diseases of the brain are a major medical and social problem. According to various statistics in the Republic of Uzbekistan for the year occurs from 60 thousand to 80 thousand new cases of stroke

Objective: To analyze and obtain reliable data on the distribution of patients with stroke in the primary health care chain

Methods: The program “stroke register” was carried out during the first 6 months of 2019 by the population-territorial method according to the questionnaire of the national stroke register of patients over 18 years of age. Information about the cases of stroke was received from ambulance stations, clinics and hospitals, as well as from the Republican Cardiology Center, the Republican Scientific Center for Emergency Medical Aid, and the Republican Centralized Anatomical Laboratory.

Results: As a result of the analysis of data on the medical care system for patients with stroke, it was found that in most cases the first medical examination was performed by an ambulance doctor (74%), less often by a local therapist (18.5%) and a neurologist at the polyclinic (7.5%) In most patients, stroke developed at home (77.9%). 76.5% of patients were hospitalized, of which about 30% were hospitalized in the first 6 hours after the onset of the disease and about 70% after 6 hours

Conclusion: Reliable data have been identified on the distribution of patients with stroke in the primary health care chain, which is valuable information for the Ministry of Health when planning a health care network.

Disclosure: Nothing to disclose

EPO1035

Ischemic stroke revealing a central nervous system vasculitis: study of 9 cases

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Background and aims: Ischemic stroke is an unusual heralding manifestation in central nervous system vasculitis. In order to make an etiologic diagnosis a comprehensive investigation need to be done. This study was conducted to analyse the clinical and radiological features and the diagnostic approach of central nervous system vasculitis revealed by an ischemic stroke.

Methods: We studied 9 patients who were admitted to the military hospital of Tunis department of neurology between 2011 and 2019 and underwent a comprehensive work up.

Results: Of the 9 cases that have been selected 3 were males, the median age was 47.3 years. All patients presented with an acute focal neurologic deficit. A first-line workup was normal. After carrying out a second line workup, 4 patients were diagnosed with a primary systemic vasculitis (2 Neurobehcet, 1 Microscopic polyangiitis, 1 Wegener's granulomatosis), 2 patients with a celiac disease, 1 patient with neuropsychiatric lupus erythematosus, 1 patient with Sjogren's syndrom and 1 patient with a primary angiitis of the central nervous system. All of them received corticosteroids and immunosuppressive therapy.

Conclusion: Ischemic stroke is an uncommon early manifestation in cerebral vasculitis, it occurs in younger adults especially females. its etiologic diagnosis remains difficult to be made and its frequently delayed, whereas its prognosis depends mainly on early treatment. Searching for extra-neurologic signs and conducting a comprehensive work up can be helpful.

Disclosure: Nothing to disclose

EPO1036

Stroke mimics: Clinical and Radiological approach

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Background and aims: Ischemic stroke is the most common cause of acute focal neurologic deficit. Nevertheless, in 30% of patients with focal neurologic deficit, the causes are non-vascular and are referred to as stroke-mimics. The broad use of MRI has been an immense factor in differentiating the causes most often misdiagnosed as ischemic stroke.

Methods: A brain MRI was performed in 134 patients with acute focal deficit, admitted to our department. Intracerebral hemorrhage was excluded with brain CT. Topographic distribution along with magnetic properties in DWI, FLAIR, T2-GRE, T2 and contrast-enhanced sequences of the lesions were evaluated.

Results: In 14 patients the final diagnosis was not stroke. The most common pathologies identified as stroke mimics were epilepsy and postictal phenomena, posterior reversible encephalopathy syndrome, herpes encephalitis, Creutzfeldt-Jakob, brain tumor, mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes, reversible cerebral vasoconstriction syndrome and medication toxicity.

Conclusion: In our department, 10.4% of cases with acute focal deficit were caused by stroke mimics. Nowadays, due to the routine use of iv stroke thrombolysis, it is crucial to identify these disorders. MRI plays a pivotal role in that area. In our diagnostic approach, first we evaluated whether DWI was normal or abnormal and then we analyzed the other sequences trying to correlate the MRI results with the clinical syndrome.

Disclosure: Nothing to disclose

EPO1037

Intracerebral hemorrhage (ICH) and epilepsy: a retrospective study

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Background and aims: Seizures are a serious complication following ICH with a frequency of 4-19%. We aimed to study the ICH patients' characteristics and try to correlate them with the occurrence of seizures and the decision to start prophylactic antiepileptic therapy.

Methods: This is a retrospective study including patients with spontaneous ICH treated in the neurologic clinic of General Hospital of Nikaia-Piraeus "Agios Panteleimon" during 2014-2017.

Results: 89 adult patients with ICH were included. Most of the ICH were in the basal ganglia (49.5%), followed by lobar subcortical hemorrhages (16.9%), lobar hemorrhages with cortical involvement (10.1%) and brainstem hemorrhages (12.4%). Other areas were affected in a much lesser percentage. Acute seizures occurred in 10 patients (11.2%), 70% of which during the first 24 hours. 6 were generalized tonic-clonic seizures, 3 were focal seizures with retained awareness and 1 was a focal seizure with impaired awareness. We prescribed prophylactic antiepileptic therapy in 12 patients (13.5%). Temporal and lobar location of the hemorrhage, intraventricular hemorrhage and cortical involvement were correlated with increased prescription of prophylactic antiepileptic drugs. Cortical involvement was found to be an independent risk factor for the development of acute seizures.

Conclusion: Our results correlate with those found in many international and randomized-control studies. There is no evidence-based recommendation for the use of prophylactic antiepileptic medication. Nonetheless, it is common practice among clinicians, especially in ICH with cortical involvement and intraventricular extension.

Disclosure: Nothing to disclose

EPO1038

Analysis of potential drug-drug interactions (pDDIs) which include angiotensin-converting enzyme (ACE) inhibitors in acute ischemic stroke patients

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Background and aims: Some studies have shown that low doses of aspirin can have the effect of reducing the antihypertensive effect of ACE inhibitors, especially enalapril. Concomitant administration of ACE inhibitors and aspirin may exacerbate heart failure. Interactions between ACE inhibitors/aspirin and ACE inhibitors/non-steroidal anti-inflammatory drugs (NSAIDs) may lead to exacerbation of renal failure and hyperkalemia. ACE inhibitors and diuretics can lead to “first-dose hypotension” and acute renal failure.

Methods: 3-year retrospective research of 696 acute ischemic stroke patients was conducted at the Clinic for Neurology, Kragujevac, Serbia. Micromedex software was used to calculate severity (major, moderate, minor) and scientific documentation (excellent, good, fair) of the pDDIs of ACE inhibitors drugs. We calculated the factors associated with exposure to these pDDIs.

Results: pDDIs which include ACE inhibitors were present in 500 (71.8%) patients. A total of 86 pDDIs were detected, which include fosinopril, enalapril, ramipril, lisinopril, perindopril and quinapril (major 35, moderate 51; excellent scientific documentation 25, good 25, fair 36). The most frequent pDDIs were aspirin-ramipril (22.84%), aspirin-enalapril (19.68%), diclofenac-ramipril (19.50%), aspirin-fosinopril (19.25%) and diclofenac-enalapril (17.38%). Fatal outcome was statistically significantly more frequent in the group of patients with this pDDIs ($\chi^2=7.595$; $p=0.004$). The risk factor for pDDIs was the total number of used drugs (OR=1.110) and the protective factor was a chronic renal failure (OR=0.466).

Conclusion: pDDIs which include ACE inhibitors are very common in patients with acute ischemic stroke. The risk factor is the number of prescribed drugs. This pDDIs may have an impact on the hospitalization outcome of patients with stroke.

Disclosure: Nothing to disclose

EPO1039

Transient alien hand syndrome in Ischemic lesions of the corpus callosum: a report of 3 cases

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Background and aims: Alien hand syndrome (AHS) is a rare neurological condition that seriously affects daily life. The common feature is the involuntary autonomic activity of the affected extremity and conflict between upper limbs. AHS has been reported most commonly in lesions of the medial frontal cortex and corpus callosum. We present three cases of AHS in the ischemic stroke of the corpus callosum, which were detected in the acute process and showed rapid improvement in clinical follow-up.

Methods: Cases: 1 female and 2 male patients were hospitalized with acute stroke either with mild hemiparesis or normal motor functions. 2 patients had ataxic gait and mild speech disorder. All patients had intermanual conflict between right and left upper limbs. 1e patient also described strange feeling like an electric current when touched to opposite arm and leg. In diffusion MRI (Magnetic resonance imaging) all patients have acute lesions of splenium of the corpus callosum. All patient improved with full recovery within 2-11 days.

Results: Because of a rich vascular structure, corpus callosal ischemic lesions are rarely seen and generally improve very rapidly. Therefore AHS due to ischemic events may resolve in a very short time. It is possible to detect AHS in the corpus callosum lesions with careful observation.

Conclusion: In addition to the limited number of cases reported in the literature, it is intended to draw attention to the presence of atypical presentiaions of lower limb involvement as in 1 of our cases.

Disclosure: Nothing to disclose

EPO1040

Ghost infarct area in a patient with an acute ischemic stroke and hemodynamic shock, a confounding factor when considering endovascular treatment

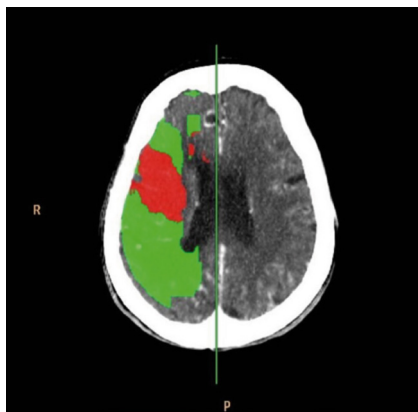
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Background and aims: Endovascular therapy (ET) has emerged as a highly effective treatment in acute ischemic stroke with large vessel occlusion. Treatment's decision is based on clinical and radiological features, such as Alberta Stroke Programme Early CT Score (ASPECTS) and CT perfusion (CTP) as well as clinical-neuroimaging mismatch. We present a case in which CTP was influenced by the patient's hemodynamic status.

Methods: We describe a 79-year-old woman with a Modified Rankin Scale (mRS) and previous history of hypertension, diabetes and bigeminated ventricular extrasystole. She presented a 2 hours right-hemispheric deficit with a National Institutes of Health Stroke Scale (NIHSS) score of 25, as well as slow atrial fibrillation with hemodynamic instability.

Results: Computed tomography (CT) and CT angiography showed an ASPECTS score of 8 and a proximal segment of the right middle cerebral artery occlusion, respectively. During the first CTP, the patient had a mean systolic blood pressure below 100mmHg, which showed a large hemispheric infarct core with no penumbra. After hemodynamic stabilization with an external pacemaker and inotropic drugs, CTP was repeated and a penumbra >30% was observed, which allowed the indication of mechanical thrombectomy. The mRS score at 3 months was 0.



CT perfusion, 6 hours after the onset of symptoms.

Conclusion: The CTP may overestimate the established infarct core in patients with hemodynamic instability and include a Ghost Infarct Area to the real infarct core. Therefore, hemodynamic status of the patients must be kept in mind during CTP interpretation in acute stroke.

Disclosure: Nothing to disclose

EPO1041

Predictors of the vertigo development in patients with posterior circulation stroke

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Background and aims: Stroke is the underlying etiology in 17-25% patients presenting with acute onset of isolated vertigo. But affected patients do not usually receive the adequate medical attention and are more likely to consult a general practitioner.

Methods: We evaluated prospectively 145 consecutive patients (85 men and 60 women) aged 32 to 85 years in acute period of ischemic posterior circulation (PC) strokes. Comprehensive examination included analysis of the baseline characteristics, risk factors; attentive clinical study; assessment of neurological status with the use of scales NIHSS, B. Hoffenberth et al. Localization and volume of the ischemic lesion were assessed with the DWI MRI.

Results: All patients were classified into two groups—with vertigo 89 (61.4%) and without vertigo— 56 (38.6%). The presence of vertigo did not correlate with distribution of ischemic lesion to proximal, middle or distal territories of PC ($p=0.073$). Patients with vertigo were predominantly females (44.9% versus 21.4%, $p=0.036$), were less likely to have focal neurological deficits (56.7% versus 86.5%, $p=0.006$), had frequently cardioembolic stroke subtype (48.1% versus 24.5%, $p=0.046$), more combined lesions in PC (46.7% versus 23.5%, $p=0.034$) and larger total infarction volume in comparison to non-vertigo patients (5.2cm^3 versus 0.68cm^3 , $p=0.003$). In age- and sex-adjusted logistic regression, an infarction location either in the cerebellum or dorsal part of brainstem and total infarction volume of $>0.54\text{cm}^3$ were found to be associated with vertigo ($p=0.002$ and $p=0.046$, accordingly).

Conclusion: Infarction location, and infarction volume are stronger predictors of vertigo in posterior circulation strokes.

Disclosure: Nothing to disclose

EPO1042

Galena vein thrombosis under Noak treatment

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Background and aims: Cerebral venous thrombosis (CVT) is a rare condition and less than 1% of stroke cases. Thrombosis of deep venous veins such as Galen vein accounts for approximately 10% of SVT cases. Clinical presentation is variable and should be kept in mind in unexplained mental state disorders.

Methods: A 65-year-old woman with nonvalvular atrial fibrillation and diabetes mellitus, receiving 20mg rivaroxaban and 2000mg metformin once daily was brought to the emergency department for three days of slowness of movement, confusion and excessive drowsiness.

Results: In neurological examination; Disorientation, bilateral dilated pupils and ataxic gait were detected. Motor and sensory deficits were not observed. Computed tomography of the brain showed hypodense lesions in the bilateral thalamic region with edema. In brain magnetic resonance imaging, T2 hyperintense in the bilateral thalamic region, T1 hypointense and diffusion-weighted imaging showed diffusion-restricted areas in the same regions. CT angiography showed thrombus in the galena vein, anticoagulant treatment, low molecular weight heparin, was initiated and the patient was admitted to the neurology clinic. There were no significant findings in the examinations performed for coagulopathy. She was discharged with warfarin treatment. There was no change in her neurological status.

Conclusion: SVT is a rare and serious condition early anticoagulant therapy should be initiated. Involvement of the deep venous structures is a rare condition and may present with a sub-acute onset. The severity of the condition may vary depending on the location of the thrombosis and the presence of collateral vessels. Diagnosis may be difficult in cases of partial thrombosis.

Disclosure: Nothing to disclose

EPO1043

Predictors of good clinical outcomes and successful revascularization after thrombolysis in acute ischemic stroke

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Background and aims: Stroke is the first cause of disability and the third cause of death. The prognosis of strokes is improved by their management within the neurovascular units by thrombolysis which represents one of the therapeutic progress whose success is conditioned by the rigorous selection of the candidates. The objective of our study is to analyze the clinical and paraclinical profile of thrombolysed patients in order to determine the factors predicting success of thrombolysis.

Methods: This is a comparative retrospective study of the records of 105 patients admitted for ischemic stroke who benefited from thrombolysis by r-tPA.

Results: The average age of our patients was 67 years, a sex ratio of 1/2, an average time to admission at 1h45min, with an average needle-holder time of 53 minutes. Their initial NIHSS score varied between 4 and 20. the success of thrombolysis was noted in 76% of patients with an improvement in the NIHSS score of more than 70% after 24 hours of thrombolysis. This success rate was explained by the rigorous selection of candidates based on several parameters which influenced the success of thromolysis to varying degrees. Among these factors, we note mainly the shortness of the needle-holder delay, the presence of a radio-clinical mismatch, the site and size of the occlusion as well as the territory of the infarction.

Conclusion: Despite its limited effectiveness in certain cases, thrombolysis constitutes the first-line treatment in the management of acute ischemic stroke, it must be implemented as quickly as possible before resorting to other therapeutic alternatives, mainly thrombectomy.

Disclosure: Nothing to disclose

EPO1044

Diffusion tensor tractography as an early predictor of functional outcome after lacunar brain infarction

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Background and aims: Lacunar infarctions (LIs) are ischemic strokes caused by occlusion of the deep penetrating arteries. They constitute about 25% of all ischemic strokes and have variable consequences based on affected tracts disruptions. The objectives of this study were to assess the role of MRI diffusion tensor imaging (DTI) fiber tractography as an early biomarker of LIs prognosis.

Methods: This work was conducted on 42 first-ever symptomatic motor or sensorimotor LIs patients submitted to stroke severity assessment using the National Institute of Health Stroke Scale (NIHSS), carotid duplex, Brain MRI to determine LIs diameter and occult small vessel disease imaging markers. Corticospinal diffusion tensor tractography (CS-DTT) was done within 48 hours from stroke onset. 38 patients continued a 3-months follow-up schedule, at the end of which their physical dependences were assessed using the Modified Barthel Index (MBI) scale which were compared with the baseline assessment parameters to determine the prognostic biomarkers.

Results: Dependent patients' group showed significant increase in their age, BMI, carotid intima media thickness and white matter hyperintensities grade than independent patients' group. The FA ratio was the earliest parameter showed significant changes which were lower in dependent than independent patients' groups. On the other hand, each of ipsilateral DTI fractional anisotropy, mean diffusivity and fiber number showed non-significant differences.

Conclusion: Reduced ipsilateral/contralateral FA ratio of the CS-DTT is a reliable early predictor of functional outcome and motor disability after motor and sensorimotor LIs.

Disclosure: Nothing to disclose

EPO1045

Predictors of early hematoma expansion after spontaneous intracerebral hemorrhage

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Background and aims: Hematoma expansion (HE) is the leading cause of early neurological deterioration, poor functional outcome and increased mortality in patients with spontaneous intracerebral hemorrhage (S-ICH). The study aimed to estimate the risks and predictors of early HE in patients with S-ICH and the effect of this HE on patient's survival and functional outcome.

Methods: This study was carried out on 72 patients with S-ICH submitted to baseline non-contrast brain CT (NCCT) and CT angiography for determination of hematoma site, size, border irregularity, blend sign and spot sign score (SSS). Rescan was done 48 hours after stroke onset or on clinical deterioration to resize the HV and diagnose HE. Modified Rankin Scale (MRS) were done 3-months after stroke onset to assess the effect of HE on patients' physical dependence.

Results: HE occurred in 28/72 (38.9%) of included patients. Risks of HE included old age, smoking, elevated baseline mean arterial blood pressure and high admission modified national institute of health stroke scale. NCCT predictors of HE included large volume, irregular border and presence of blend sign. The presence of spot sign in early CTA is more accurate than NCCT predictors with 54%, 91%, 79% and 75% for sensitivity, specificity, positive predictive value, and negative predictive value respectively.

Conclusion: HE is a major cause of early clinical deterioration, increased mortality and poor functional outcome. Early CTA for detection of spot sign is indicated in patients with large volume, irregular border and/or blend sign in NCCT.

Disclosure: Nothing to disclose

EPO1046

Arterio-arterial embolism as a cause of cerebrovascular diseases in patients with a floating structure in the carotid system

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Background and aims: Since 2016, some ultrasound laboratories have noticed the presence of a thin intraluminal mobile fragment in carotid arteries in patients (Bakhmetev A.S., Costanzo L.). Every time the previously undescribed structure was an incidental finding and in most cases remained asymptomatic. However, as the material accumulated, it was noted that about 15% of such patients had suffered a transient ischemic attack (TIA) or stroke in the absence of any other causes. The aim was to identify the connection of cerebral circulation disorders with arterio-arterial embolism from carotid arteries.

Methods: We analyzed blood flow both at extra- and intracranial levels in 28 patients with TIAs (n=24) and strokes (n=4). After an ultrasound examination and a neurological examination, 9 patients underwent bitemporal transcranial Doppler monitoring of the middle cerebral arteries (MCA) in order to detect microembolic signals (MES). Control group included 30 asymptomatic patients with FS.

Results: All patients from group I had discernible blood flow turbulence in the FS zone, some of them had regurgitation under the structure. While monitoring MCA on the side with the FS, the average number of MES was 9.5, while in the territory of contralateral MCA, as well as in patients from the control group, MES were not detected.

Conclusion: We assume the arterio-arterial nature of stroke and TIA (due to slowing of blood flow, as well as significant turbulence) in patients with FS, which is a new form of destruction of the carotid artery wall, requiring further study and consideration of preventive measures against cerebral circulation disorders.

Disclosure: Nothing to disclose

EPO1047

Infarction of the corpus callosum in a patient with bilateral carotid occlusion

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Background and aims: Infarction of the corpus callosum (CC) only represents 3-8% of ischemic strokes. We present an atypical case of a patient with progressive neurological deterioration due to a lesion of the CC secondary to occlusion of both internal carotid arteries (ICAs).

Methods: Description and review of the literature apropos of a case of infarction of the CC associated with bilateral carotid occlusion.

Results: A 37-year-old male with history of arterial hypertension, dyslipidemia, diabetes mellitus type I with microangiopathy and heavy smoker, presented with a subacute episode (2 months) of altered speech production with a fluctuating course. Neurological examination revealed bradypsychia, motor dysphasia, mild left agraphia, acalculia, left-right confusion and right faciobrachial paresis. Multimodal CT scanning showed a hypodensity in the CC with sparing of the splenium, and occlusion of both ICAs. Brain MRI confirmed a subacute ischemic lesion affecting the anterior 2 thirds of the CC (image 1), and the left centrum semiovale and frontal operculum. The ethiological study was completed in the Neurology Department and the final diagnosis was infarction of the CC secondary to bilateral atherothrombotic occlusion of the ICAs.

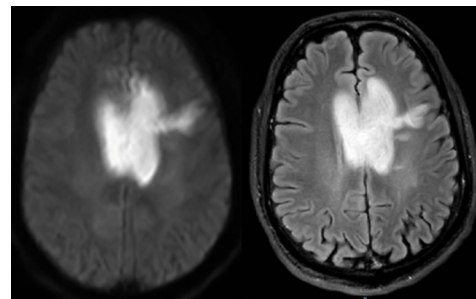


Image 1 - Brain MRI confirmed a subacute ischemic lesion affecting the anterior two thirds of the CC (image 1), and the left centrum semiovale and frontal operculum

Image 1

Conclusion: The blood supply of the anterior 2 thirds of the CC depends on perforating branches from the anterior communicating artery and the anterior cerebral artery. However, the splenium receives its blood supply from the posterior cerebral artery. Very few cases of lesions of the CC secondary to bilateral ICA occlusion have been reported. The etiopathogenic mechanisms proposed are atheroembolic or hemodynamic due to insufficient compensation via the collateral circulation.

Disclosure: Nothing to disclose

EPO1048

Cerebral venous sinus thrombosis as an uncommon complication in immune thrombocytopenia

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Background and aims: The main clinical manifestations of immune thrombocytopenia (ITP) are mucocutaneous hemorrhages. Thrombotic events are less frequent, with cerebral venous sinus thrombosis (CVT) as an uncommon complication.

Methods: Description and literature review about a case of CVT in a patient with ITP and severe thrombocytopenia.

Results: A 59-year-old woman went to the emergency room for a self-limited episode of horizontal binocular diplopia. 2 weeks earlier, she started having oppressive and intense right frontoparietal headaches. She has a history of being overweight (BMI 28) and chronic corticosteroid resistant ITP treated with Romiplostim since 1 month ago. On examination, she presented bilateral papilledema, without other relevant findings. In the analytical emergency study, a thrombopenia of 41,000 cells/ μ L and a D-dimer of 19,030 μ g/L stood out. A brain CT and CT angiography with venous phase were performed and an extensive CVT was observed without parenchymal complications (image 1), starting heparin treatment, with progressive clinical and radiological improvement. After a negative study of thrombophilia and antiphospholipid syndrome, CVT of multifactorial etiology was diagnosed (treatment with Romiplostim and overweight).



Image 1 - CT angiography with venous phase: cerebral venous sinus thrombosis with predominant involvement of the upper longitudinal sinus

Image 1

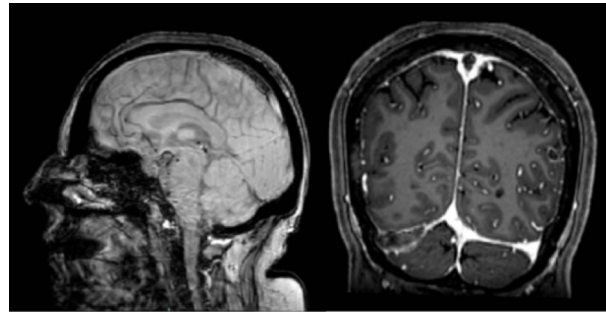


Image 2 - MRI angiography with venous phase (performed two days after heparin treatment onset): findings compatible with extensive cerebral venous sinus thrombosis, with predominant involvement of the upper longitudinal and right transverse sinus and recanalization of the left transverse sinus

Image 2

Conclusion: ITP has been associated with thrombotic events in 6-11% of cases, the most frequent being deep vein thrombosis and pulmonary thromboembolism. Thrombopoietin receptor agonists (TPA-ra), such as Romiplostim, increase thrombotic risk, although there are few described cases associated with CVT. In our patient, severe thrombocytopenia suggests that Romiplostim could increase the prothrombotic state by inducing platelet activation. Therefore, in patients with ITP in treatment with TPA-ra, we should suspect a CVT if headaches appear with warning signs.

Disclosure: Nothing to disclose

EPO1049

Etiology of first ischemic stroke and frequency of vascular risk factors in young patients

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Background and aims: Traditional risk factors (RF) may play role in the etiology of ischemic stroke (IS) also in young patients. The aim of our study was to assess the spectrum and frequency of RF in young IS patients.

Methods: In the prospective observational study, 434 consecutive patients (age 18-50, median 43 years, 56.2% males) with first IS (84%) or transient ischemic attack (16%) were enrolled. All patients underwent neuroimaging, extensive laboratory assessment, and detailed cardiologic examination. For the analysis, patients were divided into 2 groups according to age (under and over 40 years) and gender.

Results: The following types of IS were identified: atherosclerotic makroangiopathy (LVD) in 15 (3.5%), small vessel disease (SVD) in 49 (11.3%), cardioembolisation (CE) in 91 (21%), other determined cause in 76 (17.5%), undetermined cause in 149 (34%) and 2 or more causes 52 (12%) patients. Hypertension was present in 165 (37.2%) patients, hyperlipidemia (HLP) in 183 (42.4%), diabetes mellitus (DM) in 39 (9%) and smoking in 178 (43%). Among vascular RF only the presence of DM and smoking increased significantly the risk of IS recurrence OR=2.8; 95%CI:1.06-7.56 resp. OR=2.5; 95%CI:1.173-5.26), p=0.038 resp. p=0.018 in the all study population.

Conclusion: Traditional, modifiable RF occurred frequently in young IS patients. Although only the presence of DM and smoking increased the risk of recurrence in our study

Disclosure: Supported by the MH CR, grant no. 17-30101A

Cerebrovascular diseases 2

EPO1050

The study of depressive and speech disorders in post-stroke patients

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Background and aims: Determine a correlation between speech, depressive and motor disorders in patients after ischemic stroke.

Methods: A total of 95 people with ischemic stroke in the early recovery period was examined. Patients were divided into 3 groups: 30 with aphasia, 32 with dysarthria and 33 patients without speech disorders. The following research methods were applied: the Rivermid mobility index, the MMSE cognitive impairment scale, the Hamilton scale and the aphasic test.

Results: First group the average on the Hamilton scale was 10.2 points, 16.4 points on the MMSE scale and the Rivermid mobility index was 4.6. A strong correlation of $r=0.67$ was found between the motor disorders and depressive manifestations. Applying the Hamilton scale was also difficult for this group. Indirect signs of depressive manifestations were common among the patients -83%. In a group of patients with dysarthria there were determined: the mean value on the Hamilton scale of 9.7 and the index of motor disorders of 4.3; also indirect signs of depressive manifestations (36%) were found. There was a strong correlation ($r=0.78$) between the indicators of mobility index and the presence of depression on the Hamilton scale. In the second group, was 9.1 points, the cognitive impairment on the MMSE scale was 20.2 points, and the Rivermid mobility index was 4.8 points. The level of indirect signs of depressive manifestations was 20%.

Conclusion: The high prevalence of clinically significant depressive manifestations among patients with speech disorders was found.

Disclosure: Nothing to disclose

EPO1051

Preliminary analysis of M2 occlusion endovascular treatment. Cerebrovascular uncertainty management

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Background and aims: Ischemic stroke caused by arterial occlusions in the M2 segment of the Middle Cerebral Artery (MCA M2) have been ambiguous, regarding the effectiveness of mechanical thrombectomy, as they were not included in many of the pivotal clinical trials. Clinical thrombectomy guides suggest this treatment based on an expert opinion, but there is no real evidence. In daily clinical practice we find a substantial number of patients with occlusion of this segment and many of them are treated with endovascular therapy with heterogeneous results regarding clinical efficacy and complication rates. In the pivotal trials there was not intracerebral hemorrhage (ICH) found.

Methods: We analyze the epidemiological features, clinical efficacy and complication rates of MCA M2 thrombectomies of our center.

Results: Among 234 thrombectomies, 35 were MCA M2 occlusions (14%), most of them (65%) of cardioembolic etiology, with a mean age of 73 years old (44.1% men, 55.9% women), mean NIHSS 10.1 (72% NIHSS ≤ 4 , 19% ≤ 20 , 9% ≤ 25), mean onset to door time 112.8 minutes (excluding 6 wake-up strokes), onset-to-groin puncture 239.2 minutes. We observed an ICH rate of 18%, not all of them clinically significant. Clinical efficacy (3 month RankinMS ≤ 2) was favorable for 57% of the patients.

Conclusion: M2 MCA thrombectomy is performed in an important percentage of patients with stroke during clinical practice and it is advisable to communicate the results regarding clinical efficacy and complication rate outside of the ideal situation of clinical trials.

Disclosure: Nothing to disclose

EPO1052

Strokes complicating Crohn's disease

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Background and aims: Crohn's disease (CD) is associated with a significant risk of thromboembolic events. It is most often venous thrombosis of the limbs and pulmonary embolism, arterial and cerebral venous thrombosis are rare and rarely reported in this context

Methods: Mr C.R., 48 years old, with a history of ileal CD diagnosed in 2017, present; during an attack treated with oral corticosteroid therapy and Azathioprine; weakness of the left hemibody associated with sudden onset headache. The neurological examination found a left hemiplegia with facial participation and an intracranial hypertension syndrome. Cerebral angio-MRI targets a large focus of right temporo-frontal infarction with a hemorrhagic component related to cerebral thrombophlebitis of the upper longitudinal sinus, transverse sinus, right sinus, and Galen's vein. The biological assessment finds hyperplaqueotose. The patient was put on an anticoagulant, stopped after a favorable clinical course and a re-sealing of the sinuses. 4 months later, while the bowel disease is in remission, the patient has a ischemic stroke in Sylvia due to thrombosis of the right internal carotid artery. The hemostasis assessment, the thrombophilia assessment, and the cardiology assessment (electrocardiogram, cardiac ultrasound, Doppler ultrasound of the supra-aortic trunks) are without particularities.

Results: In our case both phases of the disease are involved. The treatment of these thromboses is not consensual and is done like other cerebral thromboses, the recurrence in our patient makes discuss the interest of an anti coagulation in the short court in these patients.

Conclusion: Early recognition of these complications is essential to initiating life-saving treatment.

Disclosure: Nothing to disclose

EPO1053

Ophthalmological manifestations and outcomes in patients with direct carotid-cavernous sinus fistulae – a case series

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Background and aims: The most frequent clinical manifestations at onset in patients with direct carotid-cavernous sinus fistulae (DCCFs) involve the orbital-ocular-ophthalmic nerve complex.

The aim of this case series is to present the ophthalmological clinical characteristics, treatments and outcomes in patients with DCCFs.

Methods: Case series of 14 patients admitted to our Neurology Department between 2007-2019. All patients were diagnosed with DCCF by means of digital subtraction angiography of cervical-cerebral arteries. 13 of the DCCFs were posttraumatic (6 car, 1 boat, 1 bike and 3 home accidents, and 2 victim of domestic violence), only 1 being spontaneous (ruptured carotid aneurysm). 8 patients were male and 6 female, mean age being 43.07 (20-78).

Results: The mean period between the development of signs and symptoms and diagnosis was 58.92 days (10-150). 13 patients exhibited ocular motor control ailments as to cranial nerve involvement: oculomotor (71.42%), trochlear (28.57%) and abducens (64.28%). Fundoscopy revealed abnormalities in all cases. 9 patients exhibited chemosis, 5 secondary glaucoma, 13 exophthalmos, 6 bruit and 8 decreased visual acuity. 8 patients received topical ophthalmological treatment and 12 patients received endovascular treatment (31% stent graft, 46% platinum coils, 23% detachable balloon), 1 was pending treatment and 1 DCCF closed spontaneously. Follow-up at 1 month and 3-6-9-12 months revealed ophthalmological improvement in 8 of the treated patients while 3 were stationary.

Conclusion: This case series highlights the importance of multidisciplinary management (Neurology-Ophthalmology-Interventional Neuroradiology) and ophthalmological characteristics of DCCFs as they may have decisive influence on the outcome in such cases.

Disclosure: Nothing to disclose

EPO1054

The change of transfer time of stroke patients with new pre-hospital triage in Moravian-Silesian Region (Czech Republic)

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Background and aims: The time from the onset to treatment (OTT) is important for clinical outcome in stroke. To shorten OTT, we need an effective pre-hospital triage.

Methods: Prospective multicentre study. In 2016 new pre-hospital triage has been introduced in Moravian-Silesian Region (MSR, 1.2mil. inhabitants). FAST PLUS test has started to be used (positive when severe hemiparesis was present) to predict large vessel occlusion (LVO). Patients with positive test are transported directly to mechanical thrombectomy (“mothership model”, before that we used to use “drip and ship model”). The sensitivity (93%) and specificity (47%) of FAST PLUS test in detecting of LVO have been published.

Transport time (TT) of all stroke patients treated with IVT or MT in 2015 and 2018 in all stroke centres of MSR was compared. The data were obtained from EMS of MSR database and SITS database.

Results: In 2015, 431 patients were diagnosed with ischemic stroke and treated either with tPA or mechanical thrombectomy (MT) -364 (85%) with tPA only and 89 (20%) with MT±tPA. In 2018, 691 patients were diagnosed and treated -654 (95%) with tPA only and 179 (26%) with MT±tPA. The median TT of tPA only patients was 48min both in 2015 and 2018, p=0.5. The median TT of MT±tPA patients was 118min in 2015 and 47min in 2018, p<0.001.

Conclusion: When the new triage was introduced, the TT of patients with MT was shortened, TT for IVT treated patients remained the same.

Disclosure: Supported by Ministry of Health, Czech Republic – conceptual development of research organization (FNOs/2018).

EPO1055

Contrast-enhanced transcranial Doppler for the diagnosis and monitoring of patients with patent foramen ovale and cerebral ischemic events – single center experience

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Background and aims: Patent foramen ovale (PFO) is considered one of the possible aetiologies for ischemic stroke associated with cardiac pathology and has long been dependent on transoesophageal echocardiography (TOE) for its diagnosis. Given the fact that this pathology is present in almost 25% of the population, a more accessible method for its detection was required and that is where the contrast-enhanced transcranial Doppler (c-TCD) stepped in.

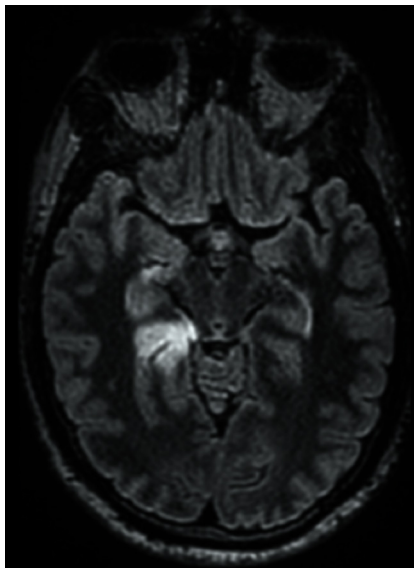
Methods: Throughout 2019, 123 patients were referred to our neurosonology laboratory after suffering an ischemic stroke/ transient ischemic attack without an identified cause or having asymptomatic ischemic lesions on the cerebral MRI. They underwent c-TCD and a TOE was recommended alongside medical treatment for those who tested positive.

Results: For 51 patients, transcranial Doppler emboli signals were detected after intravenous infusion of microbubbles and after the Valsalva manoeuvre. Spencer Logarithmic Scale was used for grading the right-to-left shunt. TOE confirmed the atrial defect for all patients who underwent this investigation. The decision for medical treatment or PFO closure by percutaneous procedure was made by a multidisciplinary team and follow-up with c-TCD was set for 1 and 6 months after the intervention.

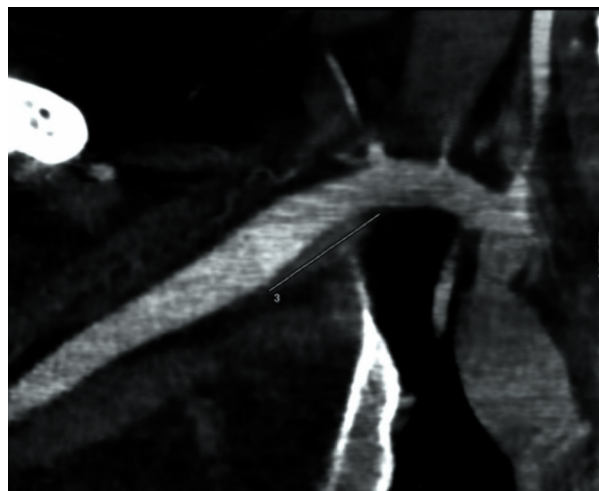
Conclusion: The purpose of this current paper is to share the data we have collected on patients diagnosed with PFO by the means of c-TCD in our clinic, bringing new evidence that this is a non-invasive valuable imaging technique, offering a high accuracy at a lower cost and at increased comfort for the patient.

Disclosure: Nothing to disclose

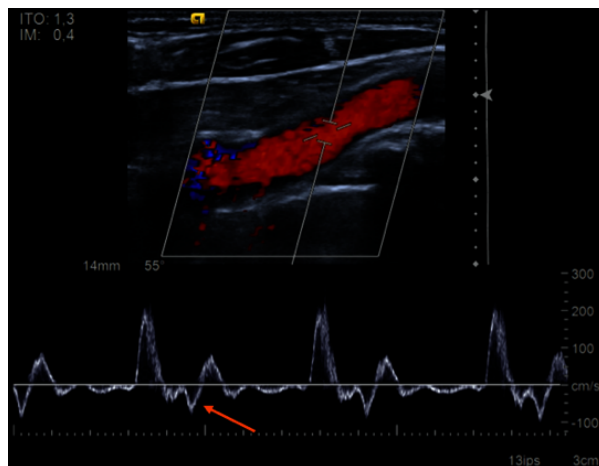
EPO1056

Posterior cerebral stroke by reverse flow embolism in thoracic outlet syndromeA. Celier¹, S. Chabay², D. Stanciu³, F. Pico⁴¹Le Chesnay, France, ²Angiology Unit, Versailles Mignot Hospital, Le Chesnay, France, ³Neurology, Versailles Mignot Hospital, Le Chesnay, France, ⁴Neurology department and Stroke Center, Versailles Mignot Hospital, Versailles, France**Background and aims:** Arterial thoracic outlet syndrome (aTOS) is a rare condition characterized by the compression of the subclavian artery in the thoracic outlet. It can be complicated by a cerebral infarction (CI). A retrograde embolism mechanism is often suspected, but rarely proven.**Methods:** A 24-year-old man presented with a transient memory disorder and paraesthesia of the left lower limb. His neurological exam was normal. In his medical history, he has a recently discovered aTOS. Surgery was planned shortly. Brain MRI revealed an CI of the right posterior cerebral artery (Fig. 1). CT angiography showed a 24.1mm thrombus in a post-stenotic aneurysm sac of the sub-clavian artery (Fig. 2). An doppler ultrasound (Fig. 3) showed retrograde reflux for approximately 0.45 seconds. During this reflux, the average maximum speed is -12.8cm/sec. Thus, the estimated amplitude of the reflux is 5.76cm. The distance from the edge of the mobile thrombus to the ostium from the right vertebral artery is 5cm. The rest of the CI work up was strictly normal. After anticoagulation, the patient underwent surgery.

FLAIR weighted brain MRI shows an hyperintense area in the right posterior cerebral artery territory



24.1mm thrombus in a post-stenotic aneurysm sac of the sub-clavian artery



Ultrasound in the sub-clavian artery showing a retrograde flux (arrow)

Results: We have found only 3 other cases in the literature with arguments in favor of an embolic mechanism by retrograde flow in CI associated with aTOS. The Doppler analysis that we report shows that the retrograde embolism mechanism was both possible and likely.**Conclusion:** Arterial thoracic outlet syndrome is a rare condition which can be complicated by a cerebral infarction linked to a retrograde embolism from a post stenotic aneurysmal sac.**Disclosure:** Nothing to disclose

EPO1057

Timing of carotid endarterectomy after intravenous thrombolysis

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Background: The aim of this study was to identify optimal timing of Carotid Endarterectomy (CEA) in a patient with acute ischemic stroke after administration of intravenous thrombolysis (IVT) and with symptomatic carotid artery stenosis. We focused on clinical outcome 3months after stroke.

Patients and methods: All CEA operated after the administration of IVT (from 2012-2019) were primary divided into the groups according to time interval between the IVT and surgery ((a) within 24 hours, (b) over 24 hours). Secondary were divided into the groups according to time interval between the IVT and surgery: within 6 hours, 6-12 hours, 12-24 hours, 24-72 hours, 72 hours- 14 days, over 14 days. Neurological deficit was assessed with National Institutes of Health Stroke Scale (NIHSS) and clinical outcome after 3 months with modified Rankin scale (mRS) with a score 0-2 for good outcome.

Results: 66 patients (44 males) were analyzed retrospectively. There was no significant difference in good clinical outcome between groups of operated patients within 24 hours and after 24 hours (76.7 vs. 75%). Median mRS after 3 months in both groups was 1. Second, in a more detailed breakdown, worse clinical outcomes are reported for groups within 6 hours and over 14 days. The good clinical outcome (mRS ≤ 2) in the groups was: within 6 hours -70%, 6-12 hours -78%, 12-24 hours -82%, 24-72 hours -77%, 72 hours -14 days -100%, over 14 days -67%.

Conclusion: The risk of stroke recurrence while waiting for CEA shows the importance of early surgery. Early CEA surgeries outside the first 6 hours following IVT administration are not burdened with a higher risk of worse clinical outcome.

Disclosure: Nothing to disclose

EPO1058

Increased brain plasmin levels following experimental ischemic stroke

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Background and aims: The fibrinolytic protease plasmin is induced by recombinant tissue-type plasminogen activator (tPA) therapy. We measured potentially harmful plasmin activity in brain tissue following experimental ischemic stroke.

Methods: We established a novel method for direct quantitative measurement of plasmin activity in mouse brain slices using a sensitive fluorescent substrate in the presence of specific protease inhibitors. This method was used in fresh coronal slices of the ipsilateral and contralateral hemispheres 3, 6 and 24 hours following permanent right middle cerebral artery occlusion (RMCAo) in wild type and tPA deficient mice. Infarct volume was measured by the TTC method.

Results: Plasmin activity was elevated in the ischemic and contralateral hemisphere after the induction of RMCAo in comparison to low levels in healthy mice ($p < 0.0001$), increased with time ($p < 0.0001$ by repeated measures ANOVA) and was significantly higher in the ischemic compared to the contralateral hemisphere 3 (1.07 ± 0.17 and 0.66 ± 0.06 , respectively, $p < 0.01$), 6 (1.04 ± 0.35 and 0.46 ± 0.07 , respectively, $p < 0.001$) and 24 hours (1.94 ± 0.50 and 0.75 ± 0.1 , respectively, $p < 0.001$) following RMCAo. Plasmin activity was concentrated in the ischemic core slices and was correlated with infarct volume ($R^2 = 0.5289$, $p < 0.01$). The specificity of the assay was verified utilizing tPA-deficient mice which had significantly 3 fold lower levels of plasmin 24 hours following ischemia compared to wild type mice ($p < 0.01$).

Conclusion: Stroke induces increased plasmin levels in the brain which may represent a therapeutic target and suggest caution in the use of rtPA.

Disclosure: Nothing to disclose

EPO1059

LncRNA-U90926 aggravates ischemic brain injury via promoting neutrophils infiltration after experimental stroke

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Background and aims: Microglia are a key immune-competent cell type that exert elaborate functions to determine the outcome of ischemic stroke. However, the detail mechanisms under the post-stroke microglial activity remain elusive. Long non-coding RNAs (LncRNAs) play a vital role in the biological function of microglia in various of diseases. In this study, we explored the role of U90926 in the microglial activity after experimental stroke.

Methods: Oxygen-glucose deprivation (OGD) and transient middle cerebral artery occlusion (tMCAO) were used as in vitro and in vivo ischemic stroke models. Real-time polymerase chain reaction (RT-qPCR) was used to detect expression of U90926 and other cytokines. Infiltrating neutrophils were quantified by FACS and immunofluorescence staining. Fluorescence in situ hybridization (FISH) assay was performed to determine the localization of U90926. Elisa assay was performed to detect the chemokine CXCL2 level. Western blot was taken to detect the expression of involved molecules. Luciferase activity and RNA pull down assays were used to explore the correlation between miR-658-3p and its target gene U90926 and CEBPB.

Results: U90926 was markedly up-regulated in microglia exposed to MCAO and OGD. Microglial U90926 knockdown definitely attenuated brain infarct size and neurological deficits after experimental stroke. Fewer neutrophils infiltrated to the infarcted brain after U90926 knockdown. U90926 functioned as an endogenous miR-7658-3p sponge, resulting in the increase of miR-7658-3p target CEBPB level, which further up-regulated neutrophil chemoattractant CXCL2.

Conclusion: U90926 aggravates ischemic brain injury through facilitating neutrophils infiltration via up-regulating microglia-modulated neutrophils chemoattractant CXCL2.

Disclosure: Nothing to disclose

EPO1060

Endovascular treatment in patients with M2 segment of the middle cerebral artery occlusions in a tertiary hospital: real-life experience

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Background and aims: The benefit of endovascular treatment (EVT) in patients with acute ischemic stroke in proximal anterior circulation is established. However, the experience with distal occlusions is limited and benefit remains unclear. We present our clinical experience among patients with occlusion of the M2 segment of the middle cerebral artery undergoing EVT.

Methods: Retrospective analysis of prospective registry of EVT in our tertiary hospital between January 2018 and November 2019. Clinical and radiological variables of patients with M2-occlusions were collected.

Results: 23 patients were identified, mean age was 64.8±16.4 years, 60.9% women. 21.7% patients were older than 80 years. The etiology was cardioembolic in a 47.8% and ESUS in a 39.1%. 56.5% patients received intravenous alteplase before EVT. 69.6% had an occlusion of the dominant branch. Successful recanalization (TICI2b-TICI 3) was achieved in 91.3%, with no significant differences between dominant and nondominant (p=0.624). There was no hemorrhagic transformation in any patient. Median NIHSS at onset was 13.9±6.3, at discharge was 6.7±6.8 (p<0.001). At 3 months 59.1% patients were independent (mRS ≤2) with no significant differences between receiving previous intravenous alteplase or not (p=0.17). This percentage of functional independence is equal for patients over 80 years old. Mortality in the first 3 months was 23%.

Conclusion: EVT in patients with M2-occlusion is associated with good functional independence and recanalization rates in our experience with no increased risk of hemorrhage. Larger studies are needed to verify the benefits of EVT for different settings of M2 occlusions.

Disclosure: Nothing to disclose

EPO1061

The association between immature platelet and the early neurological deterioration in acute ischemic stroke

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Background and aims: Early neurological deterioration (END) in acute ischemic stroke is a common event. The underlying pathomechanisms are heterogenous. Immature platelet fraction (IPF) is the useful marker of increased platelet production and turnover which could occur in patients with increased platelet activation. We investigated the association between the level of IPF and the prevalence of END in acute ischemic stroke patients.

Methods: A total 1655 of acute ischemic stroke patients in single tertiary academic center was enrolled from January 2013 to October 2018 via stroke registry. IPF levels were quantified by whole blood flow cytometry with automated assays (Sysmex XE-2100TM). High IPF was defined as the IPF level was more than 5%. Early neurological deterioration was defined as an increment change of at least one point in motor power or total National Institute of Health Stroke Scale (NIHSS) score deterioration ≥ 2 points within the first week after admission.

Results: A total of 72 patients (4.4%) experienced END. END was more prevalent in the patients with high IPF [13 (11.7%) vs 59 (3.8%), $p < 0.0001$]. Multivariate logistic regression analysis showed high IPF was an independent predictor of the prevalence of END (adjusted odds ratio=1.32; 95% confidence interval=1.03–1.70).

Conclusion: A high IPF levels was associated with the prevalence of END in acute ischemic stroke patients.

Disclosure: Nothing to disclose

EPO1062

Association of blood pressure with functional outcomes after endovascular thrombectomy in acute basilar artery occlusionB.-H. Cho¹, J.-T. Kim²¹*Korea University Anam Hospital, Seoul, Korea, Republic of,*²*Chonnam National University Hospital, Gwangju, Korea, Republic of*

Background and aims: Blood pressure (BP) is associated with clinical outcome after acute ischemic stroke, but the exact mechanism and effect of BP are not well understood. BP levels related to prognosis after endovascular thrombectomy in patients with acute basilar artery occlusion remain unclear. We aimed to investigate the association between BP and clinical outcome in acute basilar artery occlusion patients treated with endovascular thrombectomy.

Methods: This study reports a retrospective analysis of a prospective registry of a comprehensive stroke center. Patients treated with EVT due to acute basilar artery occlusion were enrolled. BP was measured hourly during the first 24h after admission. Associations of various BP parameters, including BP variability, with functional outcomes at 3m, including good outcomes (modified Rankin Scale [mRS] score of 0-2), were analyzed.

Results: Of the 79 enrolled patients (mean age; 71.5 ± 11.5 yrs, male; 53.2%), 70 (89.7%) achieved successful reperfusion after EVT, and 26 (32.9%) had good outcomes at 3m. Higher systolic successive variation (SV) (each 10% increase; OR 0.67 [0.53-0.87]) were associated with a reduced likelihood of achieving good outcomes.

Conclusion: The results showed that a higher systolic SV in patients with acute basilar artery occlusion during the first 24h of EVT reduced the likelihood of good outcomes at 3m.

Disclosure: Nothing to disclose

EPO1063

Elevated levels of D-dimer are associated with MRI hyperintensities in Patients with transient global amnesia

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Background and aims: Transient global amnesia (TGA) is a benign but self-limiting neurological syndrome, characterized by the development of anterograde and retrograde amnesia, without loss of consciousness and self-awareness. The pathophysiology of TGA remains to be obscure even after more than 60 years from its first description. The purpose of this study was to approval the hypothesis of a positive association of MRI confirmed hyperintensities with elevated D-dimer.

Methods: The study was conducted retrospectively on 33 patients diagnosed with an episode of TGA according to the criteria of Hodges and Warlow (Hodges and Warlow 1990). Out of this cohort, 24 patients (19 females, mean age 64.9) had MRI confirmed hyperintensities. D-dimer levels were taken during the admission and concurrent presence of clinical symptoms of TGA. It has been taken logistic binary regression with the presence of MRI hyperintensities (YES/NO) as dependent variable and levels of D-dimer as an independent variable. The cut-off values for D-dimer were 0.5.

Results: From the whole cohort, 21 patients (63.6%) had elevated levels of D-dimer. Presence of elevated D-dimer was connected with higher risk of hippocampal hyperintensities in 3T MRI (OR=6.000, 95% CI:1.134-31.735).

Conclusion: Positive association of MRI confirmed hyperintensities with elevated D-dimer supports the theory of small thrombi in the deep cerebral venous system as a potential pathophysiological hallmark of TGA.

Disclosure: Nothing to disclose

EPO1064

Assessing for depression following a stroke

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Background and aims: Depression is a major source of morbidity on patients following a stroke and can hinder the patients' rehabilitation potential. The aim of the study was to determine whether depression is being actively screened for in our local national hospital.

Methods: Patients who experienced an ischaemic or haemorrhagic stroke over a predefined 3-month period were identified by performing a search through the imaging database. Note was taken whether patients were started on new psychiatric medication following the stroke and whether they were referred to a mental health specialist. At 3 months from onset of symptoms, patients under the age of 65 were screened using the hospital anxiety and depression scale (HADS) while patients over the age of 65 were screened using the brief assessment schedule depression cards score (BASDEC).

Results: 59 patients were found to have suffered a stroke. 28.8% of patients had cortical ischaemia while 32% of patients had lesions in the deep white matter. The majority of patients were not screened for mood disorders. Half of these patients felt they might have benefitted from such screening. A third of patients were screened as inpatients, with up to a third of them being referred to psychiatry and starting treatment. Screening tests at 3 months revealed a third of patients were at risk of depression following a stroke with only 27% of them being seen by psychiatrist.

Conclusion: A robust way to screen post stroke patients for depression needs to be implemented. We suggest for screening to be incorporated in local guidelines.

Disclosure: Nothing to disclose

EPO1065

A Study of Clinical, Radiological & Thrombophilia Profile in Cerebral Venous Thrombosis

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Background and aims: Cerebral venous thrombosis (CVT) accounts for 10–20% of stroke in young which in turn accounts for nearly 30% of all cases of strokes in India. The study was done to describe the clinical, radiological and thrombophilia profile of CVT in an Indian population.

Methods: The study was carried out at a tertiary care multi-specialty hospital in Western Maharashtra. The study protocol was approved by the institutional ethics committee. The study design was a prospective, observational study with patients recruited over a 12 months period from December 2018 to November 2019. 45 patients were studied.

Results: Male preponderance was seen. The mean age of presentation was 30 years. Headache was the most common presenting complaint seen in 93.33%. Most common sinus involved was transverse sinus seen in 40% 43% had venous infarctions on the MRI brain. In 64% of cases, a prothrombotic state could be identified. MTHFR gene mutation (24%), Protein C deficiency (16%), APLA (12%), Factor V mutation (8%) and Protein S deficiency (4%) were seen.

Conclusion: CVT is an important cause of headache and stroke and modern MR imaging has allowed early and firm diagnosis. It is one of the treatable and reversible causes of stroke in young. Clinical presentation is extremely varied and symptoms may evolve over few weeks or even months. In contrary to recently published European guidelines, evaluation for an underlying procoagulant in provoked & unprovoked CVT, is useful for further planning of long term anticoagulation.

Disclosure: Nothing to disclose

EPO1066

Embollic stroke secondary to an aortic valve fibroelastoma: an increasingly recognized rare cause of stroke

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Background and aims: Cardiac papillary fibroelastomas (CPFEs) PFE are the second most common primary cardiac tumors after myxomas. Most PFE are found incidentally, but when they are symptomatic, stroke or TIA is the most common clinical presentation.

Methods: We report a case of a 59-year-old gentleman with sudden severe bilateral hearing loss, gait instability, dysarthria and left limbs clumsiness.

1 year before, he developed a right palmar digital artery thrombosis, without significant findings in the etiological study.

Results: A brain MRI, 15 days after the symptoms started, showed a subacute ischemic stroke involving both insular cortex and right frontotemporal lobes (Figure 1).

Blood tests, including hypercoagulability and autoimmunity, were normal. Duplex study of supraaortic arteries was normal and no potentially embolic arrhythmic events were found.

The transthoracic echocardiography (TTE) revealed a thickened aortic valve with a pediculate mobile 29mm-length mass anchored to the left coronary leaflet with preserved left ventricular ejection fraction, which suggested a vegetation or a cardiac tumor (Figure 2).

A multidisciplinary team decided on surgical treatment. After aortic valve resection a metallic aortic prosthesis was implanted, with favorable evolution.

Pathologic examination of the surgically removed pieces confirmed the CPFE diagnosis (Figure 3).

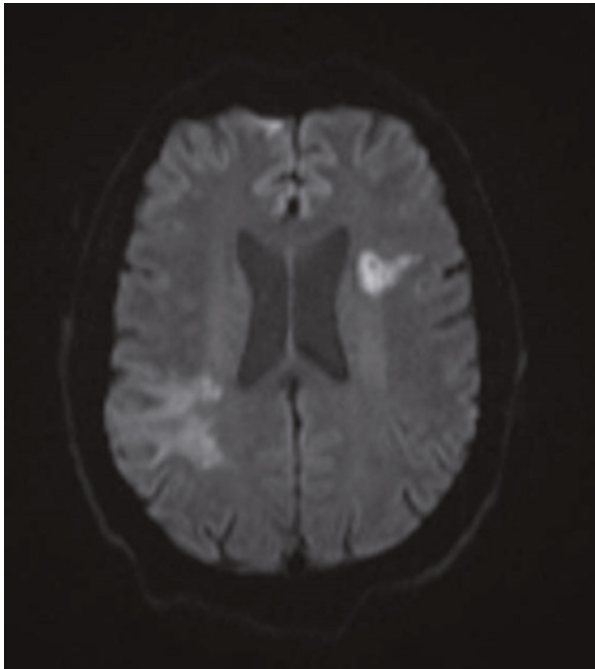


Figure 1: MRI diffusion weighted imaging of subacute ischemic stroke which involved both insular lobes and right frontotemporal lobe.

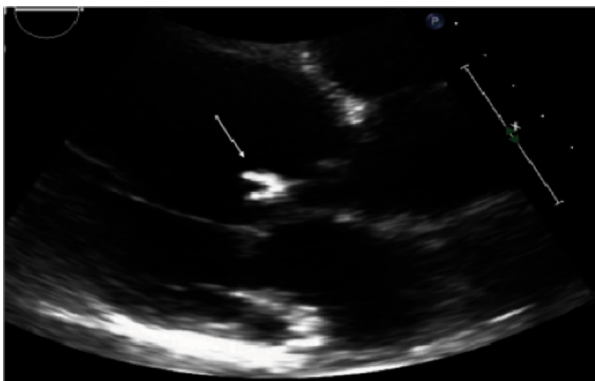


Figure 2: TTE imaging showing the thickened aortic valve with a pediculated mobile 29mm-length mass anchored to the left coronary leaflet.

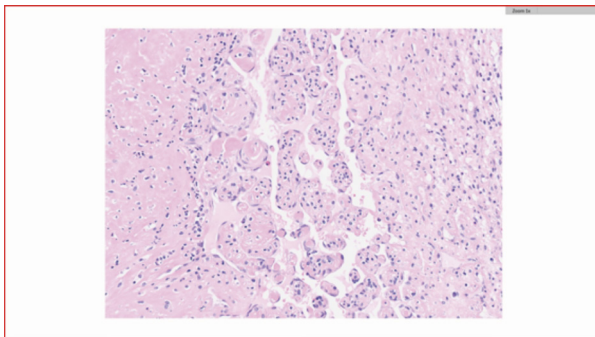


Figure 3: Pathology showed papillary structures lined by endothelium consisting of fibromyxoid stroma with dense areas of hyalinized stroma confirming the diagnosis of a papillary fibroelastoma of the aortic valve.

Conclusion: Primary cardiac tumors are an uncommon cause of systemic embolism, which can be easily diagnosed with non-invasive techniques and whose treatment eliminates the risk of recurrence. For this reason, they should be considered in the study of patients with cerebral ischemia of embolic profile without known cause.

Disclosure: Nothing to disclose

EPO1067

Cerebral amyloid angiopathy-related inflammation: a rare and treatable cause of severe subacute leukoencephalopathy

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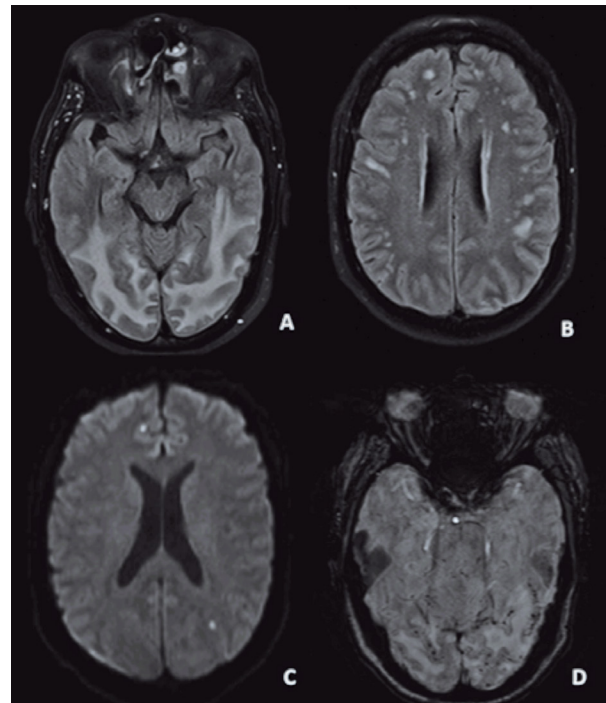
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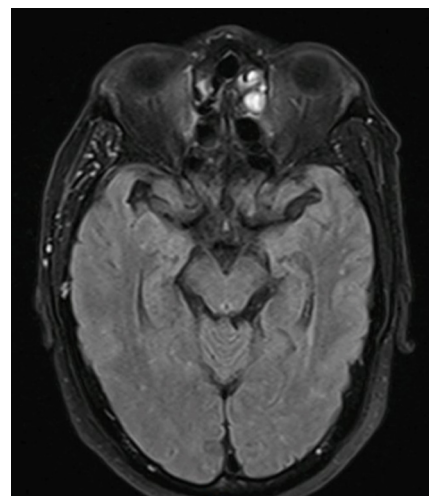
Background and aims: Cerebral amyloid angiopathy-related inflammation (CAAri) is a rare entity, characterized by inflammatory response to beta-amyloid deposits on cerebral vessels. It often presents with rapid cognitive decline and encephalopathy. Definitive diagnosis is only possible on brain biopsy, but probable diagnosis is based on characteristic clinical and imaging findings and ruling out of differential diagnosis.

Methods: Case report.

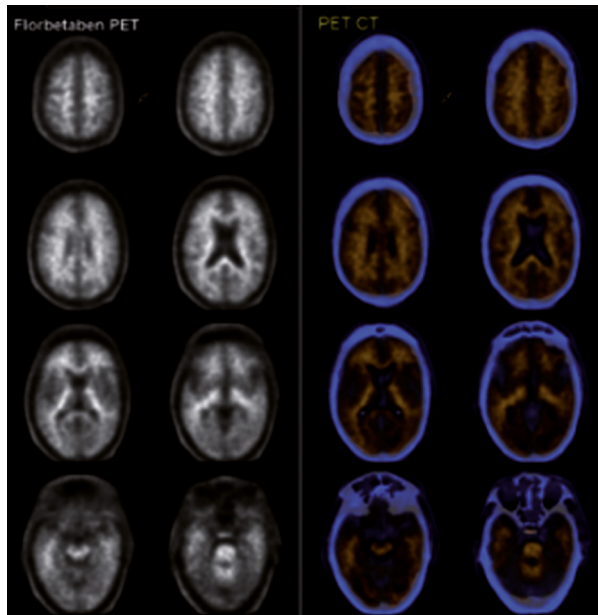
Results: 57-year-old male, presenting with acute disorientation, confusion and agitation, preceded by headache and transient upper left limb paresthesias. Blood tests were unremarkable, CT scan showed slight leukoencephalopathy and EEG had diffuse slowing without paroxysmal activity. Lumbar puncture revealed pleocytosis (107 cells/uL) with mononuclear predominance and high protein levels. Antibiotic and antiviral therapy were started, but repeat lumbar puncture revealed worsening of these parameters, and there was neurological worsening with severe cognitive deterioration, psycho-motor slowing, and marked bilateral visual deficit. Infectious and auto-immune studies were negative. MRI revealed bilateral temporo-occipital confluent white matter T2/FLAIR hiperintensity without contrast enhancement, multifocal subcortical white matter lesions (2 with restriction on DWI), and widespread cortical microbleeds. Digital angiography was unremarkable. The patient was treated with corticosteroids and cyclophosphamide, with significant cognitive and visual improvement, and remission of confluent posterior leukoencephalopathy on 3 month MRI. Florbetaben-PET showed diffuse deposition of beta-amyloid and APOE e4 was found in homozygosity, supporting the diagnosis of CAAri.



Initial MRI showing bilateral temporo-occipital confluent white matter T2/FLAIR hiperintensity (A), multifocal subcortical white matter lesions (B), 2 with restriction on DWI (C), and widespread cortical microbleeds on SWI (D).



3 month MRI showing remission of confluent posterior leukoencephalopathy.



Florbetaben-PET and PET/CT fusion images showing loss of white matter/cortex differentiation (as both take up the tracer), demonstrating abnormal beta-amyloid deposition.

Conclusion: We present an aggressive case of CAARI, a rare, probably underdiagnosed and potentially treatable cause of acute/subacute leukoencephalopathy. Studies and guidelines are in need, to clarify the best diagnostic and therapeutic approach.

Disclosure: Nothing to disclose

Cerebrovascular diseases 3

EPO1068

C-reactive protein and neutrophil-to-lymphocyte ratio may suggest early cerebral venous thrombosis

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Background and aims: Time of onset of cerebral venous thrombosis (CVT) can be difficult to ascertain at patient admission, which may have implications in therapeutic decision. Our aim was to evaluate the association between blood biomarkers levels in CVT patients at admission and the temporal pattern of CVT.

Methods: We performed a retrospective analysis of adult CVT cases admitted to a tertiary hospital from 2006 to 2019. We excluded cases of infection at admission, autoimmune inflammatory and haematological diseases. Spearman correlation test and Poisson regression were used to assess the relationship between blood biomarkers at admission and symptoms duration until CVT diagnosis. We performed a group analysis according to reported onset of symptoms: acute (<2 days), subacute (2-30 days) and chronic (>30 days).

Results: Our cohort included 78 patients, 74.4% female, median age at diagnosis of 43 years old. Median duration of symptoms of 4 days (IQR 2-11). The chronic group included 8 patients (10.3%). Spearman correlation showed a weak but significant negative correlation between duration of symptoms and absolute neutrophil counts ($p=0.028$, $r=-0.251$), C-reactive protein (CRP) ($p=0.038$, $r=-0.240$), and neutrophil-to-lymphocyte ratio (NLR) ($p=0.013$, $r=-0.282$). Poisson regression confirmed a negative relation between timing of CVT and NLR ($p=0.046$, OR 0.889, CI 0.791-0.998) and CRP ($p=0.021$, OR 0.976, CI 0.955-0.996). The latter was confirmed by analysis of chronic and non-chronic (acute and subacute) group ($p=0.037$; OR 0.804; CI 0.654-0.987).

Conclusion: In our cohort, higher CRP and NLR were associated with a shorter duration of symptoms. Nevertheless, more studies are needed to confirm these findings.

Disclosure: Nothing to disclose

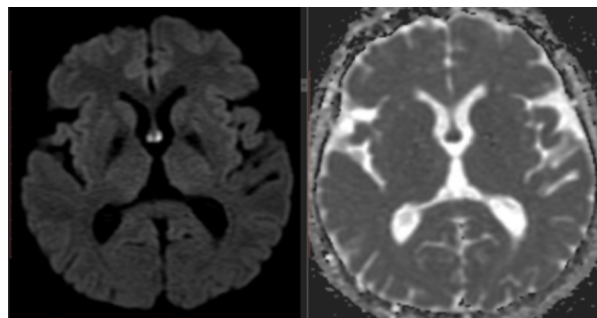
EPO1069

Exceptionally rare cause of acute anterograde amnesia: fornix infarction following subcallosal artery strokeN.I. Dima¹, L. Cozma², D. Tulbă¹, A. Lefter¹, M.C. Lupu¹, B.O. Popescu²¹*Department of Neurology, Colentina Clinical Hospital, Bucharest, Romania,* ²*“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania*

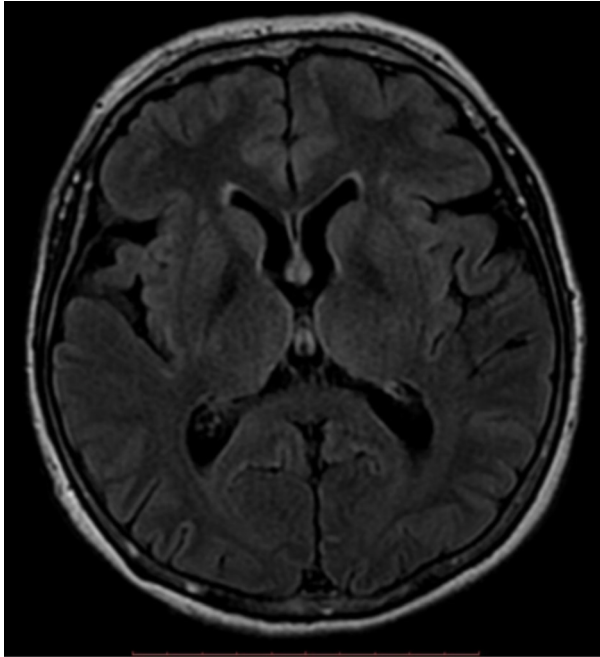
Background and aims: The fornix, as part of the Papez limbic circuit, plays an important role in the formation and consolidation of new memories. Fornix injuries cause an important spectrum of memory deficits. Although there is increasing awareness of stroke as a cause of acute isolated amnesic syndrome, fornix infarction rarely occurs.

Methods: We report the case of a 63-year-old woman with a history of untreated hypertension who presented with a sudden episode of anterograde amnesia beginning 12 hours prior to admission.

Results: Neurological evaluation revealed anterograde amnesia and disorientation in time and space. Brain computed tomography was unremarkable, but brain magnetic resonance imaging revealed restricted diffusion and increased T2/FLAIR signal in the bilateral fornix suggestive of subcallosal artery infarction. Electroencephalography and cerebrospinal fluid examination were normal. Carotid and vertebral ultrasonography showed moderate atherosclerosis and an ulcerated plaque on the internal carotid artery. The presumed pathophysiology is most likely cerebral small-vessel disease, in accordance with literature data. Concurrently, we conducted an extensive search of the literature using the Pubmed database and found 49 cases of anterograde amnesia due to fornix infarction, 28 of which were non-iatrogenic.



Brain MRI. Axial diffusion-weighted scan demonstrating restricted diffusion (increased DWI-left and decreased ADC-right signal) suggestive for a bilateral fornix infarction.



Brain MRI. Axial FLAIR-weighted imaging showing hyperintensity in fornix columns bilaterally.

Conclusion: Fornix infarction is a rare condition that should be considered in all patients presenting with acute-onset anterograde amnesia, especially if symptoms are isolated and persist for more than 24 hours.

Disclosure: Nothing to disclose

EPO1070

A right time and place for everything: - HR-MRI for the diagnosis and follow-up of primary angiitis of the central nervous system

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Introduction: Primary angiitis of the central nervous system (PACNS) is a rare disease, characterized by an exhaustive differential diagnosis and unfavorable prognosis, in the absence of aggressive therapy.

Methods: A 35-year-old, otherwise healthy female patient is hospitalized for 5 consecutive symptomatic ischemic strokes during a period of 2 months. Successive MRIs reveal consecutive ischemic strokes in the vertebrobasilar territory (right posteroinferior cerebellar, bilateral anteroinferior cerebellar and paramedian branches of basilar artery (BA). Cerebral angiography consistently showed a thrombosed distal BA, with stenosed BA branches. All recurrences are diagnosed despite intensive antithrombotic therapy. High-resolution MRI revealed basilar and vertebral arteries mural enhancement, suggesting cerebral vasculitis. An extensive diagnosis work-up included a transthoracic and transesophageal cardiac ultrasonography and lumbar puncture without pathological findings and an exploration of infectious, neoplastic and rheumatological etiologies successively excluded. Treatment induction with corticosteroids and cyclophosphamide is initiated, with no new clinical recurrences.

Results: 6-months HR-MRI follow-up revealed BA stenosis regression, with near-absence of mural enhancement. Corticosteroids are tapered over 3 years, with cyclophosphamide switched for methotrexate. Yearly HR-MRI and clinical evaluations showed absence of imagistic or clinical recurrences, thus permitting immunosuppressive treatment withdrawal after 3 years and follow-up thereafter without clinico-radiologic recrudescence.

Conclusion: Case particularities include the predilection of the vasculitic process for the vertebrobasilar territory as well as the favorable outcome, contrasting with the general disease prognosis. Our case highlights the role of HR-MRI in establishing the exclusion diagnosis of PACNS and contributing to the rapid treatment initiation and follow-up in an otherwise debilitating condition.

Disclosure: Nothing to disclose

EPO1071

Screening for atrial fibrillation in patients with cryptogenic stroke with telemonitoring

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Background and aims: Cryptogenic stroke (CS) is defined as cerebral ischemia of unknown origin and accounts for 30% of ischemic stroke. CS is more frequent in younger patients and most frequently due to cardiac embolism. The most frequent causes of cardiac embolism include paradoxical embolism via a patent foramen ovale (PFO), paroxysmal atrial-fibrillation (AF), valvular heart-disease, left ventricular aneurysm, atherosclerosis of ascending aorta. 24-hours holter-ECG is traditionally used in clinical practice. This method has some limitations especially the insufficient period for examination and the chance for misdiagnosing short episodes of AF.

The aim of the study is to find frequency of atrial fibrillation in a group of patients with cryptogenic stroke examined with telemonitoring.

Methods: The study includes 185 patients with stroke with undetermined reason. The patients were age between 33 and 75 years. Examination with monitoring system Pro Plus EHO EVENT MINI Holter was performed. The middle period for assessment of cardiac rhythm is 96 hours.

Results: Rhythmic pathology was identified in 48 patients, 3 of them were with periods of bradycardia and were transmitted for pacemaker implantation. Atrial fibrillation was diagnosed in 45 patients and anticoagulation therapy was initiated. The episodes of silent AF appeared between 24 hour and the end of examination in 31 patients. In this case, the use of 24 hour ECG holter could lead to misdiagnose.

Conclusion: Long term monitoring has advantage over 24 hour holter ECG in screening of AF in CS. New systems for telemonitoring are modern and useful approach for examination in patients with CS.

Disclosure: Nothing to disclose

EPO1072

Young cryptogenic ischemic stroke patients: a descriptive analysis of baseline epidemiologic characteristics, laboratory parameters and clinical outcomes

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Background and aims: Approximately 25% of ischemic strokes (IS) occur in young adults and despite an extensive work-up the cause of young IS remains very often cryptogenic. Thus, effectiveness of secondary prevention may be unclear. We aimed to assess the relationship between traditional vascular risk factors (VRF), baseline clinical and laboratory parameters and outcomes including recurrent IS in young cryptogenic IS patients.

Methods: The study set consisted of young acute IS patients <50 years enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). We perform extensive diagnostic work-up including specific cardiac and thrombophilia markers to assess cause of IS. 3-month clinical outcome was scored using the modified Rankin scale (mRS).

Results: Out of 294 young patients enrolled in the study, 208 (71%, mean age 41.6±7.2 years) were identified as cryptogenic. Hyperlipidemia (43%), smoking (40%) and arterial hypertension (37%) were the most frequent VRF and PFO was detected in 27% of patients. Good clinical outcome (mRS 0-2) reached 166 (80%) patients. Recurrent IS occurred in 7 (3.4%) patients during a mean time of follow up 24.2±22 months. Patients with RIS were older (47.4 vs. 41.1 years, p=0.007). Presence of VRF in patients with RIS were higher, but not significantly.

Conclusion: Despite a higher presence of VRF in young cryptogenic IS patients, the risk of recurrent IS was very low. Patients with recurrent IS were older, but did not differ in any other analyzed parameters or VRF.

Disclosure: Study was supported by the grant of Ministry of Health Czech Republic, n. 17-30101A and by the grant IGA LF UP_2019_005 and 2019_008.

EPO1073

Branch atheromatous disease in isolated pontine infarction has more peripheral arterial disease than small vessel occlusionY. Do¹, J.H. Kim²*¹Department of Neurology, Catholic university of Daegu, School of Medicine, Daegu, Korea, Republic of, ²Department of Cardiology, Gimcheon Jeil hospital, Gimcheon, Korea, Republic of*

Background and aims: Ischemic stroke patients with branch atheromatous disease (BAD) have worse neurologic deficits and prognosis compared with those with small vessel occlusion (SVO), although both disorder mechanisms are forms of deep brain infarction. The present study aimed to investigate an MRI-based etiological classification for acute isolated pontine infarctions and to assess differences in vascular risk factors and peripheral arterial disease among the etiological subtypes.

Methods: We reviewed the consecutive data of patients admitted for acute ischemic stroke or MR positive transient ischemic attack between August 2016 and July 2019. Acute isolated pontine infarcts were classified into 3 groups: BAD, SVO, and large artery atherosclerosis (LAA) according to basilar or vertebral artery steno-occlusion and infarct midline lesion extension from basal pontine surface on magnetic resonance images and angiography. The vascular risk factors, ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV) were analyzed among three groups.

Results: Among the 64 patients enrolled, BAD was the most common mechanism of isolated pontine infarct. BAD group had more frequencies of abnormal ABI (47.8%, 4.5%, $p=0.002$) and hypertension (87%, 54.5%, $p=0.023$) compared to SVO group. BAD group more frequently had abnormal ABI (47.8%, 15.8%, $p=0.048$) and hyperlipidemia (87%, 47.4%, $p=0.008$) than LAA group. There was no significant difference in either diabetes or baPWV between the BAD and SVO groups.

Conclusion: ABI and vascular risk factors in BAD group were more similar to the LAA group, rather than to the SVD group, suggesting the atherosclerotic mechanism of BAD.

Disclosure: Nothing to disclose

EPO1074

Cranio-cervical and spinal disease: two uncommon causes of sensory TIA mimics

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Background and aims: The diagnosis of transient ischemic attack (TIA) is clinical and relies on the symptoms description. Main differential diagnoses for transient sensory symptoms are migraine with aura, focal seizures and functional disorder.

Methods: We report 2 uncommon causes of TIA mimics presenting with transient sensory symptoms.

Results: Case 1

A 82-year-old woman with a history of hypertension was admitted to the Stoke Unit because of occurrence of 2 episodes of sudden right hemi-hypoesthesia, lasting for 5-20 minutes. Neurological examination disclosed a slight right hyperreflexia. The following days after admission, she continued to present 1-3 similar episodes/day. The majority occurred in orthostatic position after cephalic rotation. Brain-MRI showed a basilar invagination, with brainstem and cervical spine compression. After using cervical orthosis, she had no symptoms recurrence.

Case 2

A 54-year-old man with a history of diabetes mellitus and hypertension was referred to the TIA Clinic for 2 episodes of sudden numbness of the left limbs lasting for 1 minute. 1 month before, he had been admitted for left hemiparesis. Despite normal CT-scan, he had been discharged with diagnosis of ischemic stroke. Neurological examination disclosed left upper limb hypoesthesia. Spine-MRI revealed 2 enhancing cervical lesions (C2, C6) and brain-MRI showed multiple lesions characteristic of multiple sclerosis. Methylprednisolone was prescribed, with complete clinical resolution.

Conclusion: Atypical clinical features of transient symptoms led to the suspicion of a diagnosis other than TIA. The craniocervical junction or spinal cord may be the sites of the pathology responsible for transient sensory symptoms, and can only be diagnosed with appropriate complementary examinations.

Disclosure: Nothing to disclose

EPO1075

Sturge-Weber syndrome with an unusual location of the meningeal angiomas – a case report

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Background and aims: Sturge–Weber syndrome is a rare, sporadic neurocutaneous syndrome characterized by a classical triad of facial port wine nevus, ipsilateral meningeal angiomas and glaucoma. The incidence of Sturge-Weber syndrome is 1/50,000 live births, although it is more often underreported.

Methods: Case presentation of a 45-year-old female, diagnosed with Sturge-Weber syndrome, with a past medical history of hypertension, glaucoma, dyslipidemia, hypertensive cardiomyopathy and obesity, who was admitted for recurrent pain in the right side of her posterior vertebral thoracic region.

Results: Clinical examination revealed multiple angiomas, all of them being limited to the right side of her body (face, thorax and lower limb). Medullar thoracic magnetic resonance imaging examination showed a thoracic epidural gadolinophilic mass, suggestive for a venous malformation with an exerting mass effect on the adjacent structures. The vascular malformation was removed neurosurgically and the neurological symptoms remitted afterwards. Cerebral angiography established that the facial angiomas's arterial source was the right facial artery, without any other cerebral artery involvement. The right facial artery was subsequently ligated to diminish the size of the facial mass and to limit the extent of the future surgical excision. After 1 year, the patient underwent a new surgical intervention for the excision of the supra-orbital and infra-orbital angiomas.

Conclusion: This case emphasizes the variety of the pathological aspects of Sturge-Weber disease and the importance of extensive workup in patients with cutaneous vascular abnormalities.

Disclosure: Nothing to disclose

EPO1076

Factors affecting the fate of Raymond-Roy Grade 2

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Background and aims: Raymond-Roy Classification is the standard for evaluating aneurysms occlusion (RG1: completely excluded, RG2: neck remnant, RG3: substantial residual filling). While RG1 carries the best long-term prognosis and RG3 carries the worst prognosis; the fate of RG2 is controversial. We aim to investigate factors affecting the fate of RG2 aneurysms occlusions over a period of 6 months follow-up.

Methods: We reviewed 156 aneurysms treated with endovascular coiling aided in some cases with single or Y-configuration stenting. The radiological outcome was assessed immediately postoperative and 6 months after treatment with the grading of the angiograms on the basis of Raymond scale.

Results: In terms of the RG, the initial angiographic outcome was RG1 in 88 (56.4%) cases, RG2 in 39 (25%) cases, and RG3 in 29 (18.6%) cases, while the final angiographic outcome at 6 months was RG1 in 117 (75%) patients, RG2 in 27 (17.3%), and RG3 in 12 (7.7%). Further analysis was done for the 39 aneurysms with initial RG2. Based on the angiographic outcome after 6 months, they were classified into 2 groups: regressive to RG1 group (n=21), and non-regressive group (RG2&3) (n=18). Demographic and clinical data (age, gender, presentation), aneurysm geometry (height, width, size, neck, dome-to-neck, aspect, maximum and size ratios) and treatment-related factors (modality, stent type) were analyzed. Only the aneurysm width showed statistically significant difference between the 2 groups (p=0.046). Aneurysm width cutoff value of 0.687 had 61.1% sensitivity and 90.5% specificity.

Conclusion: About 50% of the RG2 aneurysms spontaneously regress into RG1. The most important factor that influences the process of regression is the aneurysm width.

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EPO1077

Signs and symptoms of sleep apnea and acute stroke severity: is sleep apnea neuroprotective?

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Background and aims: Previous reports suggest that brief periods of hypoxemia or ischemia render the brain tolerant to subsequent ischemic insults. Sleep apnea (SA) leads to frequent episodes of nocturnal hypoxemia and may induce ischemic tolerance. In contrast, increase risk for cardiovascular events in patients with severe SA, arguing the presence of ischemic tolerance. We undertook this study to determine differences in stroke severity and early neurologic course in patients at risk for SA as determined by a sleep questionnaire.

Methods: Patients admitted with acute ischemic stroke completed the sleep questionnaire. It examines different features of SA and classifies patients into a high, low and no risk for SA groups. NIHSS and ASPECT score were determined on admission. Age, sex, cardiovascular risk factors, stroke mechanism and outcome were determined prospectively.

Results: We enrolled 471 patients with a mean age of 66 years, 48.6% were men. Hypertension was the cardinal cardiovascular risk factor (57.5%). The SA questionnaire classified 41 patients at high risk for SA, 246 patients at low risk, while 184 patients considered with no risk. The median NIHSS and ASPECT score on admission did not differ between the 2 groups, neither the mechanism of stroke and 90 days outcome. Examined separately, we found no effect of snoring, daytime sleepiness, obesity on stroke severity and outcome.

Conclusion: A large number of stroke patients were at low risk for having SA. We were not able to show that a constellation of symptoms and features highly suggestive of SA influenced stroke severity or early neurologic course.

Disclosure: Nothing to disclose

EPO1078

Prediction of acute ischemic stroke outcome with Alberta Stroke Program Early CT Score (ASPECTS)

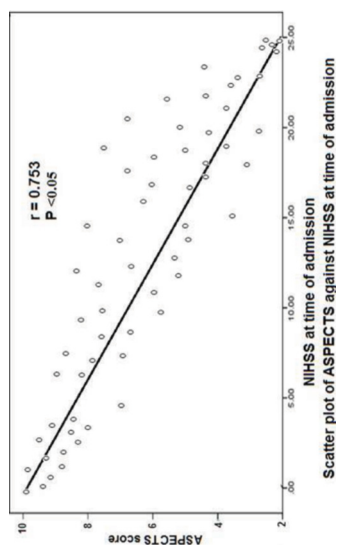
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Background and aims: CT brain used for the diagnosis of acute ischemic stroke (AIS). The aim of this study is to predict the outcome of AIS with Alberta Stroke Program Early CT Score (ASPECTS).

Methods: A prospective study was done on 150 consecutive patients presented by AIS. Vascular risk factors were determined from history taking. Glasgow Coma Scale (GCS), National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) used to assess the severity. CT brain was done initially and after 7 days using ASPECTS.

Results: ASPECTS for all patients was 8.23 ± 1.87 and ASPECT for patients with favorable and unfavorable outcomes were 8.23 ± 1.87 and 4.96 ± 2.56 respectively ($p < 0.001$). The most commonly recognized risk factor for stroke in patients group were hypertension (68%), smoking (40%), DM (26%), AF (18.6%), hyperlipidemia (14.6%), ischemic heart disease (10%) and previous stroke (6.7%). The mortality rate after 3 months was 13.3%. The initial stroke severity (NIHSS) was 12.9 ± 7 . ASPECTS was inversely correlated with NIHSS on admission in ischemic stroke ($p < 0.001$). Lower ASPECTS ≤ 7 was associated with more hospital stay ($p < 0.05$), lower GCS and development of inpatient complications ($p < 0.05$), significant higher death rates and higher mRS at 3 months follow up ($p < 0.05$).



Scatter plot of ASPECTS against NIHSS at time of admission

Table 1: Correlation between risk factors, ASPECTS and stroke outcome after 3 months

Variable	All patients	MRS 0-2 favorable outcomes	MRS 3-6 poor outcomes	P Value
Number	150	95 (63.3%)	55 (33.7%)	0.05
Age (years)	64.0 ±11.5	59.11 ±7.45	68.7 ±6.98	0.001
Male	79 (52.7%)	49 (51.5%)	30(54.5%)	0.725
Hypertension	102 (68%)	54(56.8%)	48(87.3%)	0.005
DM	39 (26%)	23(24.2%)	16(29.1%)	0.511
Smoking	60 (40%)	37(38.9%)	23(41.8%)	0.729
Hyperlipidemia	22 (14.6%)	13(13.7%)	9(16.4%)	0.654
AF	28 (18.6%)	17(17.9%)	11(20%)	0.749
IHD	15 (10%)	10 (10.5%)	5 (9.1%)	0.778
NIHSS on admission	12.9 ± 7	10.97 ± 4.64	18.92 ± 6.32	0.001
ASPECTS	8.23 ± 1.87	8.23 ± 1.87	4.96 ± 2.56	0.001

Table 1: Correlation between risk factors, ASPECTS and stroke outcome after 3 months

Table 2: Correlation of ASPECTS and stroke severity (NIHSS) Outcome variables according to ASPECTS

Variable	ASPECTS			Significance	
	Better 8-10 (n=66)	Worse			
		5-7 (n=68)	0-4 (n=16)		
Stroke severity (NIHSS)	Mild (0-5)	27	2	0	Spearman correlation 0.753 P <0.05
	Moderate (6-15)	23	16	1	
	Severe (≥ 16)	16	50	15	
Primary outcome	GCS at admission	13.77 ± 1.23	11.21 ± 3.3	8.97 ± 2.41	P < 0.05 @
	NIHSS at admission	9.78 ± 3.24	17.2 ± 5.89	20.89 ± 4.1	P < 0.05 @
	Inpatient stay (days)	3.65 ± 4.87	12.08 ±6.67	15.66 ± 6.2	P < 0.05 @
	Inpatient complications	10 (15.1%)	20 (29.4%)	7 (43.8%)	P < 0.05 @
Secondary outcome	Death (N) 20 (13.3%)	3 (4.5%)	12 (17.6%)	5 (31.3%)	P < 0.05
	mRS at 3 months	1.23 ± 0.93	3.31 ±1.36	4.96 ± 1.04	P < 0.05

@ Significant only for group 1 & 3. mRS: modified Rankin Scale

Table 2: Correlation of ASPECTS and stroke severity (NIHSS) Outcome variables according to ASPECTS

Conclusion: ASPECTS is a simple, easy practical scale for assessment of prognosis of AIS and may predict 3 months outcome in ischemic strokes.

Disclosure: Nothing to disclose

EPO1079

How to choose the right patients when you have limited resources – the clinical utility of AS5F score in detecting paroxysmal atrial fibrillation in stroke patients

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Background and aims: AS5F (Age and Stroke Severity NIHSS >5 to Find AF) is a risk score based on clinical parameters developed for selecting patients with cryptogenic stroke for prolonged Holter-ECG monitoring to detect paroxysmal atrial fibrillation (pAF). We aimed to determine the utility of the AS5F score in current clinical practice in a group of patients with stroke of undetermined etiology.

Methods: We retrospectively assessed clinical data of 768 patients with acute ischemic stroke hospitalized in our department between 1st of January 2018 and 31st of December 2018, 51.7% (n=397) having a stroke of undetermined etiology (according to TOAST classification) for whom we calculated the AS5F score.

Results: The cut-off value for patients with high risk of developing pAF is 67.5 points. 50.2% had AS5F score greater/equal to 67.5. Compared to the low-risk group, the high-risk patients were older (78 years versus 63 years), more frequently women (51.76% versus 41.76%), had higher median NIHSS (8 versus 3) and a higher mortality (26.79% versus 3.53%). When compared with the group of cardioembolic stroke patients, the high-risk group had a similar profile for age, gender distribution, stroke severity and in-hospital mortality. Patients underwent Holter monitoring at the request of treating physicians and, by chance, 29.4% were in the low-risk group and only 15.3% patients in the high-risk group.

Conclusion: Considering the lack of sufficient resources in low and middle income countries, AS5F score can be extremely useful for the management of acute stroke patients in order to efficiently prioritize those needing prolonged-Holter monitoring.

Disclosure: Nothing to disclose

EPO1080

Black hole sign for predicting in-hospital and 90-day mortality

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Background and aims: Spontaneous intracerebral hemorrhages constitute about 15% of all strokes and have a high mortality rate. Black hole sign is a novel computerized tomography (CT) finding which is shown to predict hemorrhage expansion and poor prognosis. We aimed to analyze the effect of black hole sign on prognosis and mortality.

Methods: We included spontaneous intracerebral hemorrhage patients who were admitted to our hospital between September 2018 and October 2019 and have a CT performed within 6 hours of onset. Hemorrhages related to secondary causes were excluded and patients who underwent to surgery were excluded from prognosis analysis. Demographic data and medical history were collected on admission. CT is examined for presence of black hole sign, ventricular extension of hemorrhage and hematoma volume using ABC/2 method. Modified Rankin Scale (mRS) was assessed on day 10 and 90.

Results: Of 88 patients admitted, 66 were included in the study. 47 of the patients were male and mean age was 63.08±14.33. Black hole positive patients had more anti-coagulant use, higher creatinine and initial hematoma volumes compared to black hole negative patients. 7 of the patients underwent surgery. Black hole positive patients had more in-hospital mortality (p=0.028) and 90-day mortality (p=0.028). Comparison of median mRS at day 10 (p=0.081) and 90 (p=0.059) between groups did not reach significance.

Conclusion: Black hole sign may be related to poor prognosis and can be used to predict mortality. It may be a useful marker for classifying patients for management and clinical studies.

Disclosure: Nothing to disclose

EPO1081

The perils of an elongated styloid process: carotid artery type Eagle syndrome

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Background and aims: Eagle syndrome (EagleS) is a rare condition due to an elongation of the styloid process and/or calcification of the stylohyoid ligament. EagleS is divided in a classic type, with impingement of the last 4 cranial nerves, and a carotid artery type, with impingement of the external or internal carotid arteries.

Methods: We describe a patient with a carotid artery type EagleS.

Results: A 47-year-old male presented at the emergency department (ED) with a 1-week, left-sided, hemifacial pain and paresthesias. He described a sudden-onset, constrictive and persistent pain, despite treatment with nonsteroidal anti-inflammatory drugs, acetaminophen and opioids. Ipsilateral conjunctival injection and tearing were initially present, but temporal evolution was not suggestive of cluster headache. He denied nausea, vomiting or photophobia. At first observation, he had no focal signs and brain computed tomography (CT) was normal. Latter re-evaluation showed a mild left ptosis and anisocoria (OD>OS). Careful history review revealed a blunt left cervical trauma prior to symptom onset. Angio-CT revealed a left internal carotid artery (ICA) dissection and reformatted images showed a bilateral elongated styloid process (right: 47mm, left: 41mm), near to the ICA. The patient was admitted to stroke unit and treated according to the legis artis. He was latter discharged with no deficits, waiting for surgical correction.

Conclusion: EagleS diagnosis needs a strong clinical suspicion, since it may present with ordinary symptoms. This case highlights the importance of a structured evaluation, even in a busy ED.

Disclosure: Nothing to disclose

PO1082

Brainstem cavernoma presenting as a rare etiology of Benedikt syndrome

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Background and aims: Benedikt syndrome is characterized by a third nerve palsy with contralateral pyramidal signs and Holmes tremor (rest, postural and intentional tremor in increasing order of intensity) and localizes the lesion to the mesencephalon. It is most commonly associated with ischemic or hemorrhagic stroke. In rare cases, a cavernoma is the underlying cause and usually manifests as a partial syndrome.

Methods: Case report.

Results: We present the case of a 50-year-old male with hypertension but no other relevant medical or family history. The symptoms began 7 years before he presented to our department, with progressive worsening of continuous involuntary movements of the left limbs. Mild ipsilateral weakness and binocular diplopia were also noted. He presented to our emergency department due to the subacute worsening of his abnormal movements. His neurological exam revealed right ptosis and limitation of vertical movements of the right eye suggestive of a third cranial nerve lesion, as well as left central-type facial palsy, mild left hemiparesis, and Holmes tremor, leading to a diagnosis of a Benedikt syndrome. Dystonic posturing of the upper limb and subtle involuntary movements of the leg were also present. MRI revealed a right ponto-mesencephalic lesion, strongly hypointense on SWI, compatible with a cavernoma. There were no signs of recent hemorrhage. There was a moderate improvement of tremor with Clonazepam (2,5mg/day). Surgical resection is planned.

Conclusion: Although rare, cavernomas should be considered in the differential diagnosis of Benedikt syndrome. Medical and surgical management may be required for optimal treatment.

Disclosure: Nothing to disclose

EPO1083

The role of blood flow and cerebrospinal fluid flow disturbances in the development of cognitive impairment in cerebral small vessel disease

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Background and aims: Cerebral small vessel disease, cSVD, is the main cause of vascular cognitive impairment(CI) and the leading cause of mixed dementia. The objective of our study was to assess the role of arterial, venous blood flow and CSF-flow and their relationships in the development of CI in cSVDpatients.

Methods: 96 patients (64 female, mean age 60.6±6.3 years) with cognitive complaints and cSVD, according to the STRIVE criteria, were examined. The severity of CI was assessed based on the cognitive tests (MoCA, 10 words test, TMT B-A) and ADL scale. The phase-contrast MRI (PC-MRI,3T scanner) was used to measure blood flow in the internal carotid and vertebral arteries (the total arterial blood flow was taken into account), internal jugular veins (level of C2-C3vertebrae), in the straight and superior sagittal sinuses; CSF-flow in aqueduct.

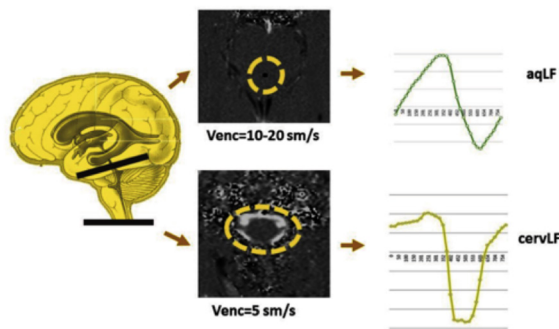


Fig.3

Results: Dementia and severe memory impairment were associated with an increase of arterial pulsation index, the intracranial compliance index and the aqueduct CSF-flow; severe executive dysfunction was additionally associated with a decrease in arterial blood flow, venous blood flow in the straight and superior sagittal sinuses. Parameters of blood flow and CSF-flow were interrelated, the arterial pulsation index had an influence on all parameters.

Conclusion: PC-MRI is simple and rapid way of performing noninvasive evaluation of vascular and CSF-flow and their dynamic coupling in cSVD patients throughout disease progression. The specific changes in blood flow and CSF-flow and their interrelation in patients with CI due to cSVD suggest the pathogenetic importance of cerebral hydrodynamic disturbances in the aetiology of brain damage and the development of CI in cSVD.

Disclosure: Nothing to disclose

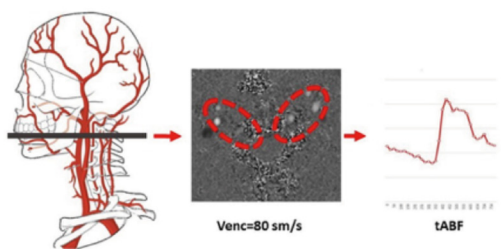


Fig.1

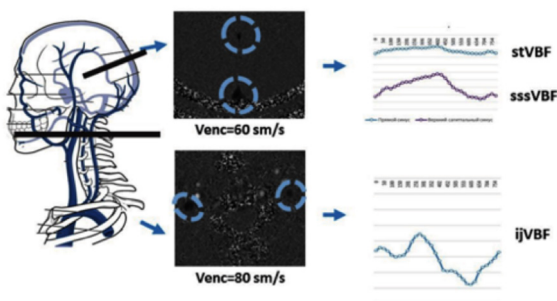


Fig.2

EPO1084

Taking a closer look at brain hemorrhage. A comparative study between hypertensive and amyloid etiologies

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Background and aims: Cerebral hemorrhage carries a very high mortality rate. There are few studies evaluating the relationship between hemorrhage etiology and prognosis.

The object of this work is to describe the baseline characteristics and prognosis of patients with hypertensive (HTAh) and probable amyloid (Ah) cerebral hemorrhage.

Methods: We retrospectively analyzed the demographic characteristics, functional prognosis and mortality rate of patients with HTAh and Ah, admitted to our Neurology department between January 2014 and January 2016.

Results: There were 158 patients (90HTAh and 68Ah). Both groups had similar proportion of females (52% and 51.5% respectively), as well as similar median age (76 vs 77).

In the first group, there were more patients with hypertension (72% vs 68%) and with oral anticoagulants (21 vs 16%), less percentage of dyslipaemia (31 vs 41%) and smoking (11 vs 18%). Diabetes mellitus (18 and 20%), median systolic blood pressure (161 vs 158mmHg), ICH scale score (2.1 vs 1.8) and initial NIHSS (11 vs 10) were similar in HTAh and Ah groups.

We found a very high and similar mortality rate (34% in HTAh vs 33% in Ah), but there were more patients functionally independent (mRS \leq 2) at discharge in the HTAh group (37% vs 28%).

Conclusion: Patients with HTAh and Ah have a high median age and high proportion of cerebrovascular risk factors. Although both groups have similar mortality rate, there is a trend towards a better functional outcome in those with HTAh. Larger and prospective studies are needed.

Disclosure: Nothing to disclose

EPO1085

Assessment of stroke risk in patients with atrial fibrillation – a different tale of an old clinical conundrum

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Background and aims: Patients with atrial fibrillation (AF) are at high risk for suffering a stroke but the risk is not the same for all patients. Several risk stratification scores with different performance are available to guide anticoagulation therapy in primary and secondary prevention.

Methods: We performed a cross-sectional study on 246 patients with AF admitted for acute ischemic stroke; CHADS2, CHA2DS2-VASC and modified ATRIA scores were calculated for all patients with and without taking the index stroke into account. Patients were grouped according to embolic risk: low risk (CHADS2 0-1; CHA2DS2-VASC 0; ATRIA 0-5), intermediate risk (CHADS2 2-3; CHA2DS2-VASC 1; ATRIA 6) and high risk (CHADS2 score 4-6; CHA2DS2-VASC score \geq 2; ATRIA 7-15).

Results: Mean age of the patients was 75.4 years and 58.8% were females. Our patients had the following estimated cardioembolic risk prior to suffering the stroke: CHADS2: 21.1% high risk, 53.7% intermediate risk, 25.2% low risk; CHA2DS2-VASC: 97.9% high risk, 2.1% medium risk; ATRIA: 66.3% high risk, 8.9% moderate risk, 24.8% low risk. After suffering the index stroke, the patients were classified according to the 3 risk scores as follows: CHADS2 -67.7% high risk, 33.3% intermediate risk, CHA2DS2-VASC and ATRIA - all patients were classified as high risk.

Conclusion: CHA2DS2-VASC was the score that most accurately predicted the high risk of cardioembolism in patients who suffered an ischemic stroke, while post stroke calculated CHA2DS2-VASC and ATRIA had similar performance in estimating the risk for subsequent cardioembolic events.

Disclosure: Nothing to disclose

Child neurology/developmental neurology

EPO1086

Specific Language Impairment (SLI) in children may be caused by epileptic brain activity

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Background and aims: The objective of this study was to find out if there is a possible association and the impact of epilepsy and epileptiform activity in children with SLI.

Methods: The study was conducted on 80 children suffering from SLI and 80 age and sex match healthy control children. CT brain was performed and EEG was recorded for children. IQ level, cognitive age, social and phoniatic assessment were done for all patients.

Results: 80 children with SLI (51 males and 29 females) with a mean age of 4.11±1.93. Patients with SLI, showed significantly higher rates of abnormal EEGs ($p = 0.006$) and epilepsy ($p < 0.001$) compared to the control group. Spearman correlation showed a highly negative significant correlation between the language, IQ with abnormal EEG and epilepsy ($r = -0.91$, $p < 0.01$ and $r = -0.91$, $p < 0.01$ respectively). Also, there was a moderately negative significant correlation between the cognitive age, social with abnormal EEG and epilepsy ($r = -0.70$, $p < 0.05$ and $r = -0.65$, $p < 0.05$ respectively).

Conclusion: Epileptiform activities even without epilepsy in preschool children may alter normal language function. SLI was associated with lower IQ levels, social and cognitive age.

Disclosure: Nothing to disclose

EPO1087

Pediatric optic neuritis

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Background and aims: Optic neuritis (ON) is rare in children in comparison to adults, but accounts for approximately 25% of pediatric acute demyelinating syndroms.

Methods: We conducted a retrospective study including 25 patients followed up for ON.

Results: The sex-ratio M/F was 0.27. The mean age of onset was 11.39 years (2-17). ON was characterized by acute or subacute vision loss, bilateral onset, pain with eye movement and dyschromatopsia in 73.9%, 69.5%, 30.4% and 14% of cases, respectively. All patients presented visual acuity worse than 5/10. 31 of patients had a mildly edematous optic disc. Visual evoked potentials revealed a demyelinating mechanism in 82.6% of cases. Orbit MRI showed enhancement of affected optic nerve in 38% of cases. Brain and spine MRI were abnormal in 52.3% and 37% of cases, respectively. Oligoclonal bands were identified in cerebral spinal fluid in 26% of cases. ON was inaugural of a neuroinflammatory disease in 21% of cases. The etiologies were dominated by idiopathic optic neuritis (11 patients) and multiple sclerosis (9 patients). 3 patients were diagnosed with neuromyelitis spectrum disease: 1 of them had AQP4-antibodies and the other had MOG-antibodies. 1 patient was diagnosed with acute demyelinating encephalomyelitis, and 1 with Behçet-disease. Visual disturbance resolves in 95% of cases after corticosteroids. The incidence of recurrence was 17.4%.

Conclusion: Compared to adults, ON in children is more likely to be bilateral, to occur following infection or vaccination, with poor presenting visual acuity, lack of pain, and anterior involvement. The majority of children experience full visual recovery.

Disclosure: Nothing to disclose

EPO1088

Slowly but surely: the possible relationship between electroencephalographic slow wave activity and brain myelination during early childhood

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Background and aims: Ratio of frontal/occipital slow wave (1-4.5 Hz) activity (SWA) – F/O, observed within the stage of slow-wave sleep, is considered as a marker of myelination (Kurth S. et al., 2017; LeBourgeois M.K. et al., 2019). The reasoning of the choice of SWA during the sleep for the calculation of F/O ratio refers to the fact that SWA is more prominent during the sleep as well as to the observation of enhanced transcription in several genes involved in phospholipid synthesis and myelination during the sleep. However, we suppose that F/O-ratio during wakefulness remains rather informative index. It is well known, that preterm children are characterized by delay in myelination in central neuronal system.

Methods: Based on mentioned above, we calculated F/O-ratio (frontal electrodes: 10,11,15,16,18; occipital electrodes: 71,74,75,76,82) in two samples: 8 preterm infants (gestational age (GA) – 32.25 (SD=1.28) weeks; corrected age (CA)–5.0 (SD=0.66) months); 20 term infants (GA – 39.7 (SD=0.97) weeks; CA – 5.7 (SD=0.21) months).

Results: There were no significant between-group differences ($p=0.051$). However, effect size (Cohen's d) was rather big ($d=0.9$), that allows us to suggest presence of significant differences with a sufficient increase of the sample. Values of F/O-ratio were 0.77 (SD=0.29) and 0.53 (SD=0.19) in term infants and preterm infants respectively, pointing to a relatively more pronounced «frontalization» of SWA in control group.

Conclusion: «Frontalization», apparently, correlates with better myelination. Given to the all mentioned above, we consider that it is possible to use F/O-ratio computed during wakefulness as a correlate of myelination.

Disclosure: This work was supported by a grant of Russian Science Foundation, 20-18-00343

EPO1089

Video labeling software for general movements assessment classification aim in machine learning field

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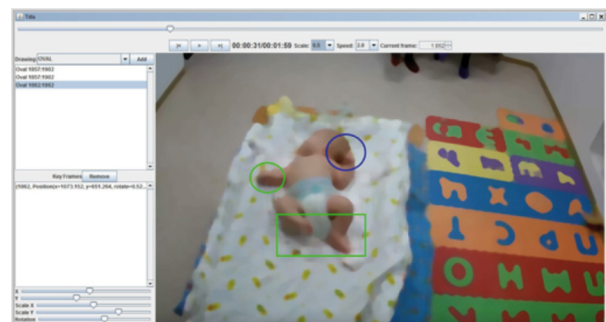
Background and aims: A common problem with automated general movements assessment (GMA) is that there is only a general expert assessment. It involves every event that needs to be distinguished from each other. These events happen arbitrarily during the child observation.

There are two approaches to solve the problem. First, collect a huge dataset with any possible examples. Secondly, manually label necessary events on video with expert involvement.

Methods: Our research used the second approach. The program goal was labeling events and objects on video that corresponded to analysis by Prechtl's method. Labeling was carried out manually by certified expert. The option with automatic recognition of objects and generation of markup based on previously marked data is considered in future work.

Results: Available elements were rectangle and ellipse for highlighting an interest region. It was possible to rotate and scale these shapes. The rejection of more complex shapes was made deliberately in order to simplify the software interface.

The elements position was set using two key frames. Another elements position was calculated by linear interpolation between them. Also there was an opportunity to set up its name and color for each shape. It was necessary to distinguish different types of movements that appeared at the same time. In addition, it was possible to export both to video file with superimposed markup, and to independent json file, which contained only markup data (image).



Conclusion: The software helped to create dataset, which was suitable for test of GMA algorithmization hypothesis in the machine learning paradigm.

Disclosure: This work was supported by a grant of the Russian Science Foundation, 20-18-00343

EPO1090

Sleep architecture in Valproate-induced nocturnal enuresis in primary school and preschool children.

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Background and aims: Nocturnal enuresis (NE) is a common pediatric problems related to sleep.

Objective: We aimed at studying the sleep architecture, to evaluate the occurrence and the characters of nocturnal enuresis in children secondary to valproic acid antiepileptic drug.

Patients and methods: A retrospective study carried out in 260 pediatric patients diagnosed as idiopathic epilepsy and kept up on valproic acid antiepileptic drug. 28 children developed secondary nocturnal enuresis aged 5-12 years were subjected to a single overnight polysomnography and compared to 28 child age and sex matched controls.

Results: Enuretic children had significantly prolonged sleep latency and higher stage N1 percentage, less total sleep time, lower sleep efficiency, and lower rapid eye movement sleep percentage compared with the control group. Multivariate logistic regression, demonstrated that the independent factors associated with nocturnal enuresis, were younger age (OR 2.31, p=0.004), followed by weight and Serum level of valproic acid (OR 1.44, p=0.05 and OR 1.39, p=0.05 respectively). While, the therapeutic dose, or the treatment duration with valproic acid, were not significantly associated with the incidence of enuresis (OR 0.98, p=0.09 and OR 0.86, p=0.12 respectively).

Conclusion: Nocturnal enuresis is a common reversible side effect that accompanied the valproic acid use in children. The underlying mechanism may be related to increase sleep depth with valproic acid.

Disclosure: Nothing to disclose

EPO1091

Clinical characteristics of tuberous sclerosis patients with refractory epilepsy

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Background and aims: Refractory epilepsy is a common clinical manifestation in patients with tuberous sclerosis (TSC). In this study, we aimed to evaluate the clinical and neuroimaging characteristics of tuberous sclerosis patients with refractory epilepsy.

Methods: A total of 113 patients with tuberous sclerosis who were followed up at the Istanbul University Tuberous Sclerosis Unit between January 2010- June 2018 were included. Neurological and psychological examinations of all patients, characteristics of seizures, electroencephalography (EEG) and cranial magnetic resonance imaging (MRI) findings were recorded.

Results: Of the 113 patients screened, 85.8% had seizures at any time during life. Of the epilepsy patients, 62.9% developed refractory epilepsy. Onset of seizures occurred within the first year of life in 75.4% of these patients, and after the age of one in 51.4% ($p < 0.05$). Clinical follow-up was available for 57% of these patients. 59.6% of those who were followed up developed multiple seizures. The difference between this group and that without resistant seizures was statistically significant ($p < 0.05$). 67 patients underwent psychiatric and developmental assessment. Of the patients with refractory epilepsy, 59.5% had intellectual disability (ID) and 37.5% had autism spectrum disorder (ASD). In those without refractory epilepsy, 16.7% had ID and 13.3% had ASD. The difference was statistically significant ($p < 0.05$).

Conclusion: This study suggests that refractory epilepsy has a close relationship with multiple types of seizures and psychiatric comorbidities. In order for the differences to be explained, detailed genetic examinations in large cohorts should be performed.

Disclosure: Nothing to disclose

EPO1092

The role of pro-inflammatory cytokines in different types of epilepsies in children

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Background and aims: The etiology of epilepsy is a definitive determinant of clinical course and prognosis. Following modern studies in experimental models were established the important role of the inflammation as a trigger in epileptogenesis. Activation of glial cells, disturbed completeness of hemato-encephalic barrier by the influence of cytokines present great pathogenic value in epileptogenesis, especially in resistant epilepsies and encephalopathies in childhood. Thus pro-inflammatory markers can reflect the pathogenesis of seizure generation and exacerbation.

We aimed to assess the clinical and predictive meaning of expressions of pro-inflammatory markers, which may have an elucidated role in the generation of seizure and the resistance in epilepsies. We measured in serum comparably unknown pro-inflammatory factors, in the particularly Vascular cell adhesion molecule 1 (VCAM-1), chemokines, including macrophage inflammatory protein (CCL2, CCL3, CCL 4), eotaxin (CCL11), prostaglandin-PGE2 in different types of epilepsies.

Methods: Serum samples were collected from children in both gender 0-16 age with pharmacosensitive epilepsies (N=20), with intractable, drug-resistant epilepsy children (N=20) and afebrile nonepileptic controls (N=16)

Results: Preliminary findings from the recently completed assessments demonstrated cytokines that were significantly elevated in patients with epilepsies in comparison to the control group: prostaglandin-PGE2 and CCL3, CCL4, CCL5. Furthermore, Prostaglandin-PGE2 and CCL3 levels were higher in resistant seizure patients than in pharmacosensitive group ($p < 0.05$).

Conclusion: Precise correlation between expressions of pro-inflammatory markers, their quantitative concentrations, and levels of repeating seizures should be discussed as a prediction of resistance and supports possible future strategies of anti-inflammatory drugs as targeted, essential or additional therapy for prevention of recurrent epileptic seizures.

Disclosure: This work was supported by Shota Rustaveli National Science Foundation of Georgia Fundamental Research Foundation grant FR-18-16052.

EPO1093

Adaptive skills in 5-24 month-old children with family risk of autistic spectrum disorders

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Background and aims: Adaptive behavior includes the ability to cope with environment requirements and daily needs. Infants use various skills (communication, motor activity, health and safety, self-regulation). The aim of the research was to assess the adaptive skills in children at 5-24 months age stage with family risk autistic spectrum disorders (ASD)

Methods: Cohort-study design. Experimental group included children with family risk ASD. Control group included typically development full-term infants without pathologies, matched by age and gender. The Bayley-III Adaptive Behavior Scale was used for assessment adaptive behavior at points: 5, 10, 14, 24 months

Results: There were no significant differences between groups at 5 and 10 month-stage (12 infants, mean age 6.0±1 months, 8 males; 17 babies, 10.8±0.8 months, 10 males). At 14 months-stage (15 toddlers; 14.6±0.4 months, 9 males) there were significant differences in scores Home Living (t=2.8 p=0.01), Self Direction (t=2.3 p=0.03), integrative skill Social communication (t=2.5 p=0.02). But at 24 months-stage (13 toddlers, 24.3±0.4 months, 6 males) there were significant differences (the Mann-Whitney test U) in scores Community Use (p=0.02); Home Living (p=0.001), Health & Safety (p=0.006) Self Care (p=0.003) Self Direction (p=.002), Motor (p=0.03).

Conclusion: There is an accumulation the number of adaptive skills with lower indicators in the group of children with family risk of ASD by the 24-months age compared to control group. The most differences were observed in the skills that can be taught by parents

Disclosure: The research was supported by the grant of the Russian Foundation for basic research №17-36-01100

EPO1094

Severe SCN8A-developmental and epileptic encephalopathy in a preterm infant presenting with malignant migrating focal seizures and early-onset movement disorder

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Background and aims: In the preterm neonates, most seizures are often an early indication of acute brain injury including intraventricular hemorrhage. While genetic epileptic encephalopathy is rarer in the preterm than the term neonates, there is growing evidence that specific genetic conditions are important etiologies of neonatal epilepsy.

Methods: We describe a preterm neonate diagnosed as severe SCN8A-developmental and epileptic encephalopathy presenting with malignant migrating focal seizures and severe non-epileptic movements.

Results: A female neonate presented paroxysmal non-epileptic episodes of severe tremor and hyperekplexia-like startles several hours after she was delivered at 32 and 1/7 weeks. Since the first week of life, she showed intractable focal or generalized seizures in the form of malignant migrating focal seizures or status epilepticus. Electroencephalography during the ictal period showed epileptiform discharges from left temporoparietal or bilateral frontal regions. Brain magnetic resonance imaging and metabolic tests were normal. Sequencing of the SCN8A gene revealed a de novo heterozygous missense mutation; c.2911C>G; p.Leu971Val (NM_014191.3). Her seizures have been well controlled with multiple sodium channel blockers including oxcarbazepine, zonisamide, phenytoin, and lamotrigine. However, she has been on the support of home mechanical ventilator and gavage feeding due to severe global development delay.

Conclusion: This case is the preterm neonate with early and severe clinical phenotypes linked to the SCN8A gene mutation. A high index of suspicion for the genetic etiology of seizures in the preterm neonate must be kept in mind when confronted with intractable seizures and abnormal movements.

Disclosure: Nothing to disclose

EPO1096
Cancelled

EPO1097
Cancelled

EPO1099

Cancelled

EPO1100

The results of MRI and CT imaging in children with arterial ischemic stroke – experience from one medical center

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Background: Arterial ischemic stroke (AIS) in pediatric population is a rare condition. It's prevalence is estimated at 0.58 to 7.9 new stroke onset in 100,000 children a year. Risk factors for pediatric AIS as well as its clinical presentation and outcome are recently better known for the results of IPSS (International Paediatric Ischemic Stroke) research. Aim of the study was to analyze clinical presentation of pediatric AIS and outcomes in consideration of neuroimaging (CT, computed tomography and/or magnetic resonance imaging, MRI of brain) results.

Material and methods: The analysed group of patients consisted of 78 children (32 girls and 46 boys) at the age of 9 months to 18 years at stroke onset (mean age 9.25 ± 5.48 years); the mean age of the children at follow-up was 11.86 ± 6.01 years. The diagnosis of stroke was based on applicable criteria by thorough past history, neurological examination and results of neuroimaging (CT and/or MRI), in most cases also MR angiography and classical angiography. The study was retrospective. The consent of Ethical Committee was obtained.

Results: In analyzed group of patients AIS was more common in boys than girls, the mean age for stroke onset was 8.4 years. The most common type of stroke was TACI, ischemic focus was most commonly located in temporal lobe and in middle cerebral artery. It occurred most commonly in sleep and winter.

Conclusion: AIS occurs most commonly in boys than girls. Correlation between clinical presentation and neuroimaging results was found.

Disclosure: Nothing to disclose

EPO1101

Rett syndrome: analysis of 23 cases

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Background and aims: Rett syndrome (RTT) is an X-linked neurodevelopmental disorder which mostly affects females and in 95% caused by mutation in MECP2.

Aim: To provide clinical characteristics of RTT in 23 patients.

Methods: There are 23 patients with RTT under our observation, all of them - girls. Average age - 6.4 years old (range 2.6-12.4). MECP2 mutations were found in 20 (87.0%) cases, 3 (23.0%) were diagnosed clinically.

Results: Average age at onset of RTT was 16 months (from 6 to 24). 14 (61.0%) patients had walking skills before the onset, another 4 (17.4%) started walking later, 5 (21.7%) girls did not start walking at the time of the study. Speech was present in 19 (82.6%) patients before the onset and later it was lost in 18 (78.2%) cases. The most common comorbidity was abnormal breathing affecting 21 (91.3%) of the patients and appeared from 8 months to 5 years of age. Types of breathing disturbances included hyperventilation 7 (33.3%), apnoea 1 (4.7%) and combination of hyperventilation and apnoea 13 (62%). 11 (47.8%) patients of the cohort had epilepsy. Onset of seizures ranged from 1.9 to 6 years of age. 5 (45.5%) girls developed drug resistant epilepsy. 2 (18.2%) of them used ketogenic diet which decreased seizure frequency in the first case by 64.9% during the first quarter and 35.2% during the second quarter, in the second case - by 100%. Scoliosis was noted in 15 (65.2%) patients, sleep disturbance in 10 (43.5%).

Conclusion: Abnormal breathing, scoliosis and epilepsy are the most common comorbidity in RTT. A ketogenic diet may be effective in drug resistant epilepsy.

Disclosure: Nothing to disclose

EPO1102

Exogenous flupirtine and flupirtine aromatic carbamate derivative as potential treatment for CLN3 disease

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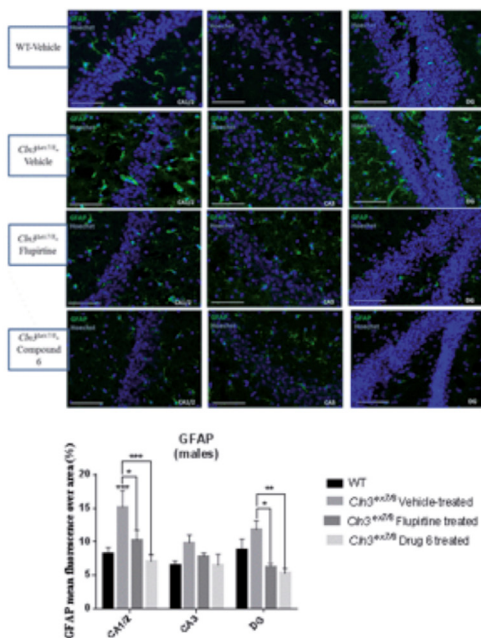
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Background and aims: CLN3 disease is the most common form of Neuronal Ceroid Lipofuscinoses (a group of childhood neurodegenerative diseases). Hallmarks include brain atrophy, retinitis pigmentosa, accelerated apoptosis and ceramide elevation. Treatment regimens are symptomatic. Flupirtine and its novel aromatic carbamate derivative (compound 6) exert anti-apoptotic and neuroprotective effects, in vitro. This study aims at investigating, in vivo, beneficial effects of orally supplied flupirtine and compound 6 in Cln3Δex7/8 knock-in mice.

Methods: WT and Cln3Δex7/8 mice received flupirtine, compound 6 or vehicle for a period of 15 weeks. Effect of flupirtine or compound 6 on Cln3Δex7/8 mice was determined by performing behavioral tests (open field, pole climbing, Morris water maze, rotarod, wire suspension test), and biochemical tests (gene expression, proteome profiler assay, TUNEL assay, subunit C storage, astrogliosis and neuronal cell counts).

Results: Flupirtine and compound 6 were able to attenuate mobility, enhance gait locomotor measures, and increase exploratory behavior in Cln3Δex7/8 mice. Both were able to enhance spatial learning navigation and memory retention in Cln3Δex7/8 mice. Various apoptosis genes with dysregulated expression in Cln3Δex7/8 knock-in mice were restored to normal levels. NOSTRIN gene in males and XPA gene in female mouse brain were differentially modulated in response to Flupirtine/Compound 6 treatment as compared to Cln3Δex7/8 vehicle-treated mouse. Anti-apoptotic protein XIAP and BDNF were downregulated in Cln3Δex7/8 vehicle treated mice. Finally, high levels of astrogliosis in male Cln3Δex7/8 brains were significantly lowered after treatment with both drugs.



Conclusion: These findings establish that compounds analogous to flupirtine demonstrate anti-apoptotic activity with potential for treatment of CLN3 disease.

Disclosure: Nothing to disclose

EPO1103

Gilles de la Tourette syndrome: a Moroccan experience

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Background and aims: Gilles de la Tourette syndrome (GTS) is a neuropsychiatric disorder that is characterized by motor and vocal tics and psychiatric comorbidities, including attention deficit/hyperactivity disorder and obsessive-compulsive disorder. Our aim is to review the epidemiological, clinical, comorbidities as well as the various treatment options of GTS.

Methods: We performed a retrospective data analysis of patients diagnosed with GTS according to DSM V criteria over a period of 12 years. The severity of GTS was assessed through the Hopkins Motor and Vocal Tic Scale.

Results: 20 patients were included with an average age at onset of 8 years and a sex ratio M/F of 4. In past medical history we found repetitive angina and parents with tics. All patients had simple motor or vocal tics and 50% had complex motor or vocal tics. The most common phenomena associated with tics were self-harm (62.5%), arithmomania (60%), and touching (50%). GTS was mild in 3 cases; moderate in 7 cases; moderately severe in 4 cases and severe in 6 cases. The most commonly used treatments were SSRIs/Benzodiazepines (90%), haloperidol (65%), risperidone (40%) with improvement in the majority of patients.

Conclusion: GTS is a heterogeneous disease which treatments are discussed according to the severity of tics; it is essential to educate the patient and his entourage about the impact of disease on daily life. Our study has the advantage of being the first to report characteristics of GTS in Morocco. These characteristics do not seem to differ from those of the literature.

Disclosure: Nothing to disclose

Education in neurology; History in neurology; Ethics in neurology

EPO1104

Evaluation and treatment of mild traumatic brain injury in general medical practice in view of the need for further harmonization in advanced postgraduate medical education

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Background and aims: There are some common problems and controversies in evaluation and treatment of patients with mild traumatic brain injury (MTBI) in neurological as well as in general medical practice despite the introduction of modern standard clinical protocols. Our objective was to clarify the most significant issues in the management of MTBI patients for the further improvement of the program of advanced training of medical specialists.

Methods: We analyzed 215 medical records of consecutive admissions and referrals concerning MTBI twice during the last 5 years. Besides, we conducted structural interviews among neurologists and general practitioners in regard to the most difficult and relevant topics for advanced training of medical specialists.

Results: Standard protocols have been recently in use more often i.e. up to 79% of cases. At least 2 groups of difficulties and typical problems were identified. Along with the proper evaluation and interpretation of clinical symptoms some difficulties were revealed in regard to indications and timing of the appointment of CT, MRI and skull radiography during the initial management of MTBI (48%). The second group of problems was associated with the adequate medical treatment, pain control, follow-up recommendations, return to work, neurorehabilitation, detection and interpretation of possible posttraumatic consequences. Additionally, there exist some differences in approach to management of MTBI patients in neurological as well as in general medical practice.

Conclusion: The obtained data could be used as a basis for elaborating special advanced training programs for different categories of medical specialists.

Disclosure: Nothing to disclose

EPO1105

An observational survey 3 years after the French law on continuous and deep sedation until death (CDS)

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Background and aims: Continuous and deep sedation until death (CDS) is a new right open to the patient under conditions since the Claeys-Leonetti Act of February 2016. It represents a new end-of-life medical practice for patients with serious and incurable diseases including neurological diseases. So far, there has been little data to assess its implementation in the field

Methods: After an initial national survey in 2018, the National Centre for Palliative and End-of-Life Care conducted a new survey, in April 2019, over a given week, in 14 hospitals throughout France. The objective was to characterize and account for CDS among palliative sedation practices.

Results: 36 CDS were identified ; these included 6 requests by patients and 30 proposals by physicians in the context of limiting or stopping active therapies in non-communicating patients. A collegial procedure was carried out in 33/36 cases. Information to families was provided in all cases. The average doses of midazolam and morphine at the time of death were 9.2mg/h and 5.5mg/h respectively with an average survival time of 33.5 hours.

Conclusion: The survey results show large differences in dosages and survival time, notably between the limitation of invasive treatments including assisted ventilation and the limitation of artificial feeding and hydration. Furthermore, the study highlights the persistent difficulty of characterizing CDS among palliative sedation end-of-life practices.

Disclosure: Nothing to disclose

EPO1106

Abnormal findings in peer neurological examination – ethical and management approaches after two “clinical” cases

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Background and aims: Peer Physical Examination (PPE), in which a medical student is used as a model or students examine each other, is a common approach to teach undergraduate neurology. It can, however, bring unpredicted events, namely “incidental findings”. The recent occurrence of two of these situations in our department raised a reflection that we find appropriate to share.

Methods: Case report.

Results: Case1- Abnormalities were found in an extraocular motricity examination performed by the instructor in a 22-year-old male student. After the class, the abnormalities were explained to the student and the Neurological Examination (NE) was completed. The student agreed in pursuing the investigation and a diagnosis of multiple sclerosis was determined.

Case2 - An absent right corneal reflex was found in a 22-year-old female student in a PPE. Since she remained anxious, the NE was performed after the class and was unremarkable. She agreed to undergo on a brain MRI which showed a sequaleae in the paramedian left pons. Clinical and imaging follow-up was made during the following year and then suspended by student request.

Conclusion: NE performed by peers carry some issues related to the possibility of finding abnormalities. This seems to occur despite absent awareness about it, since no results appear in a PubMed search. We discuss aspects related to the exigence of the NE teaching to undergraduate Medical Students in terms of amount of practice, recognition of normal anatomy and non-pathological findings and the risk of finding unexpected signs during Peer Neurological Evaluation, but also how to prevent and deal with them.

Disclosure: Nothing to disclose

EPO1107

Training in Epilepsy at the Psychiatric Hospital of Bouakée. Ivory Coast Does the training reduce the cultural and health gap?

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Background and aims: Epilepsy has a high prevalence in Ivory Coast. It's a chronic and dynamic pathology that requires medical monitoring. Specialized health training in Ivory Coast is limited. Health personnel with general training take care of patients. The culture associates epilepsy with spirits, damns and religion. This beliefs are common even among the health personnel themselves, causing great stigmatization of patients. Some patients are not considered as sick, being separated from society in prayer fields. Most are valued by traditional medicine and a minority resorts to conventional medicine. The motley semiology of epileptic seizures makes them valued by Psychiatry. In this context, a Neurocooperation project in epilepsy is carried out

Methods: It has been made an intensive 3-day and 20-hour total course, in November 2019, at the Bouakée Psychiatric Hospital, to local healthcare staff by 3 Spanish neurologists
Results: There were 11 participants, 1 Psychiatrist and 2 fellow, with 34.5 years old on average.

They attend an average of 14 patients/day, 10.5 of them with neurological pathology. Pretraining test is performed, results are showed at figures. The main topics were adjusted according to the results and suggestions from participants. Misconceptions persist about epilepsy. Drug availability is limited. The EEG study is not carried out due to lack of training resources. Training will continue for 1 year online with the aim of improving knowledge about epilepsy. The main topics will be reinforced with subsequent examination to know the formative impact.



EPO1108

Lev Yakovlevich Livshits – the founder of an effective original method for the surgical treatment of trigeminal neuralgia in the USSR in the middle of the 20th century

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Background and aims: The history of Russian neurosurgery as a practical science that studies the surgical treatment of trigeminal neuralgia is closely connected with the name of the famous neurosurgeon Lev Yakovlevich Livshits (1928-2005).

Methods: An important stage in the research biography of L.Ya. Livshits was his study on the surgical treatment of drug-resistant forms of trigeminal neuralgia by the method of directed hydrothermal destruction of its sensitive root by inserting a needle into the Meccel cavity through the oval foramen. As a physical factor of destruction, boiling distilled water was used; it was introduced fractionally with the total volume of 1.5ml, and the interval between portions reached 3-4 minutes.

Results: In 1968, L.Ya. Livshits successfully defended his dissertation on the topic: “Trigeminal neuralgia and its treatment by the method of directed hydrothermal destruction of a sensitive trigeminal root”. Putting the results of this work into practice brought relief to thousands of patients in the Soviet Union. Livshits became the head of the first Pain Center in Russia, which was located in Saratov and carried out the examination and treatment of patients from all over the USSR.

Conclusion: The concept of “growing radicalism” created by Professor Livshits allowed his students elaborating algorithms for treating severe chronic pain syndromes of any localization and etiology.

Disclosure: Nothing to disclose

Conclusion: Education programmes are a necessary tool to reduce the health and cultural gap in the treatment of epilepsy

Disclosure: Nothing to disclose

EPO1109

Descriptive analysis of absenteeism in patients with a first given appointment in an ambulatory neurological care office

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Background and aims: Non-attendance in outpatient appointments represents human resources under-utilization, time lost, financial costs as well as possible health implications for absentee subjects. Our goal is to determine the main features of the non-attenders to a first given outpatient neurological appointment.

Methods: This is an observational case-control study based on patients sent to one outpatient neurology clinic of a third-level hospital. Data available electronically from patients who miss a first-given appointment between August 2018 and May 2019 (n=85) were prospectively recorded and compared to a control group of 187 consecutive first-time visitors.

Results: Non-attendance rate was 9.8% for the first appointment made in a neurological consultation. The mean age of the defaulters was 63 years (range: 15-96), of which 55.3% were older than 65 years and 57.6% were women. The most frequent reasons for reference in patients who miss appointments were cognitive impairment (32.9%) and headache (22.4%) followed by neuromuscular diseases (22.8%) and movement disorders (9.4%). 60% of the absentees were sent by their General Practitioner [GP], 21.1% came from Specialized Care [SP] and 18.8% were referred from the Emergency Department [ER]. No differences between attenders and defaulters were observed in age ($p>0.05$), gender ($p>0.05$), or reasons for reference ($p=0.097$). A significantly higher percentage of patients referred from GP (79.7%) and lower from ER (13.3%) and SP (6.4%) was found among the attenders.

Conclusion: Patients referred by their GP, with continued follow-up, present less absenteeism in a neurological consultation. Hence, educational patient-centred approaches are required in order to reduce neurological non-attendance.

Disclosure: Nothing to disclose

EPO1110

The history of aspirin use in neurology

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Background and aims: Acetylsalicylic acid (aspirin) is one of the most widespread drugs – and the history of its use in neurology (in cerebrovascular disease, in particular) is quite remarkable. We present here a timeline of aspirin discovery with a special emphasis on its debut on the neurological “scene”.

Methods: A number of various scientific literary and historical works have been analysed.

Results: The medicinal use of salix has been dated back to ancient Egypt (15-16th centuries BC). It was widely used in ancient Greece and Rome. In the XVIIIth century Rev. Edward Stone described an infusion of salix alba which he used as “cure of agues”. It was he who in 1763 described salicylic acid. In 1852, Charles Gerhardt was the first to synthesize acetylsalicylic acid. In 1897, 29 year old Felix Hoffmann from Friderich Bayer & Co developed a more stable form of ASA - he was working under the supervision of Prof. Arthur Eichengrün. For nearly half a century aspirin was used as an anti-inflammatory drug until the early 1950s when Dr. Lawrence Craven started prescribing small doses of ASA for prevention of coronary and carotid thrombosis. This launched the use of aspirin in stroke prevention with numerous clinical trials which followed.

Conclusion: The history of aspirin depicts how old, well-known drugs offer new clinical possibilities which may totally shift the current therapeutic paradigm.

Disclosure: Nothing to disclose

EPO1111

Differentiating neuronal circuits to store an auditory information from those to define a sequence of sounds

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Background and aims: Auditory memory is one of the sensory memories. This study aimed to evaluate medical students' auditory memory.

Methods: Volunteers were 35 third year medical students (aged 19 to 31 years), 20 women. They listened to 3 samples of rock and 3 of classical songs. Soon after, answered 8 questions (Q). Q1-Q2: what was the position of the song in the sequence (5th and 1st); Q3-Q4: what was the song listened in a given position (2nd and 4th); Q5-Q6: what song they had not listened; Q7-Q8: what song they had listened. Q3- Q8: they had to choose among 3 presented songs. We got written approval from all of them.

Results: Q1: 46.7% males and 50% females got the right answer. For Q2:73.3% and 60%, respectively. Q3:6.7% and 15%. Q4: 0% and 20%. Q5, Q7 and Q8: 100%. Q6:95%.

Conclusion: Only about half of the students could remember the position of the song when it was the 5th. A higher percentage of students could remember the first song listened, particularly men. When we mentioned the position and they had to choose among 3, they scored poorly. In this case, women got higher scores. Our data suggests that the process of memorizing a sequence of sounds is much less effective than the 1 to store the auditory information. For medical students it is of great importance to recall the sequence of information they get from a patient. Therefore, it is of relevance to develop training methods to improve that ability.

Disclosure: Nothing to disclose

EPO1112

Monosynaptic Reflexes (MSR) – the first systematically used parameters for psycho-physiological activation. History of methods and results

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Background and aims: The importance of testing reflexes is evident to every neurologist, little is known of systematic studies of MSR as indicator of tonic and phasic activation. Only recently the author noticed that MSR were the first parameters used in psychophysiology, even before electrodermal parameters.

Methods: A literature overview is given on history of research on monosynaptic reflexes.

Results: Lombard (1887, first volume of *AmJPsychol*) with his hammer of defined drop height and registration of reflex amplitudes in millimeters found variations under many conditions (e.g. fatigue, exciting vs. relaxing music or literature, sudden external stimuli). Bowditch & Warren (1890) with their complicated pendulum apparatus for eliciting reflexes after defined stimuli (auditory, visual, an even touch by air blasts) showed activation curves in the time range up to 2000ms, similar to those in later studies of activation with other parameters.

Paillard (1955) was the first to study simultaneously mechanically elicited T reflexes and electrically H reflexes, T reflexes being more reactive to activation. Later investigations (Bathien and coll., 1969, 1971, Brunia 1970, 1971, Sczesni & Kröner 1985) will be presented.

The technical features, representing the best technologies of their times, neurophysiological and neuropsychological aspects, and limitations of the methods are discussed.

Conclusion: H reflexes are more sensitive than T reflexes. Changes can represent phasic as well as tonic influences. MSR in some areas of research were used for decades with some profit, but they were no longer carried out, presumably because of the vast technical equipment needed.

Key words: monosynaptic reflexes, activation,, relaxation, psychophysiology

Disclosure: Nothing to disclose

EPO1113

The history of neurological service of Kyiv Institute of traumatology and orthopedics

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Background and aims: In June 2019, the Institute celebrated its 100 years since establishment.

Methods: We researched archive materials of the institution.

Results: In 1919, in country seat of Count Shteingel Kyiv Institute of the crippled child was organized. In 1924, it was transformed into All-Ukrainian state pediatric orthopedic institute with maternity department, later transferred to building on 7 Revoliutsii Str. 1919–1941 at Institute worked neuroscientist Arinshtein. He gave professional advice to children with congenital malformations of musculoskeletal system, consequences of poliomyelitis, neurological complications of bone tuberculosis, consequences of infantile cerebral paralysis. During postwar years, consultative neurological service of Institute was headed by doctor O. Rabinovych. Scientific neurological activity began in late 1950s, when methods of conservative, surgical treatment of children with poliomyelitis, spastic paralysis began to develop. Significant contribution to study of pathology was made by Frumin, Talko, Haiko, Putilina, Mezhenina. Since 1976, Ulis was neurological consultant at in-patient hospital, who in 2013 published monograph “Neuro-ortopedia”. 1985–2001, Guba worked as consultant of outpatient department, which in 1997 published “Handbook of neuro-orthopedics”. 1982–1988 at Institute was department of involuntary nervous system diseases. In 1990, laboratory of neuro-orthopedics and pain issues was established within department of rehabilitation of Institute, which since May 2006 became independent scientific unit. Today laboratory staff solve clinical, theoretical issues of pain of people with kinetics, musculoskeletal pathologies and conduct diagnostic monitoring of neurological disorders of such patients; develop new, improve existing treatments for acute, chronic pain syndromes. Activity of laboratory gained international recognition.

Conclusion: Issues of neuroorthopaedy need to be further deeply studied.

Disclosure: Nothing to disclose

Epilepsy 1

EPO1114

Combination of advanced structural and functional MRI methods in the pre-surgical evaluation of patients with drug-resistant epilepsy

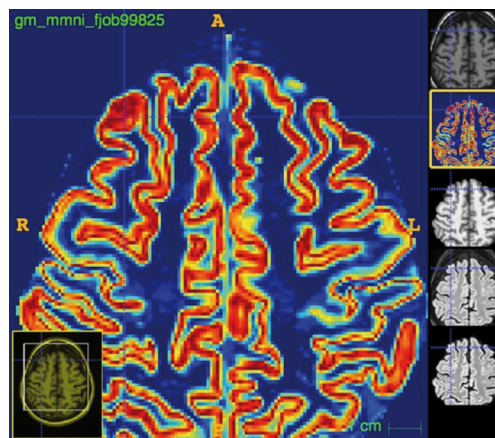
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Savvas", Athens, Greece

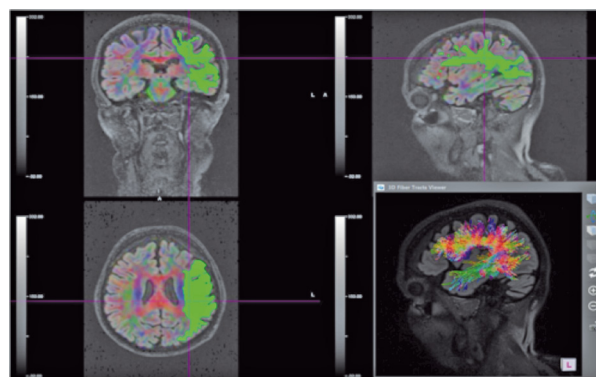
Background and aims: Epilepsy surgery leads in significant seizure reduction in patients with drug resistant focal onset epilepsy. Localization of the epileptogenic zone is required for surgical planning prior to a focal cortical resection. Odds of becoming seizure-free after surgery are 2.5 times higher in patients with MRI lesions related to epileptogenic network. Conventional imaging often fails to reveal these lesions, demanding the practice of harmonized neuroimaging of epilepsy structural sequences-(HARNES)-MRI protocol and post-processing methods such as Volumetry.

Methods: We selected eleven patients with drug-resistant epilepsy and a "non-lesional" MRI. They were further examined with advanced MRI techniques by 3D-T1 before and after administration of 15ml Gadovist, 3D-T2 weighted and 3D-FLAIR sequences. Echo-planar BOLD (Blood Oxygenation Level Dependent) for task-based and resting state fMRI (RS-fMRI), and diffusion tensor imaging (DTI) were acquired for language/memory lateralization, and if possible, to visualize epileptogenic zones.

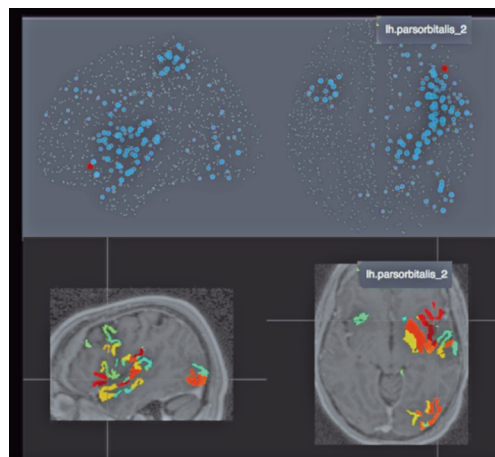
Results: All eleven patients had a "non-lesional" MRI. Applying advanced and quantitative imaging techniques, abnormal findings were revealed in six patients. After surgery, five out of six patients were free of disabling seizures (Engel class I), with one-year follow-up. Among five patients with the non-lesional MRI, only one was free of disabling seizures after surgery.



Volumetry



DTI



RestingState fMRI

Conclusion: Revealing lesions unseen with conventional imaging, the HARNES-MRI protocol and advanced and quantitative imaging techniques transforms MRI-negative into MRI-positive cases. Thereby, applying the technical advances and developments in neuroimaging more systematically in everyday clinical routine, we succeed in offering the life-changing benefits of epilepsy surgery to a greater number of patients.

Disclosure: Nothing to disclose

EPO1115

Clinical features of patients treated with very-low dose of anti-epileptic drugs in focal epilepsy

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Background and aims: The prescription of a dose of antiepileptic drugs (AED) below the minimum effective dose stipulated in the summary of product characteristics (SmPC) is a relatively common situation, mainly for patients with or at risk of cognitive and/or behavioural disorders. We aimed to determine the clinical features of the patients treated with very-low dose of lamotrigine, lacosamide and levetiracetam and to display factors associated with a diminution of the dose.

Methods: In this retrospective study (between November 2017 and October 2018), adult patients with focal epilepsy and a stable dose of lamotrigine, lacosamide or levetiracetam (more than 3 months) hospitalized in Lille university medical centre were included. They were divided into 2 groups: treated with a dose above or below the guidelines of the SmPC.

Results: 118 patients with complete data were included (age= 65±18 years old; H/F=0.75; age of onset of epilepsy= 59 years old; 79% of structural cause). 90 were treated with a dose in agreement the SCP guidelines and 28 were treated with a dose below the guidelines). A history of neurovascular or neurodegenerative disease and a history of delirium during the preceding year were associated with a AED dose below the guidelines (OR=3.43 [1.1;10.7] and OR=16.7 [3.8;74.9] respectively) but age, weight and creatinine clearance were not.

Conclusion: Physicians spontaneously adapted the dose of AED by relying on clinical factors. The efficacy of very-low dose AED needs to be investigated even if this strategy seems to be relevant for fragile patients.

Disclosure: Nothing to disclose

EPO1116

Is it easy to switch antiepileptic treatment from valproate to others?

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Background and aims: Although prospective studies have provided information on the teratogenicity, patients on valproate (VPA) are generally reluctant to change treatment. We present the results of our epilepsy department patients whose the treatment regimens were switched from VPA.

Methods: We evaluated the patient files whose VPA were switched. Age, daily dosage of VPA, seizure type, alternative regimen (lamotrigine:LMT or levetiracetam: LEV) choice, maintenance dosage, seizure frequency before and after switching, side effects and pregnancies during treatment were evaluated.

Results: Total of 20 patients in our outpatient clinic were on VPA in childbearing age. Average age of 29.45 years (±5.80). VPA dosage 787.50 mg/daily (±259.99). 11 of 20 were having myoclonic-tonic-clonic and 9 were having tonic-clonic sz. Maintenance dosage of LEV was 1308 mg/daily (±809mg) and LMT was 239mg/daily (±124mg). Sz freedom in 2 of LEV, 50%- 75% sz reduction in 3 LEV patients were achieved. Sz free on VPA were still sz free in 4 LEV and in 6 LMT patients. Increase in sz frequency was observed in 2 of LEV and in 2 LMT patients. Skin rash was the only side effect in one LMT patient. Increased aggression were seen in 3 LEV patients. Three patients had healthy pregnancy and deliveries.

Conclusion: Either LEV or LMT are both safe alternatives. Although treatment switching procedure might have idiosyncratic problems as stated here, each patient should be handled individually and VPA should be switched as recommended.

Disclosure: Nothing to disclose

EPO1117

Relationship between plasma concentrations and clinical effects of perampanel. An observational study

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Background and aims: To investigate the correlation between plasma concentrations of perampanel (PMP) with both tolerability and seizure control in adults and children with drug-resistant epilepsy.

Methods: Plasma samples were collected in the morning at 12-h distance from once-a-day bedtime PMP dose. Patients had to be on stable therapy for at least 3 weeks. Tolerability was assessed on the day of drug monitoring by clinical examination and patients' interview. The response was based on average seizure frequency estimation and defined as $\geq 50\%$ decrease from PMP pretreatment. The main outcomes were the comparisons of PMP plasma concentration-to-weight-adjusted dose ratio (C/D) [$(\mu\text{g/mL})/(\text{mg/kg})$] between patients with and without adverse effects (AEs) and between responders and non-responders.

Results: 79 patients (52 males) aged (mean \pm SD) 36 ± 14 years (range 12-70 years) were enrolled. The mean PMP dose was $6.7\pm 2.2\text{mg}$ (range, 2-12mg), drug treatment averaged 46 ± 34 weeks (6-161 weeks). The mean plasma concentration was $376\pm 295\text{ng/mL}$ (39-1641ng/mL). 39 patients (40%) reported AEs, mainly agitation and irritability. No significant difference was found in median PMP C/Ds between patients with (3.02) and without (2.79) AEs. 45 patients (46%) resulted in responders, at a median PMP C/D of 3.16, similar to the value of 2.80 found in non-responders. These 2 groups also overlapped for all the above mentioned clinical and therapeutic variables.

Conclusion: PMP plasma levels largely varied in relation to both tolerability and efficacy. We did not identify a reliable reference range for PMP plasma concentrations in our cohort of patients.

Disclosure: none

EPO1118

Evaluation of cognitive and language side effects of topiramate in patients with epilepsy, and effectiveness of counseling and speech therapy interventions

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Background and aims: Topiramate (TPM) is a highly effective antiepileptic drug. Up to 10% of patients experience TPM-related cognitive side effects, especially on language (impaired word finding and verbal fluency), with a drug discontinuation rate up to 70%. We investigated early cognitive and language deficits in patients on TPM for epilepsy and the possible favorable effect of counseling and speech therapy interventions.

Methods: Patients enrollment: age ≥ 18 years, on TPM therapy for epilepsy with good efficacy and tolerability, MMSE >23 . Baseline evaluation: clinical-functional (TIB, mRS, VAS-Depression) and cognitive-linguistic (Verbal Fluency, Token Test, naming and calculation tests, Digit Span, Corsi Test, Symbol Digit Modalities Test, FAB). Administration of 4 biweekly outpatient sessions of lexical enhancement exercises by a speech therapist, and inter-session home exercises. After the 2-month treatment the cognitive-linguistic assessment was repeated, patients were provided with maintenance home exercises and re-evaluated 4 months later.

Results: Out of 380 outpatients screened, 29 were on TPM and 10 met the study inclusion criteria. All patients showed good participation and increasing engagement in the study, excepting for 1 who discontinued it for personal reasons. At baseline all participants showed normal verbal and total IQ scores. 5 patients (56%) showed frankly pathological verbal fluency, either phonemic or semantic, and improved up to normal values at the end of treatment ($p<0.05$). This improvement persisted after the 4-month maintenance period.

Conclusion: Our results suggest the effectiveness and feasibility of a counseling and speech therapy treatment in patients with TPM-related language involvement, warranting future studies on wider sample and follow-up.

Disclosure: Nothing to disclose

EPO1119

The effects of GPR39 agonist on BDNF signaling in the pentylenetetrazole model of epilepsy

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Background and aims: The G-protein coupled receptor 39 (GPR39) is activated by zinc ions and has been suggested as a novel drug target for epilepsy. However, the results which have been obtained by our group generally argue against the hypothesis that activation of GPR39 alleviates seizure. We found, e.g., that TC-G 1008, a potent and selective GPR39 agonist, facilitated the development of pentylenetetrazole (PTZ) kindling. Here, we aimed at assessing the mechanisms that may underlie the effects observed after administration of TC-G 1008 in the PTZ model of epilepsy.

Methods: Male Albino Swiss mice received TC-G 1008 (10mg/kg i.p.) 30min (based on previous pharmacokinetic analysis), zinc chloride (ZnCl₂) (8mg Zn/kg) or valproic acid (VPA) (150mg/kg) before each dose of PTZ. Following completion of the kindling paradigm, the expression levels of proteins: phosphorylated CREB (p-CREB), brain-derived neurotrophic factor (BDNF) and phosphorylated high-affinity tropomyosine-related kinase B receptor (p-TrkB) were measured using western blot in the hippocampi (Hp).

Results: PTZ kindling significantly increased p-CREB and p-TrkB in the Hp of mice. There was also a tendency towards increased BDNF level. Administration of TC-G 1008, ZnCl₂ and VPA significantly decreased the level of p-CREB in the Hp of kindled mice. Moreover, there was a tendency towards decreased p-TrkB level in the Hp of kindled mice after treatment with these compounds.

Conclusion: Although inhibition of BDNF signaling has been suggested as a strategy for the treatment of epilepsy, our data shows that facilitation of epileptogenesis may also be associated with inhibition of BDNF signaling.

Disclosure: The study was supported by a grant from the National Science Centre, Poland (2016/20/S/NZ7/00424)

EPO1120

Prediction of vagal nerve stimulation efficacy – validation of statistic model on external data set, pilot study

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Background and aims: Vagal nerve stimulation (VNS) offers a possibility for a substantial seizure reduction in approximately 50% of implanted patients. However, there is a large group of patients who do not profit significantly from this therapy. At the moment, there is no widely-accepted method for prediction of VNS efficacy based on pre-implantation data. Our group has developed and published a statistic classifier based on pre-implantation routine EEG, which was able to predict VNS response in a given patient with high accuracy. The crucial limitation of our previous work was its monocentric nature and the use of only one type of EEG recording system.

Methods: We retrospectively identified a pre-implantation EEG in a group of patients with drug-resistant epilepsy treated with VNS (all EEG recorded by different EEG system than in our previous work). The EEG was mathematically post-processed the same way as in our previous work. Subsequently, the patients were classified by their statistic outcome (statistic responders vs. statistic non-responders). The statistic outcome was compared to the patients' real-life outcomes (real-life responders vs. real-life non-responders).

Results: We identified 10 patients with drug-resistant epilepsy treated with VNS: 9 real-life responders and one real-life non-responder. We were able to predict their response by our classifier with 0.750 accuracy, 0.714 sensitivity, and 1 specificity.

Conclusion: We managed to prove the possibility of applying our statistic classifier in different EEG systems. This universal application is a crucial step for design a prospective multicenter study which we plan to initiate in the future.

Disclosure: The project is supported by the Ministry of Health of the Czech Republic, grant NV19-04-00343.

EPO1121

Results of TMS using in patients with pharmacoresistant epilepsy which using levetiracetam

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Background and aims: The TMS is promising for additional therapy of patients with pharmacoresistant epilepsy, but there is no unambiguous data on its use in patients taking using different AED.

Methods: We examined 35 patients with pharmacoresistant epilepsy with focal seizures with or without evolution to tonic-clonic seizures. All patients took AED in adequate doses. The AED regimen was stable for at least 3 months before being included in the study. All patients used Levetiracetam as AED.

The frequency of seizures was evaluated. For evaluation severity of seizures NHS3 scale was used.

Patients were observed for 3 months before the course of TMS and 6 months after the course of TMS.

TMS was done in the sitting position to the occipital zone of the head fixedly. Exposition was 10 seconds, pulse induction of 2.0T and a frequency of 5Hz by a biphasic pulse generation. The interval between the series was 20 seconds, the number of series-20, total duration-10 minutes. Stimulation was carried out daily for 20 days with a break of 5 days after the first 10.

Results: There was a positive effect - decreasing number of seizures compared to the baseline level, which was short-term (decreasing frequency of more than 50% - 82% and 86%, respectively) and after 6 months there was no significant difference from the baseline level. Similar data were obtained by dynamic evaluation using NHS3 scale.

Conclusion: Thus, effect of TMS is extremely unstable. After 6 months, the frequency of seizures and their severity return to the original level.

Disclosure: Nothing to disclose

EPO1122

Valproate-induced nocturnal enuresis in children

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Objective: The objective of this research study was to evaluate the occurrence and the characters of nocturnal enuresis in children secondary to valproic acid antiepileptic drug and to discuss the suspected reasons.

Methods: A retrospective study carried out in pediatric patients (aged 5 to 15 years) diagnosed as idiopathic epilepsy and kept up on valproic acid antiepileptic drug. Side effects recorded by parents were reported at each subsequent visit especially enuresis. The occurrence of enuresis was assessed and its association with different factors.

Results: 260 children (153 males and 107 females) aged 5 to 15 years were investigated for nocturnal enuresis which, was reported in 28 (10.7%) of the cases after a mean exposure time to valproate of 18.78±8.4 days. Enuresis halted in most of cases either spontaneously or after cessation of valproic acid. Multivariate logistic regression, demonstrated that the independent factors associated with nocturnal enuresis, were younger age (OR 2.31, p=0.004), followed by weight and Serum level of valproic acid (OR 1.44, p=0.05 and OR 1.39, p=0.05 respectively). While, the therapeutic dose, or the treatment duration with valproic acid, were not significantly associated with the incidence of enuresis (OR 0.98, p=0.09 and OR 0.86, p=0.12 respectively)

Conclusion: Nocturnal enuresis is a common side effect that accompanied the valproic acid use in children, which is mostly reversible. The underlying mechanism is unclear may be related to increase sleep depth with valproic acid which require further studies with polysomnography.

Disclosure: Nothing to disclose

EPO1123

The influence of neonate convulsion on the neurodevelopment of the child

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Background and aims: Neonatal seizures are a common neurological dysfunction of the neonatal period, apparently from birth to the end of the neonatal period. The incidence of neonatal seizures is in range of $1^{5/3}$ per $1^{/000}$ live births, in the neonatal period - with an index of 1.2. the evolution of neonatal seizures is often dependent on the cause that led to seizures.

Methods: The results on the neurodevelopment of 67 newborn children who had neonatal seizures of various etiologies werw evaluated. Assessment period - 5 years. Examinations were performed: neurophysiological, imagistic.

Results: Among the 67 children who had neonatal seizures during the newborn period, the following neurodevelopmental problems were registered: behavioral disorders (42 children, 63%), cognitive disorders (35 children, 53.7%), speech and language disorders (39 children, 58%), attention disorders (49 children, 73%), hyperactivity disorder (33 children, 49%), socializing disorders (31 children, 46%), epilepsy (20 children, 30%), cerebral palsy (22 children, 33%), intellectual disability (19 children, 28%).

Conclusion: Triggering causes of neonatal seizures determine long-term prognosis and outcomes, as they are associated with various brain injuries, can have a negative impact on the child's neurodevelopmental outcomes.

Disclosure: Nothing to disclose

EPO1124

Evaluation of quality of life and stigma among epileptic patients in French-speaking Belgium

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Background and aims: Epilepsy has been associated with poor life quality especially with poor seizure control. 30% of patients remain refractory to currently available treatment and more than 30% of treated patients experience adverse events compromising life quality. Lack of access to knowledge about the disease might have a negative influence on disease outcome and result in a poorer life quality and more stigma. This survey evaluate life quality of epileptic patients in French-speaking Belgium.

Methods: An online survey was published and addressed to epilepsy patients including demographic data, open-ended questions (based on Gilliam's paper 1997), a life quality scale (QOLIE 31) and the stigma scale of epilepsy (SSE). Linear regression was applied to different scores and sub-scores and compared on the demographics.

Results: 279 patients responded to the online questionnaire. The mean age at the time of the first seizure was 20 ± 13.33 years and the time between first seizure and diagnosis was 4 ± 9.91 years. Demographically, there was a significantly higher representation of single and unemployed patients. The life quality is lower than in the control population, mainly in men, patients with no qualifications, or with a high seizure frequency. Seizure frequency also influences stigma. There is a correlation between reduced life quality and stigma.

Conclusion: Life quality is reduced in patients with epilepsy, decreasing mainly with increasing seizure frequency, or in low level of education. Stigma also increases with seizure frequency. Public educational programs on epilepsy for epileptic patients and epileptic-free population should be developed to prevent stigma.

Disclosure: Nothing to disclose

EPO1125

Impact of ammonia measurement on therapy decisions in an adult status epilepticus cohort treated with valproic acid

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Background and aims: Status epilepticus (SE) is a neurological emergency in which immediate intervention is required to prevent permanent brain damage and death. Intravenous (IV) valproic acid (VPA) is considered a safe drug and is frequently used for the treatment of SE. However, IV VPA frequently increases blood ammonia levels, the clinical relevance of which is uncertain. In this retrospective observational study, we highlight the impact of increased ammonia levels on further treatment management

Methods: We retrospectively included adult patients (≥ 18 years) treated at Oslo University Hospital between January 2006 and October 2019. All patients were admitted to the hospital with the clinical presentation of SE, were treated with IV VPA, and had at least one ammonia level measurement. Laboratory results and clinical information from medical records were registered. Correlations were tested using the Pearson's correlation coefficient. Patients were also graded after the West Haven Criteria to assess signs of encephalopathy.

Results: 30 out of 31 patients had increased ammonia level during IV VPA treatment. In 16 out of 30 patients, VPA was discontinued and in 6 patients the dose was reduced. Other blood tests related to liver function at time of the peak ammonia level were within normal range.

Conclusion: Increased blood ammonia level is common in SE patients treated with IV VPA. In our patient material increased blood ammonia level had a substantial impact on further treatment management. To date, no guideline exists on how to handle VPA induced hyperammonemia. As treatment outcome could potentially be affected, further studies are warranted.

Disclosure: Nothing to disclose

EPO1126

Side effects, tolerance and abandonment of perampanel in the neurology service of the General University Hospital of Ciudad Real

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Background and aims: We describe the baseline characteristics of our patients treated with Perampanel.

Methods: We selected the total patients of our service in whom Perampanel was indicated during the years 2016, 2017 and 2018, a total of 99 patients (43% women and 57% men).

Results: In our patients, the main indication was epilepsy treatment, 71%. In 95% of cases it was indicated as an adjuvant drug, and in 5% as a single treatment. The second indication, 29% of patients, was control of tremor and other non-epileptic involuntary hyperkinetic disorders. Regarding adverse effects: 17% abandoned treatment due to side effects. Of these, 70% were older than 75 years of age ($>75y$) and 65% were male. Among the most common side effects were: 60% dizziness and instability of gait. 68% $>75y$ and 67% were male. Greater with associated pluri-pathology. Psycho-behavioral alterations were also evident in 25%, higher in patients with previous intellectual disability (21%), cognitive impairment (11%) and $>75y$ (43%). Changes in the sleep cycle, were seen in 15%. Also more frequent in $>75y$ (79%) and with cognitive impairment (13%) or prior intellectual disability (24%) The incidence of side effects was lower both with lower doses, regardless of age group or cognitive situation.

Conclusion: According to our results, it would be necessary to conduct studies that support both a dose or a dose escalation schedule according to specific groups of patients. Probably the addition of a marker or titration of the serum levels of the drug would help in the selection of the dose to be used.

Disclosure: Nothing to disclose

EPO1127

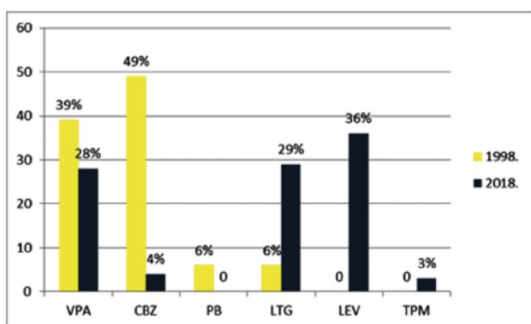
Changes in prescription pattern of first antiepileptic drug for childhood and adolescent epilepsy over the last two decades

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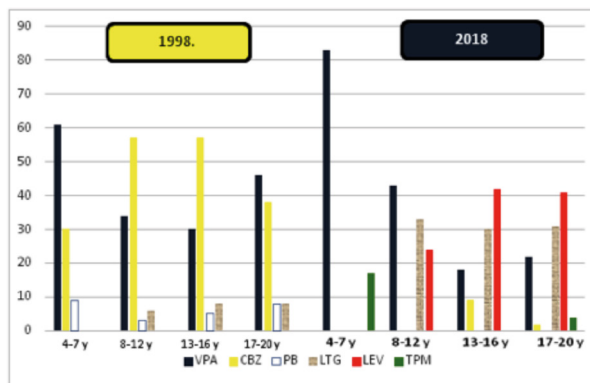
Background and aims: Newer generation of antiepileptic drugs (AED) and conventional AED are equally heterogeneous groups in terms of their mechanism of action and pharmacological characteristics. However, newer AED are prioritized primarily due to their improved safety profile even in patients with well-controlled seizures.

Methods: This was a retrospective and prospective cross-sectional study of medical records of children and adolescents with epilepsy, who were admitted as inpatients or outpatients at a tertiary referral center in Novi Sad, Serbia during 1997-1998 and 2017-2018.

Results: In 1997/98, the most commonly initially prescribed AED was carbamazepine (49%), followed by valproate (39%), phenobarbitone and lamotrigine (6%). In 2017/18, the most commonly initially prescribed AED was levetiracetam (36%), followed by lamotrigine (29%), valproate (28%), carbamazepine (4%), topiramate (3%), while phenobarbitone was not prescribed as the initial AED. Comparing the results between 1997/98 and 2017/18 regarding the seizure type and type of epilepsy with respect to newer and older generation of AED, we noticed that pattern of prescribing initial AED has been significantly reversed. The most important difference was reflected in the treatment of generalized seizures and in the population of adolescents. The prevalence of valproate usage in the population of girls at puberty has decreased significantly during 2017/18, compared to the 1997/98.



Percentile representation of initially prescribed AED during 1997/98 and 2017/18



Age related percentile representation of initially prescribed AED during 1997/98 and 2017/18

N (%)	VPA		CBZ		PB		LTG		LEV		TPM		statistic P
	1998	2018	1998	2018	1998	2018	1998	2018	1998	2018	1998	2018	
4-7 y	14 (32)	5 (17)	7 (13)	0 (0)	2 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33)	0.46
8-12 y	12 (28)	9 (30)	20 (38)	0 (0)	1 (1)	0 (0)	2 (3)	7 (23)	0 (0)	5 (15)	0 (0)	0 (0)	0.00
13-16 y	11 (26)	6 (20)	21 (40)	3 (7)	2 (3)	0 (0)	3 (5)	10 (32)	0 (0)	14 (37)	0 (0)	0 (0)	0.00
17-19 y	6 (14)	10 (33)	5 (9)	1 (2)	1 (1)	0 (0)	1 (1)	14 (45)	0 (0)	19 (50)	0 (0)	2 (6)	0.00
boys	17 (40)	22 (73)	32 (60)	3 (7)	1 (1)	0 (0)	3 (5)	6 (19)	0 (0)	4 (11)	0 (0)	1 (3)	0.07
girls	26 (60)	8 (27)	21 (39)	1 (2)	5 (8)	0 (0)	3 (5)	25 (81)	0 (0)	34 (89)	0 (0)	2 (6)	0.00
focal seizures	1 (2)	7 (23)	25 (47)	3 (7)	0 (0)	0 (0)	3 (5)	4 (13)	0 (0)	4 (10)	0 (0)	0 (0)	0.08
general. seizures	41 (96)	16 (54)	27 (51)	0 (0)	6 (10)	0 (0)	3 (5)	8 (26)	0 (0)	23 (61)	0 (0)	1 (3)	0.00
both seizures	1 (2)	7 (23)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	19 (61)	0 (0)	11 (29)	0 (0)	2 (6)	0.81
idiop. etiol.	19 (44)	20 (67)	2 (4)	0 (0)	1 (1)	0 (0)	0 (0)	6 (19)	0 (0)	22 (58)	0 (0)	1 (3)	0.00
crypt. etiol.	19 (44)	6 (20)	32 (60)	2 (5)	4 (6)	0 (0)	5 (8)	16 (52)	0 (0)	8 (21)	0 (0)	1 (3)	0.00
sympt. etiol.	5 (12)	4 (13)	19 (36)	2 (5)	1 (1)	0 (0)	1 (1)	9 (29)	0 (0)	8 (21)	0 (0)	1 (3)	0.00
total (%)	43 (100)	30 (100)	53 (100)	4 (100)	6 (100)	0 (100)	6 (100)	31 (100)	0 (100)	38 (100)	0 (100)	3 (100)	108/106 (100)

Comprehensive comparison between 1997/98 and 2017/18 result data in regard to age, gender, seizure type and etiology of epilepsy with respect to newer and older generation of AED

Conclusion: The trend of prescribing initial AED has changed significantly over the last 20 years. Newer generation AED are significantly represented primarily in the female adolescent population. The results are in line with modern guides and recommendations.

Disclosure: Nothing to disclose

EPO1128

Analysis of sleep-related movement disorders, parasomnias and physiological sleep variants in adult patients with generalized epilepsy: a polysomnographic study

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Background and aims: The interplay between epilepsy and sleep is widely recognized. In particular, in Genetic Generalized Epilepsies (GGE), a close link of seizures to the sleep-wake cycle has been demonstrated. The objective of our study is to evaluate the frequency of sleep disorders and physiological sleep variants in patients with GGE as compared with controls, by means of polysomnography.

Methods: We performed a retrospective observational study in the Neurological Clinic of the University of Catania. We enrolled patients with diagnosis of GGE and controls without epilepsy who underwent a polysomnography in the 2007-2019 period. Exclusion criteria were: obstructive sleep apnoea syndrome and epileptic encephalopathy. The following sleep disorders were considered: disorders of arousal from NREM, REM sleep behaviour disorder, periodic sleep movements in sleep, bruxism, propriospinal myoclonus at sleep onset, alternating leg muscle activation, excessive fragmentary myoclonus, and neck myoclonus.

Results: 30 patients (mean age 28.7 ± 12.3 years, 11 [36.7%] males) and 56 controls (mean age 32.7 ± 11.5 years, 18 [32.1%] males) were enrolled. A significant higher percentage of sleep disorders was found in patients (83.3% vs 50%, $p=0.002$) compared to controls. In particular, we found a higher frequency of disorders of arousal from NREM (60% vs 30.3%; $p=0.01$), bruxism (26.7% vs 5.3%; $p=0.005$) and neck myoclonus (26.7% vs 5.3%; $p=0.01$) in patients.

Conclusion: Our study demonstrated a high frequency of sleep disorders in patients with GGE. This should be taken into account in order to ensure an optimal seizures control in these patients.

Disclosure: Nothing to disclose

Epilepsy 2

EPO1129

Seizure freedom in patients treated with lacosamide and levetiracetam

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Background and aims: Lacosamide is a sodium channel blocker (SCB) approved as adjunctive therapy for partial onset seizures and more recently as monotherapy. We wanted to evaluate the effectiveness of lacosamide and levetiracetam compared to the other combinations.

Methods: We have evaluated the patients treated with lacosamide in the last 10 years in a secondary hospital obtaining a total of 99 patients of which, 14 were treated with levetiracetam and 48 were treated with other double therapies of antiepileptics. Other treatments with less than 5 patients and sodium channel blocker drugs were not evaluated. The minimum follow-up was 6 months.

Results: Comparing the double therapy of lacosamide and levetiracetam with the other combinations it shows a clear tendency to seizures free patients [64.28% Vs 33.33 (OR=3.6; p=0.077)]. On the other hand, the percentage of seizures reduction of lacosamide and levetiracetam is 71.66% (SD 44.68) Vs 62.56% (SD 38.51) without levetiracetam. In general, no combination has shown to be more effective than others regarding the percentage of seizures reduction (f unilateral=0.16 ; p=0.85).

Conclusion: The addition of lacosamide and levetiracetam in our series achieve a tendency of greater proportion of seizure free patients in comparison to other treatments, which is important to consider in our daily medical practice. It is necessary to have studies with greater sample to confirm the results.

Disclosure: Nothing to disclose

EPO1130

Long-term efficacy and safety of adjunctive cenobamate in patients with uncontrolled focal seizures: experience in a single center

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Background and aims: To assess the long-term efficacy and safety of cenobamate in adult patients with focal onset seizures participating in an open-label, safety and pharmacokinetic study of cenobamate as adjunctive therapy (study C021).

Methods: Review of adult patients with focal epilepsy treated with at least a single dose of cenobamate as adjunctive therapy. Outcomes included analysis of responder and seizure-free rates at 6 and 12 months (compared with the mean monthly seizure frequency in a 3-month baseline period), frequency and severity of adverse events and retention rates at 6 and 12 months and for the entire evaluation period.

Results: 14 patients older than 18 years with drug-resistant focal epilepsy [mean epilepsy duration 25.5 years (1-20 years), mean number of concomitant AEDs 2.6 and previous AEDs 9] were included. Responder rates at 6 and 12 months were 57% (8/14 patients) and 61.5% (8/13 patients). 6-month and 12-month retention rates were 85.7% and 84.6%. 9 patients continued on cenobamate for a mean follow-up period of 32 months (28-34 months), the majority (78%) with sustained seizure frequency reductions of 50% or more. 4 patients (30%) were seizure-free for the last 12-months (mean dose=266mg/day, range=150-400mg/day). The most common adverse effect was somnolence (13/14 patients) which was usually mild and led to drug discontinuation in 2 patients.

Conclusion: Our results show high and sustained efficacy of cenobamate as adjunctive therapy for the treatment of drug-resistant focal seizures. Adverse effects were common but usually well-tolerated rendering high long-term retention rates.

Disclosure: JM Serratosa has been invited speaker or participated in advisory boards for Eisai, UCB, Esteve, Bial, Arvelle Therapeutics, UNEEG medical

EPO1131

Cefepime-Induced Neurotoxicity (CIN): Report of three cases and systematic review of the literature

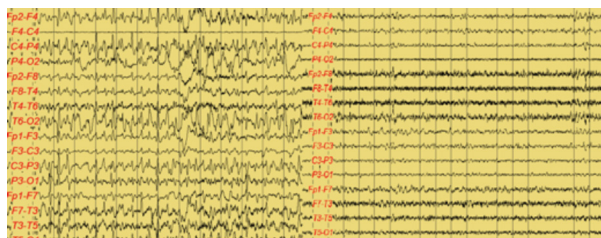
Z. Grana, P. Stamatelos, D. Georgouli, N. Markoglou, A. Sarantis, P. Gklinos, H. Leloudas, E. Papathanasiou, G. Aposporos, M. Terzoudi, E. Makri, A. Agathonikou
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Background and aims: Cefepime is a 4th generation cephalosporin antibiotic. Its use is associated with neurotoxicity (CIN), including encephalopathy, myoclonus and non-convulsive status epilepticus (NCSE).

Methods: We present 3 cases of NCSE induced by cefepime in our hospital. We also performed a systematic review of the literature, searching for case reports or series of patients with CIN. The search was applied to MEDLINE and we initially identified 82 articles. After screening titles, abstracts and references of the selected articles, 55 articles were included.

Results: Our patients were 2 females (82 and 86 years old) and 1 male (60 years old). All of them had acute impairment of level of consciousness during Cefepime treatment, with EEG findings compatible with NCSE. No patient had a history of epilepsy and 1 patient had impaired renal function. After cessation of Cefepime there was a rapid clinical and electrophysiological improvement in 1 patient (Image), while the other 2 patients were also treated with antiepileptic drugs (AED's), with a favorable outcome.

After literature review we found 18 retrospective Case-Series, 35 Case-Reports and 2 review articles. The most common presentations are impaired level of consciousness, NCSE and epileptic seizures (including myoclonus). The predisposing factors are age and impaired renal function. Cessation of Cefepime combined in selected cases with AED'S is the treatment of choice.



Generalized spike-waves 2,5 Hz on the 3rd day of Cefepime treatment (left). Rapid improvement after cessation of Cefepime, with only few bursts of theta waves (right).

Conclusion: Physicians must be alert for CIN in hospitalized patients taking Cefepime, especially among the elderly and those with renal failure. Early diagnosis is essential for the favorable prognosis of these patients.

Disclosure: Nothing to disclose

EPO1132

MRI changes in status epilepticus patients with unknown etiology

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Background and aims: Our purpose was to investigate MRI (Magnetic resonance imaging) signal changes in patients with status epilepticus (SE) and to evaluate clinical semiology, seizure type, corresponding electroencephalography (EEG) findings and prognosis.

Methods: A retrospective review of our records from 2013 to 2019 identified 210 patients with SE. The patients had any intracranial pathology were excluded. We analyzed the demographics, medical history, provocative factors, EEG records, localization of MRI signal changes attributable to SE of all patients admitted to our hospital.

Results: 44 patients who met the inclusion criteria were found to have significant abnormalities. Series of 44 patients (15 men, 29 women, mean age 56.5 years) with non-convulsive SE (13/29.5%) and convulsive SE (31/70.5%). On diffusion weighted imaging (DWI), the neocortex was affected in 20/45.5% cases, often in combination with other brain areas (18/40.9%), in particular the hippocampus was affected in 11/25% patients. Bilateral DWI and susceptibility weighted imaging (SWI) changes were found in respectively 22/50% and 6/14.6% patients. No correlation with a provocative factor was observed. EEG abnormalities correlated with lateralization of MRI abnormalities in 11/25% patients. MRI and EEG with corresponding clinical semiology were found in respectively 30/68.2% and 15/34.1% patients. Brain atrophy, the presence of epilepsy, age, seizure type showed no difference in prognosis. 3rd step therapy was correlated with poor prognosis ($p < 0.001$).

Conclusion: Combined MRI and EEG analysis provides clues to seizure localization and propagation. These findings demonstrates MRI can be useful as EEG to evaluate SE patients have unknown etiology.

Disclosure: Nothing to disclose

EPO1133

De Morsier syndrome as etiology of drug-resistant epilepsy: case review

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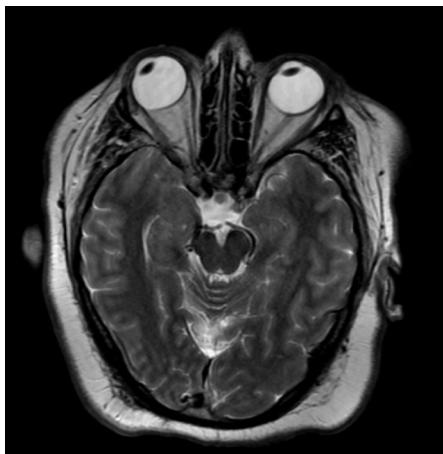
Background and aims: Septo-optic dysplasia (SOD) or De Morsier syndrome is a rare disorder (1/10000) characterised by classic triad of absence of septum pellucidum, optic nerve hypoplasia and pituitary dysfunction, which is only complete in 30%. It's called SOD-plus when associates disorders of cortical organization.

Methods: We report 3 patients with SOD assisted in our epilepsy clinic.

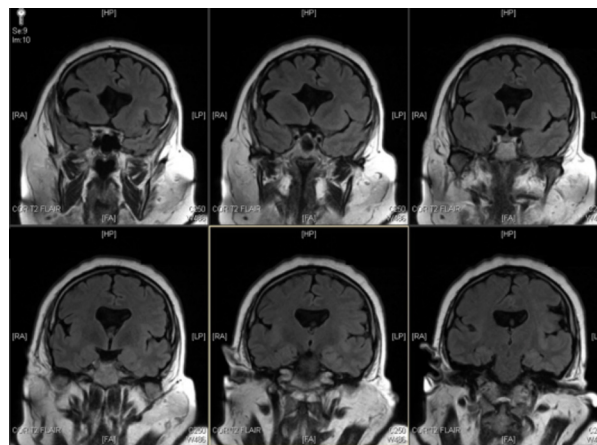
Results: Patient 1: 40-year-old woman, diabetes mellitus since age 6 and development generalized seizures since 8. Diagnosed at childhood of SOD-plus with absence of septum pellucidum and hypoplasia of optic chiasm and nerves, frontal left lobe schizencephaly and left frontoparietotemporal cortical dysplasia and polymicrogyria. After 10 years seizure-free with phenobarbital and carbamazepine, developed atonic seizures that showed response to levetiracetam and implantation of VNS.

Patient 2: 66-year-old man, moderate psychomotor retardation since childhood. Started at age 50 with focal aware seizures with non-motor onset, not controlled with lamotrigine, zonisamide and carbamazepine. MRI showed partial absence of corpus callosum and septum pellucidum and hypoplasia of optic chiasm and nerves.

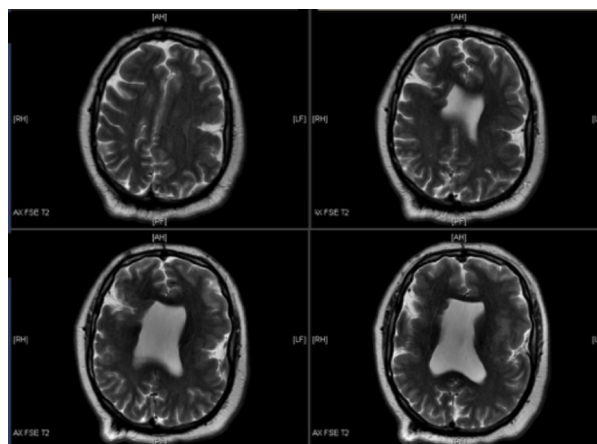
Patient 3: 28-year-old man with normal psychomotor development. At age 11 started with daily focal impaired awareness seizures, not controlled with lacosamide and levetiracetam. MRI showed SOD-plus with absence of septum pellucidum and hypoplasia of left optic nerve, as well as parietal right lobe schizencephaly and left external capsule polymicrogyria.



MRI, sagittal T2. Bilateral optic nerves hypoplasia



MRI, coronal FLAIR. Absence of septum pellucidum



MRI, axial FSE T2. Frontal right lobe schizencephaly and left frontoparietotemporal cortical dysplasia

Conclusion: De Morsier syndrome is a rare disorder that frequently associates other cerebral malformations. Clinical manifestations are variable, with drug-resistant epilepsy being an important source of morbidity. Seizures tended to be multifocal and they are not usually good surgical candidates.

Disclosure: Nothing to disclose

EPO1134

The quality of life of the patients with idiopathic epilepsy

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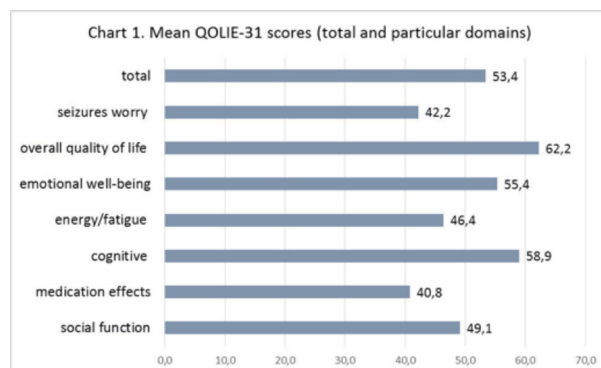
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Background and aims: The aim of the study was to assess the quality of life (QOL) in the patients with idiopathic epilepsy with regard to demographic, clinical and psychological factors.

Methods: The study was conducted in a group of 50 patients with idiopathic epilepsy (44 women and 6 men, average age 35,6 years). Quality of Life in Epilepsy Inventory (QOLIE-31) was used for the assessment of the quality of life and Beck Depression Inventory (BDI-II) - of depression. Their results were referred to demographic and clinical data based on medical records.

Results: Mean total QOLIE-31 score in the patients was 53.4 ± 19.1 , with the highest score in overall QOL (62.2 ± 18.3) and the lowest – in medication effects (40.8 ± 31.2) domain (Chart 1). According to BDI, 21 patients were depressed (9 – mildly, 6 – moderately and 6 – severely). Frequency of seizures, duration of the disease, focal epilepsy, concomitant psychogenic non-epileptic seizures, as well as coexisting diseases and low level of education negatively influenced the total QOLIE-31 score (Table 1). No such relationships were found for polytherapy or abnormal interictal electroencephalographic findings. QOLIE-31 scores in most domains were lower in the subgroup of patients with subjective cognitive complaints. QOLIE-31 scores correlated significantly with BDI results (Table 2).



Factor	p-value
total	
low education	p=0,0188
longer epilepsy length	p=0,0358
focal epilepsy	p=0,0464
higher seizure frequency	p=0,0025
concomitant psychogenic seizures	p=0,0307
concomitant somatic diseases	p=0,0396
complains of cognitive dysfunction	p=0,00004
seizures worry	
higher seizure frequency	p=0,0296
complains of cognitive dysfunction	p=0,00278
overall quality of life	
higher seizure frequency	p=0,0090
complains of cognitive dysfunction	p=0,0391
emotional well-being	
complains of cognitive dysfunction	p=0,0412
cognitive	
higher seizure frequency	p=0,0363
concomitant psychogenic seizures	p=0,0177
concomitant somatic diseases	p=0,0224
complains of cognitive dysfunction	p=0,00000
medication effects	
complains of cognitive dysfunction	p=0,0176
social function	
low education	p=0,0109
unemployment	p=0,0427
focal epilepsy	p=0,0269
higher seizure frequency	p=0,0001
concomitant psychogenic seizures	p=0,00067
concomitant somatic diseases	p=0,0113
concomitant mental disorders	p=0,0459
complains of cognitive dysfunction	p=0,0129

QOLIE-31	BDI-II
total	p=0,00000
seizures worry	p=0,00003
overall quality of life	p=0,00000
emotional well-being	p=0,00000
energy/fatigue	p=0,00000
cognitive	p=0,00000
medication effects	p=0,00359
social function	p=0,00533

Conclusion: The patients with idiopathic epilepsy declare low quality of life, especially associated with fear of seizures and side effects of medications. Epilepsy-related factors, as well as concomitant depression, cognitive dysfunction and other comorbidities significantly affect the quality of life.

Disclosure: Nothing to disclose

EPO1135

Adjusting to a life with epilepsy: does seizure control equate to a good quality of life?

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Background and aims: Depression is well recognized among patients with epilepsy (PWE); Although it is associated with increased seizure frequency and exacerbated by polypharmacy, many PWE with infrequent seizures report fears regarding the ongoing risk of seizures and this impacts on quality of life. This adjustment response to living with a chronic condition has been identified in other fields such as cardiology, but is not well recognized in PWE. We characterized the extent and nature of adjustment symptoms in PWE in a UK tertiary center, the QEBH Birmingham.

Methods: The well validated NDDI-E and QOLIE-10-P were given to patients to self-report prior to their consultation. Those lacking capacity to complete the questionnaires independently were excluded from data collection.

Results: 43 completed questionnaires were analysed. 23 patients were depressed (NIDDIE >15) of whom 14 (60.1%) had good seizure control of ≤ 1 seizure/month. 29 had reduced quality of life (QOLIE 10P Q11 ≤ 3) despite 11 (37.9%) having good seizure control. Despite having good seizure control 13 patients (30.2%) reported fear of having a seizure in the subsequent month.

Conclusion: PWE struggle with low mood and adjusting to living with a chronic condition, often in spite of attaining good seizure control. These patients would potentially benefit from early psychological support to reduce their fears around the risk of future seizures and help to maintain their sense of role in the wider community.

Disclosure: Nothing to disclose

EPO1136

The impact of irregular dosage regimens on levetiracetam plasma concentration: pharmacokinetic modeling

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Background and aims: Levetiracetam is a frequently used antiepileptic drug with high efficacy on seizure control, predictable pharmacokinetics and minimal drug interactions. Both therapeutic and adverse toxic effects of levetiracetam are related to plasma concentration. The aim of this study was to investigate the influence of dosage regimens on the concentration range of levetiracetam.

Methods: Levetiracetam plasma concentration was calculated by means of a one-compartment pharmacokinetic model with 1st order kinetics. Parameters of the model were taken from published pharmacokinetics studies. The dosage regimens had a structure of 2 drug-consumption periods separated by 2 drug-free periods. They reflected dosing habits of patients from our department (n=68).

Results: In the 1st part we characterized the impact of dosing regimen parameters on the minimum and maximum concentrations and in the 2nd part we calculated the maximum and minimum concentrations for dosing regimens reported by the patients. With pharmacokinetic parameters set at representative values, the minimum concentration decreased, in comparison to the perfect regular dosing, by 9% at median and 27% at the lower range; the maximum concentration increased by 4% at median and 21% at the upper range, respectively.

Conclusion: Dosing regimens, considered by epileptic patients as an acceptable therapy adherence, comprises different drug intake habits. The extreme plasma concentrations reached in these dosing regimens differ up to tens of percents from the perfect regular dosing. In some cases, changing the drug intake habit could possibly improve seizure control similarly to drug dose increase.

Disclosure: Supported by Charles University (PROGRES P35/3LF).

EPO1137

Internalized stigma in people with epilepsy

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Background and aims: Epilepsy is a strongly stigmatized health condition. Some people with epilepsy internalize public stigma, which may have negative impact on their psychosocial functioning.

Aims: To investigate the level of internalized stigma and its associations with social network, depression and life satisfaction among patients with epilepsy.

Methods: A total of 65 patients diagnosed with epilepsy (mean age 42.9 years, 24 males) were recruited from a neurological ward and neurological outpatient clinic at the Institute of Psychiatry and Neurology. They were assessed with the Internalized Stigma of Mental Illness (ISMI) scale adapted for epilepsy, the abbreviated version of the Lubben Social Network Scale (LSNS-6), the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R), and the Satisfaction with Life Scale (SWLS).

Results: The ISMI total score was 1.89* (SD=0.56), meaning a relatively low level of internalized stigma. Pearson correlations indicated significant positive associations of stigma with the intensity of depressive symptoms ($r=0.43$, $p<0.001$) and significant negative associations with the size of social network ($r=-0.52$, $p<0.0001$), and with the degree of life satisfaction ($r=-0.51$, $p<0.0001$).

*Possible scores range from 1 to 4, with higher scores indicating more severe internalized stigma. According to Ritsher & Phelan (2004), scores above the midpoint of the scale denote high internalized stigma.

Conclusion: Since internalized stigma is related to various indicators of psychosocial functioning, it should be considered as important target of treatment and rehabilitation of people with epilepsy.

Disclosure: Nothing to disclose

EPO1138

Ictal EEG quantification in epilepsy of infancy with migrating focal seizures (EIMFS): from seizure dynamics to EEG-based markers

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Background and aims: We aimed to quantify EIMFS seizures related to the KCNT1 mutation, to determine if these seizures diffused randomly or not, and specific EEG markers.

Methods: We included EEGs of 7 EIMFS patients with KCNT1 mutations (115 seizures) and of 17 patients with other early-onset epilepsies (30 seizures). 1st, we developed an algorithm to detect seizures' onset and offset in each EEG channels. Then, we quantified seizures spatiotemporal characteristics and analyzed their dynamics using chronograms and phase coherence. Finally, we compared these data with other epileptic syndromes in children under one year of age to determine specific EEG markers.

Results: Seizures started and were localized predominantly in temporal and occipital areas, and evolved with a stable frequency (4-10 Hz). They showed inter and intrahemispheric migrations in 60% of them with high intraindividual reproducibility of temporo-spatial dynamics. Interhemispheric migrating spread in 71% from temporal or occipital areas to the homologous contralateral ones. Intrahemispheric seizures involved mainly frontal-temporal, temporal and occipital channels. In migrating seizures, we found causality links between ictal activities. Finally, time delay index (based on delays between the ictal onsets) and phase correlation index (based on coherence of ictal activities) identified EIMFS seizures and non-EIMFS seizures (specificity of 91.2% and sensitivity of 84.4%).

Conclusion: This study characterized migration as a specific pattern of propagation. The EEG markers could facilitate the diagnosis of EIFMS at early stage. In addition, these results will help to validate future computational models.

Disclosure: This work was supported by funds from the French Pediatric Society (PhD 1-year grant) and the French Institute of Health and Medical Research (PhD 2-year grant: poste d'accueil Inserm, M.K.). This work was carried out with the support of the Institute of Clinical Neurosciences in Rennes (INCR).

EPO1139

Lacosamide as add-on in combination with other sodium channel blocker

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Background and aims: Lacosamide is a sodium channel blocker (SCB) approved as adjunctive therapy for partial onset seizures and more recently as monotherapy. We wanted to evaluate the effectivity of this drug when is used in combination with other SCB versus when is combined with other antiepileptic drugs.

Methods: We have evaluated the patients treated with lacosamide in the last 10 years in a secondary hospital obtaining a total of 99 patients of which, 75 were in polytherapy (35 as second drug, 30 as 3rd drug, 7 as 4th drug and 3 as 5th drug) in the moment when lacosamide was started and 40 of them were treated with other SCB.

Results: The combination of lacosamide with antiepileptic drugs, other than SCB, shows more effectivity in the percentage of reduction of seizures (62.86% [SD 40.23%] vs. 22.95% [SD 74.43%]) and an increase in seizure free patients (OR=3.778, p=0.018) than the combination with others that act on the same channels.

Conclusion: Lacosamide, as was previously known, is effective in polytherapy, and more if is combined with other drugs with a mechanism of action other than SCB so we must take this into consideration when prescribing lacosamide to a patient.

Disclosure: Nothing to disclose

EPO1140

Status epilepticus with prominent motor symptoms: a retrospective single-center cohort study

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Background and aims: Status epilepticus (SE) is a neurological emergency associated with high mortality and morbidity. The purpose of this study is to evaluate the demographic data, clinical presentation, etiology, treatment and outcome of a cohort of patients with SE with prominent motor symptoms.

Methods: Retrospective cohort study (2012-2019) of adults with SE with prominent motor symptoms, excluding myoclonic SE. We used the latest International League Against Epilepsy (ILAE) definition and classification of SE.

Results: Among 52 patients with SE with prominent motor symptoms, 15 (28.8%) had generalized convulsive SE and 37 (71.2%) had focal motor SE (29 repeated focal motor, 7 *epilepsia partialis continua* and 1 *adversive*). 26 (50%) females and 26 (50%) males, with a median age of 70 years (18-95 years), 17 (32.7%) with a previous epilepsy. Etiology was identified in 47 (90.4%) of patients being the most common systemic infections (n=19, 36.5%), cerebrovascular disease (n=18, 34.6%) and metabolic disease (n=13, 25%). Most patients (n=37, 71.2%) required 2 or 3 antiepileptic drugs (AED), being levetiracetam (n=48, 92.3%), valproate (n=33, 63.5%) and phenytoin (n=22, 42.3%) the most commonly used. 14 patients (26.9%) progressed to refractory SE, 12 had sequelae (23.1%) and 7 (13.5%) died in hospital.

Conclusion: Etiologies were similar to those described in other studies except for the higher rate of infection. In this cohort SE was challenging to treat, requiring multiple AED and often progressing to refractoriness. In-hospital mortality and morbidity was significant.

Disclosure: Nothing to disclose

EPO1141

Defining EEG stages in Lafora disease

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Background and aims: Lafora disease (LD) is an ultra rare form of Progressive Myoclonus Epilepsy. Since the evolution of the EEG is not well defined, we aimed to investigate the EEG changes in different stages.

Methods: We performed a cross sectional study of LD patients seen in our center during 2019. Patients were classified according to a clinical scale based on seizure control, cognitive impairment, motor function and performance of daily living activities. We reviewed EEGs (background activity, reactivity to eye opening, frequency of epileptiform activity and photosensitivity).

Results: We studied 11 patients. Patients in presymptomatic stage (2/11) had normal EEG or slow background activity (6-7 Hz), with non-continuous focal and generalized epileptiform activity. Patients in early stage (4/11) had normal or slow background activity (6-7 Hz), normal reactivity, mostly preserved sleep stages and very frequent focal and generalized epileptiform activity. Patients in middle stage (2/11) had slow background activity (4-5 Hz), absence of reactivity, moderate loss of sleep stages and almost continuous focal and generalized epileptiform activity. Patients in advanced stage (3/11) had slow background activity (3-4 Hz), absence of reactivity, loss of sleep stages and continuous focal and generalized epileptiform activity. In all patients epileptiform discharges decreased during sleep, almost disappearing in early stages. Only 4 patients had photosensitivity (1 presymptomatic, 2 early stages, 2 advanced stages)

Conclusion: We can differentiate 3 EEG stages in LD with good correlation with clinical stages. During sleep, epileptiform activity decreases significantly. The EEG may be a valid biomarker to follow the progression of LD and can detect presymptomatic individuals.

Disclosure: Part of this work was founded by Ionis Pharmaceuticals and Valerion Therapeutics.

EPO1142

Sub-Saharan study of photoparoxysmal response in a reference epilepsy lab

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Background and aims: The photoparoxysmal response (PPR) is defined as the occurrence of generalized spike, spike-wave or polyspike-wave discharges consistently elicited by intermittent photic stimulation (IPS). PPR is not well studied in African black subject.

Methods: We prospectively studied the epidemiological, clinical and EEG characteristics of PPR among consecutive epileptic patients seen in the EEG laboratory at Fann University Hospital at Dakar in Senegal.

Results: Among 3065 pathological EEG for 1 year, we collected 56 EEG (1.8%) with PPR, including 31 women and 25 men (sex ratio: 0.8). The mean age was 13.3 years (range: 8 months to 59 years). The peak of photosensitivity was found in the range of 6 to 10 years. Of the PPR cases, 12 had had clinical manifestations during IPS. Generalized epilepsy was diagnosed in 23 (41%) patients and 18 (32%) had focal epilepsies. The most epileptogenic stimulation frequencies are between 12 and 24 Hz. PPR were obtained most often when the eyes are closed (64%) and 41 patients (73% of patients) were classified as Type 4 (Waltz classification).

Conclusion: Our results suggests lower rates of photosensitivity in sub-Saharan people compared with Caucasians. Therefore, subject to consistent larger cohort's data, it would be interesting to study a probable epigenetic protective value of sunshine against photosensitivity.

Disclosure: Nothing to disclose

EPO1143

Sleep features of patients with psychogenic non-epileptic seizures (PNES)

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Background and aims: Sleep complaints are frequently reported by patients with psychogenic non-epileptic seizures (PNES) but, up to now, few studies evaluated hypnic features by means of polysomnography. Objective of our study was to assess the polysomnographic sleep features of a group of patients with PNES.

Methods: We performed a retrospective observational study in the Neurological Clinic of the University of Catania. We enrolled patients for whom a diagnosis of PNES was made, after excluding all other possible diagnoses. We also enrolled a group of controls without epilepsy and a group of drug-naïve patients with newly diagnosed epilepsy. We excluded subject who were taking antiepileptic treatment. All subjects underwent a long-term EEG monitoring, including at least one night of sleep.

Results: 33 patients with PNES [mean age 33.4 ± 13.7 years; M=9 (27.3%)], 34 controls [mean age 38 ± 15.5 years; M=17 (47.1%)] and 46 patients with epilepsy [mean age 29.5 ± 15.3 years; M=17 (37.0%)] were enrolled. At the multivariate analysis, adjusting for age, sex and psychotropic therapy, patients with PNES displayed a significant reduced latency of REM sleep (73.2 ± 22.1 , mean) both compared to controls (98 ± 54.8 , $p=0.025$) and patients with epilepsy (110.5 ± 51.6 , $p<0.0001$), while an increase in REM sleep percentage (22.8 ± 6.4) was recorded compared to patients with epilepsy (18.2 ± 5.2 , $p=0.005$).

Conclusion: The results of our study show significant differences, mainly in REM sleep structure, in patients with PNES, resembling the sleep structure of patients with mood disorders.

Disclosure: Nothing to disclose

Headache and pain 1

EPO1144

The PEARL study protocol: a pan-european prospective observational study of fremanezumab effectiveness in patients with chronic or episodic migraine in the real world

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Background and aims: Migraine is a common but highly disabling disease, and adherence to traditional migraine preventive treatment is low. Fremanezumab is a fully-humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP) and has been approved in the US and EU for the preventive treatment of migraine in adults. The PEARL study aims to provide real-world evidence of fremanezumab treatment outcomes in European clinical practice in patients with episodic migraine (EM) or chronic migraine (CM).

Methods: PEARL is a 36-month (12-month recruitment and 24-month follow-up), multicenter, pan-European, prospective, observational study conducted in adults with EM (≥ 4 migraine days per month) or CM in real-world clinical practice. The primary endpoint is the proportion of patients reaching $\geq 50\%$ reduction in monthly average number of migraine days during the 6-month period after the 1st dose of study drug. Secondary effectiveness endpoints include changes from baseline in monthly average number of migraine days, disability scores, and monthly average number of days of acute headache medication use. Adherence and persistence with fremanezumab treatment over the 24-month follow-up, as well as reasons for and outcomes of fremanezumab cessation and re-initiation, will also be examined.

Results: The study is planned to be conducted in approximately 100 centers in 11 European countries, with an estimated sample size of 850 patients.

Conclusion: Through the assessment of a range of effectiveness outcomes and patient-reported measures in clinical practice, PEARL will generate precious information about real-world effectiveness, treatment adherence, and treatment persistence of fremanezumab in patients with EM or CM.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPO1145

Correction of biomechanical disorders by the original method of biofeedback for cervicogenic headache

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Background and aims: Determine the role of correction of biomechanical disorders in cervicogenic headache.

Methods: 71 patients with cervicogenic headache (CGH) were examined. The average age is 32.7 ± 3.6 years. Patients were divided into 2 groups (35 and 36 participants). The 1st group: pharmacotherapy+physiotherapy. The 2nd group: pharmacotherapy+stabilometric training. Biomechanical parameters (biauricular, biacromial lines) were assessed by visual-optical analysis (VOA). Stabilometric parameters were studied: the statokinesiogram area, displacement of the center of pressure, energy spent.

Results: The method of correction of biomechanical disorders in CGH based on the principle of biofeedback has been developed and tested. After treatment: 67.6% of patients relapse of CGH occurred a month later after pharmacological treatment, 32.4% - after pharmacological treatment and treatment on the stabilometric training ($p < 0.05$). The 'statokinesiogram parameters': the best dynamics of return to the norm of the 2nd group was $107 \pm 10.3 \text{ mm}^2$, while in the 1st only $151 \pm 10.7 \text{ mm}^2$. The degree of displacement of the center of pressure in the 1st group decreased by 17.1%, in the 2nd group by 52.8%. Analysis VOA showed a significant approximation of the degree of deviation of biauricular, biacromial lines to the norm in the 2nd group of participants.

Conclusion: Clinical manifestations of CGH are mainly associated with biomechanical disorders in the cervical region. The use of the biofeedback method (the stabilometric training) for the correction of biomechanical disorders improves the diagnosis and results of the treatment of CGH.

Disclosure: Nothing to disclose

EPO1146

The effects of repetitive pericranial nerve blocks on neutrophil / lymphocyte, platelet / lymphocyte ratios and mean red cell distribution width in patients with chronic migraine

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Background and aims: The pathophysiology of migraine is attributed to neurogenic inflammation and neurovascular disorder in which contractile dysfunction of cranial blood vessels plays a role. There is a limited number of studies evaluating the changes of inflammatory markers such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLO) and Mean Red Cell Distribution Width (RDW) following the treatment of chronic migraine. The aim of this study was to investigate the effects of repetitive pericranial nerve blocks on inflammatory markers.

Methods: The diagnosis of migraine was made according to the ICHD 3rd edition version. The socio-demographic and clinical characteristics were recorded for 16 patients with chronic migraine who underwent at least 3 pericranial nerve blocks with local anaesthetics (great occipital, supraorbital, infraorbital nerves and sphenopalatine ganglion) and attended at least 4 follow-up appointments. Change in the Numeric Pain Rating Scale (NPRS) was used to assess the response to GON blocks.

Results: The mean age of patients was 42.375±11.18 years; 94% were female. The duration of the headache was 20.10±11.15 years. From 3-months post-treatment, a significant decrease in NPRS and number of headache days were found ($p<0.001$). There were no statistically significant changes in the mean NLR, PLO and RDW values before and after the injections ($p=0.616$, $p=0.677$, and $p=0.720$).

Conclusion: Although repetitive pericranial nerve blocks are an effective interventional treatment option for chronic migraine, no significant decrease in RDW, neutrophil/lymphocyte and platelet/lymphocyte ratios within 3 months after injections supports that these inflammatory markers do not play an important role in prognosis monitoring for migraine.

Disclosure: Nothing to disclose

EPO1147

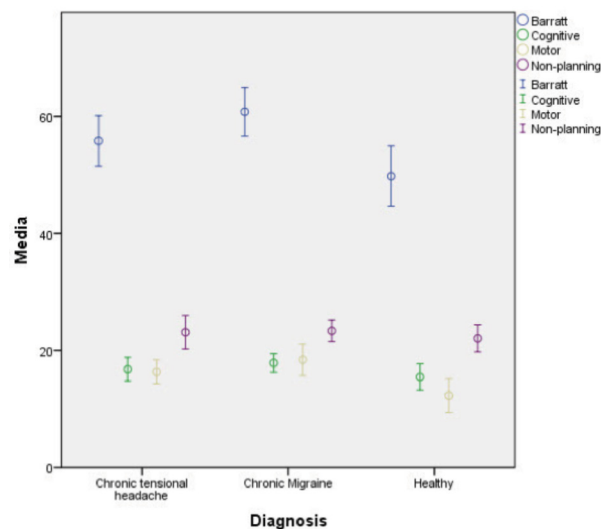
Impulsivity traits between chronic headache and healthy population

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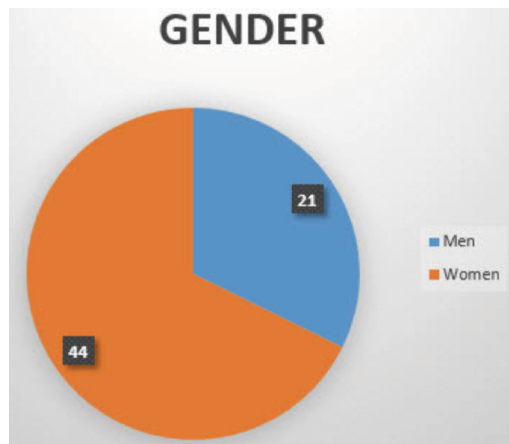
Background and aims: Chronic migraine and tensional headache are associated with psychological and psychiatric comorbidities. Amongst those comorbidities, impulsivity has been poorly explored. This survey aims to evaluate impulsivity traits between healthy people and patients with chronic headache (migraine and tensional headache).

Methods: The Barrat Impulsivity Scale (BIS) was filled by patients with chronic headache (migraine or tensional headache). Data about gender, age, type of headache, number of days with headache and days taking medication were collected and analysed by SPSS software.

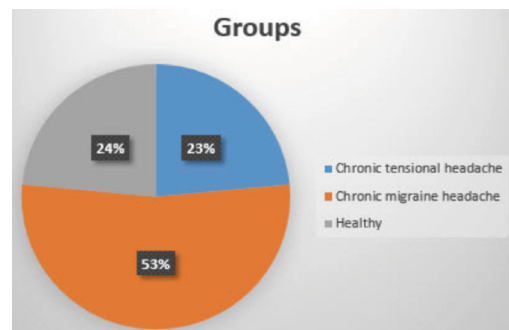
Results: A total of 65 patients filled the tests, the mean age was 37.5 years-old (SD 11.84); 44 (67.7%) were women. 16 (24.6%) had a chronic tensional headache, 33 migraine (50.8%) and 16 (24.6%) were healthy. The mean BIS score was 60.79 in migraine patients, 55.81 in tensional headache and 49.81 in healthy people ($p=0.04$). Furthermore, the mean score of the Motor subset of the BIS was 18.42; 16.37 and 12.31 respectively ($p=0.01$). The mean days with painkillers was 12.6 in migraine patients and 18 in tensional headache group ($p=0.2$). Moreover, the mean days with headache was 25.69 and 20.27 in patients with migraine and tensional headache respectively ($p=0.01$).



BIS



GENDER



GROUPS

Conclusion: BIS and the motor subset score showed significant differences between healthy and patients with chronic headache. These findings are not related to the use of analgesics as we demonstrated in a previous study of impulsivity and medication overuse headache.

Disclosure: Nothing to disclose

EPO1148

Cerebrospinal fluid oligoclonal bands in headache with neurological deficits and lymphocytosis (HaNDL) do not support an immune-mediated pathogenesis

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Background and aims: The syndrome of headache with neurological deficits and lymphocytosis (HaNDL) is an entity with an unknown pathogenesis. An autoimmune etiology has been postulated, with some attempts to relate it to specific antibodies. Nevertheless, there are not specific studies of intrathecal synthesis of antibodies in HaNDL.

Methods: Retrospective study of cases fulfilling diagnostic criteria for HaNDL (ICH-3) who underwent CSF study for the presence of IgG and IgM oligoclonal bands (OCB).

Results: A total of 16 patients were included (6 males, median age 28 years, range 15-51). Neurological deficits were aphasia in 15 patients, hemiparesis in 7, hemihypoesthesia in 5 and hemianopia in 3, with 12 patients showing more than 1 deficit. Median lymphocytic count in CSF was 59 (range 17-351). Median of episodes was 1.5 (range 1-6), with a median duration of 72 hours (range 3-720). 5 patients displayed minor alterations in MRI (leptomeningeal enhancement or unspecific white matter hyperintensities). Positive IgG OCB were present in 2 patients (6.25%) while mirror pattern was found in other 2. IgM OCB were negative in the 13 patients studied. There were no differences in clinical presentation or CSF or MRI findings between positive and negative OCB groups, except for higher frequency of hemianopsia in positive OCB group (100% vs 7.1%, p 0.025). Positive PCR for HHV-7 was detected in one patient with positive OCB.

Conclusion: CSF OCB, indicative of specific intrathecal immune activation, are uncommon in HaNDL. Our findings suggest that HaNDL may have a heterogeneous ethio-pathogenesis and an

infectious/parainfectious etiology cannot be ruled out.

Disclosure: Nothing to disclose

EPO1149

Chronorisk in a chronic cluster headache patient: analysis of 2292 attacks

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Background and aims: A key finding of cluster headache (CH) is the presence of a chronobiological rhythm. This characteristic is quite relevant in episodic cluster headache, but has also been described in chronic CH (cCH). We report the time analysis of attacks in a 59-year-old male with a 19 year history of cCH.

Methods: Retrospective analysis of 15 years of attacks in a single case of cCH. Study variables include date, intensity, starting hour of an attack and intensity (rated in a VAS scale 0-10).

Results: There were 2292 CH attacks in 5049 days of registry, corresponding to an attack every 2.2 days and 3678 days (72%) free of headache, showing that attacks tend to cluster. The most frequent hour of attack was 10-10:59PM (n=596) and mean attack intensity was 4.55 (s=0.94). The majority of attacks (59%) occurred in the late evening, between 8-12PM (n=1346), which also corresponded to the highest mean attack intensity (4.76 vs 4.25, p<0.001). There was a correlation between attack hour frequency and intensity of an attack (p=0.324, p<0.01). Attack frequency and mean attack intensity was unrelated to months with >12 hours of sunlight (March-September) and months with <12 hours of sunlight (October-February) (p=0.16). Although the patient reported an aggravation of attack intensity in warmer months (June-September), this was not confirmed when compared to the other seasons; p=0.056).

Conclusion: Chronorisk analysis in CH patients could become an important tool for new acute and prophylactic therapeutic strategies and pathophysiological knowledge of CH.

Disclosure: Nothing to disclose

EPO1150

Megadose of botulinum toxin type A in chronic migraine: our experience in a tertiary hospital in Madrid

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Background and aims: Chronic migraine is a disabling neurologic condition that affects 2% of the general population. Patients with chronic migraine have headaches on at least 15 days a month, with at least eight days a month on which their headaches and associated symptoms meet diagnostic criteria for migraine. The PREEMT studies have already demonstrated the effectiveness of Onabotulinumtoxin A in the treatment of chronic migraine at a maximum dose of 195U.

Methods: Describing our experience with doses of botulinum toxin type A between 250-300U in patients with chronic migraine refractory to the standard dose.

Results: We identified 16 patients with chronic migraine refractory to the dose of 195U in whom we used doses between 250-300U. 12 of them presented a partial subjective improvement measured in decrease of days and intensity of headache and more effectiveness to triptans, with few treatment-related adverse events.

Conclusion: Chronic migraine is a disabling neurologic condition, associated with a substantially greater personal and societal burden, more frequent comorbidities, and possibly persistent and progressive brain abnormalities. Many patients are poorly responsive to, or noncompliant with, conventional preventive therapies. Higher dose of Onabotulinumtoxin A (195U) has demonstrated to be superior to standard dose (155U) in several trial. We thought, as occurs in many drugs, a higher dose in some patients will be beneficial. In our experience, higher doses (250-300U) in selected patients could be a good alternative before adding new oral medication (usually bad tolerated) or new anti CGRP monoclonal antibodies. It's necessary to perform more studies to confirm our experience.

Disclosure: Nothing to disclose

EPO1151

Slovenian experience with erenumab

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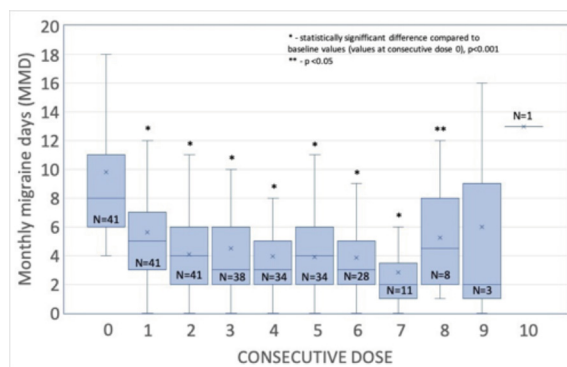
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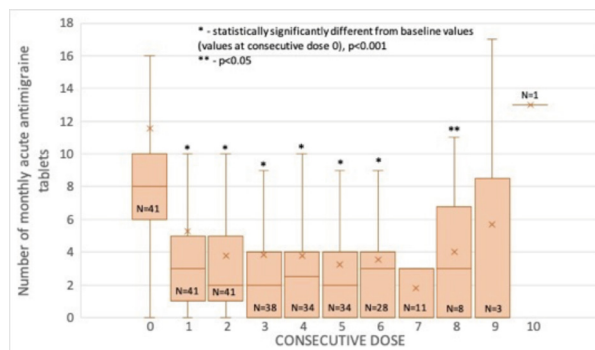
Background and aims: Erenumab is novel monoclonal antibody against canonical CGRP receptor for prophylaxis of migraine. In Slovenia its use is approved for the treatment of patients with 4 or more monthly migraine days and 2 or more failed prophylactic drugs.

Methods: We are prospectively monitoring 41 patients that have received erenumab from December 2018. We are recording number of monthly migraine headache days (MMD) and number of monthly acute antimigraine tablets (MMT) as well as side effects.

Results: These are interim results of a one-year study. Mean age of patients is 44.4 ± 10.4 years and there are 35 (85%) women. In patients treated at least 3 months (N=38) baseline MMD was 9.1 ± 0.7 and was reduced to 4.7 ± 0.4 for 3-month period ($p < 0.001$). In patients treated at least 6 months (N=28) baseline MMD was 11.3 ± 2.8 and was reduced to 4.2 ± 0.6 for 6-month period ($p < 0.001$). Similar results were observed for MMT (box plots 1 and 2). The most common side effects were constipation (41%), reaction at the site of applicator (17%) and fatigue (12%). Other reported side effects were signs upper respiratory tract infection, muscle cramps, flue-like symptoms and anxiety. There were no serious side effects noted.



Box plot 1. Number of monthly migraine days at consecutive doses of erenumab.



Box plot 2. Number of monthly acute antimigraine tablets at consecutive doses of erenumab.

Conclusion: In our experience erenumab is effective and safe for reducing migraine burden in patients with 2 or more failed prophylactic treatments. This is in line with previously published data from clinical randomized studies.

Disclosure: Nothing to disclose

EPO1152

**Sinus headache:
an overdiagnosed problem**

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Background: Although the International Classification of Headache Disorders (ICHD-3) recommends avoiding the term “sinus headache”, it is still widely used in daily practice. Recent series show that over 80% of these patients have other types of headache, mostly migraine.

Aims: Identify the types of headache diagnosed as “sinus headache”. Recognize barriers to the correct diagnosis.

Methods: We performed an observational and prospective study, and included adult patients diagnosed with “sinus headache”, from March to November 2019. We applied a structured questionnaire and classified the headache according to ICHD-3.

Results: We included 18 adult patients with the initial diagnosis of “sinus headache”, 15 (83.3%) were female. Mean age was 41.3 (18-61 years). After our evaluation, 2 patients (11.1%) had headache attributed to chronic or recurring rhinosinusitis. 1 patient (5.6%) had chronic tension-type headache. The remaining 15 patients (83.3%) fulfilled the criteria for migraine: 2 patients (11.1%) had migraine without aura, 5 (27.8%) migraine with typical aura, 1 (5.6%) probable migraine with aura, 6 (33.3%) chronic migraine and 1 (5.6%) chronic migraine and non-opioid analgesic-overuse headache. Atypical features in these patients included: atypical location – bifrontal and/or paranasal (73.3%), nasal congestion (60.0%) and worsening with exposure to allergens (26.7%), weather changes (33.3%) and altitude changes (33.3%).

Conclusion: Many patients with “sinus headache” actually have migraine. The most common barriers to the correct diagnosis appear to be atypical location and worsening/association of the headache with well-known symptoms and triggers of sinus disorders.

Disclosure: Nothing to disclose

EPO1153

Neurophysiological, biomolecular and psychological predictors of response to Erenumab in chronic migraine

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Background and aims: The aim of this study is to investigate the role of neurophysiological, biomolecular and psychological parameters as potential predictors of the clinical outcome of Erenumab treatment in chronic migraine (CM) with or without medication overuse (MO).

Methods: We enrolled 36 patients, 30 of whom had MO. All patients were treated with 3 doses of Erenumab (every 28 days). The study protocol included: V1: baseline; V2: 28 days after V1; V3: end of study, 56 days after V2.

At V1, V2 and V3 we recorded headache days (HDs) and days of drug intake (DDs).

At V1 and V3 all subjects underwent neurophysiological recording of the Nociceptive Withdrawal Reflex (RTh: Reflex threshold), blood essays for micro-RNAs expression (miR-382-5p and miR-34a-5p), and a psychological assessment.

Results: HDs and DDs markedly and progressively decreased over time ($p=0.001$ for both). At V3, 52.7% were considered Responder as they achieved a reduction in HDs of 50% or more.

Responder patients showed a significant lower baseline RTh and a longer duration of chronic migraine ($p=0.019$ and 0.035 respectively). A multivariate analysis confirmed a pivotal role of RTh even after a statistical correction for age, sex, MO, preventive therapy and disability scale. Biomolecular and psychological parameters significantly improved at the end of treatment, but we fail to find a significant association with clinical outcomes.

Conclusion: Neurophysiological recorded spinal sensitization may represent a predictor of response of Erenumab in the management of CM associated or not with MO.

Disclosure: Nothing to disclose

EPO1154

Stroke-like Migraine Attacks after Radiation Therapy (SMART) Syndrome – two new cases and systematic review of the literature

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Background and aims: SMART Syndrome is characterized by reversible episodes of headache with cortical neurological symptoms occurring as a late complication of cranial irradiation.

Methods: We report 2 male patients (38 and 47 years old), treated with cranial radiation for cerebellar astrocytoma at ages 14 and 8. We performed a systematic review of Pubmed and Cochrane Library and report all published cases of SMART Syndrome up to date.

Results: The younger patient presented with headache and visual disturbance. Initial MRI was normal but 4 days later revealed right subcortical occipital acute lesion. He suffered 2 more episodes, in which MRI showed reversible right temporal-parieto-occipital gyriiform enhancement. The older patient presented a migraine-like attack with visual disturbances and psychomotor slowing. Cranial MRI showed reversible right occipito-temporal cortical enhancement; he had 3 further similar episodes. Regarding systematic review, 51 manuscripts were included, total of 100 patients (60 males); median age at presentation was 48 years (5-81). 59 patients had cranial irradiation for primary brain tumor with cumulative dose from 12 to 134.8 Gy. Clinical presentation included focal signs in all patients, headache (81%), seizures (52%) and encephalopathy (31%). Symptoms were reversible in most patients, lasting 30 minutes to 8 months. 82% of patients had cortical gyral enhancement in MRI, that reverted in 4 days to 6 months. Treatment included antiepileptic drugs, steroids, and aspirin.

Conclusion: SMART Syndrome should be considered in patients with history of cranial radiotherapy that present neurological symptoms and headache. Clinic is not always reversible and there is no consensual treatment.

Disclosure: Nothing to disclose

EPO1155

Lacrimal neuralgia: seven new cases of an emerging pain syndrome

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Background and aims: Lacrimal nerve is one of the 3 terminal branches of the ophthalmic nerve. It supplies the lateral upper eyelid and a small part of temporal periorbital skin. Lacrimal neuralgia was first described in 2013 and proposed diagnostic criteria included pain in the skin area supplied by the nerve, tenderness upon palpation on its emergence, and relief with an anaesthetic blockade. Only 9 cases have been published. We aim to describe clinical characteristics of a series of 7 new cases of lacrimal neuralgia.

Methods: From October 2013 to December 2019, we prospectively screened all patients fulfilling the proposed diagnostic criteria of lacrimal neuralgia in a headache clinic in a tertiary hospital. We gathered their clinical and demographic characteristics.

Results: We included 7 patients (1 male, 6 females). Neuroimaging was obtained in all cases to exclude underlying lesions. Left side was affected in 6 patients. Mean age at onset was 33.5 ± 21.1 years (8-70) and latency between onset and diagnosis was 44.4 ± 47.5 months (4-120). In 3 patients the neuralgia was triggered by a mild trauma. In 6 cases there was an oppressive or burning background pain with intensity of 6.6 ± 2.7 (3-10), and in 3 electric or stabbing paroxysms rated as 8 in all cases. In 3 patients there were spontaneous remissions and the 3 post-traumatic cases presented only background pain with no exacerbations.

Conclusion: Lacrimal neuralgia is uncommon and probably difficult to diagnose, but must be taken into account in patients with orbital and periorbital pain. We need further reports to better characterize its phenotype.

Disclosure: Nothing to disclose

EPO1156

Premonitory symptoms in patients with episodic migraineH. Güven, B. Güven*Neurology, Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, University of Health Sciences, Ankara, Turkey*

Background and aims: It is important to understand the premonitory phase of the migraine both for elucidating the pathophysiology of the events that initiate the migraine attack and for early treatment. The aim of this study is to investigate the frequency of premonitory symptoms (PSs) during migraine attacks and its association with different characteristics of migraine.

Methods: Patients with episodic migraine with or without aura were evaluated using questionnaires and diaries to determine the characteristics of headache and PSs.

Results: Of the 330 patients included in the study, 196 had PSs during migraine attacks (59.4%). The most common PSs in patients with migraine were neck stiffness (21.2%) and yawning (19.1%). Older age ($p=0.025$), female gender ($p=0.021$), migraine with aura ($p=0.020$), longer disease duration ($p<0.001$), more severe headache ($p=0.030$), unilateral+ bilateral lateralization of headache ($p=0.003$) and pure menstrual or menstrually related migraine attacks ($p=0.045$) were more frequent in patients with PSs compared to without. Accompanying vomiting, photophobia, cranial autonomic symptoms, and cutaneous allodynia were also more common in patients with PSs ($p=0.026$, $p=0.026$, $p=0.047$ and $p<0.001$, respectively). In multivariate logistic regression analysis, PSs were independently associated with duration of disease, headache severity, and allodynia ($p=0.005$, $p=0.026$ and $p=0.016$, respectively). Longer disease duration and accompanying photophobia were more common in patients having >3 PSs than those with 1 symptom ($p=0.005$ and $p=0.010$).

Conclusion: Longer disease duration and diversity of accompanying symptoms in patients with PSs may suggest that these symptoms facilitate the occurrence of each other and reflect the increase in brain excitability over time.

Disclosure: Nothing to disclose

EPO1157

Do patients with chronic migraine and daily headache respond to preventatives? Analysis of a series of 265 patients treated with Onabotulinumtoxin AI. Hernandez¹, M. Gutiérrez Sánchez de la Fuente¹, B. Talavera de la Esperanza¹, C. Martínez Badillo², C. García Iglesias³, A. Sierra Mencia⁴, D. García Azorín³, A.L. Guerrero Peral³*¹Neurology Service, Valladolid, Spain, ²Headache Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ³Valladolid, Spain, ⁴Valladolid, Castilla y Leon, Spain*

Background and aims: Efficacy and safety of Onabotulinumtoxin A (OnabotA) in Chronic Migraine (CM) have been established in controlled trials and real-world data. We have less information regarding patients with daily headache, commonly excluded from clinical trials. We aim to evaluate efficacy and predictors of response in a large single-center series of CM patients treated with OnabotA.

Methods: From May 2012, we offered OnabotA to adult CM patients not responding to previous treatment 2 preventatives including topiramate. OnabotA was administered according to PREEMPT protocol. We gathered clinical and demographical variables. Efficacy was assessed 3 months after 2 procedures and it was defined as a reduction of at least 50% in number of headaches per month.

Results: We included 265 patients (230 female, 35 male). 84 (31.6%) with daily headache and 204 (77%) with symptomatic medication overuse. Efficacy was achieved in 185 patients (69.8%). Among responders we observed a shorter duration of migraine (22.6 ± 12.2 vs 26.6 ± 14.0 years, $p=0.04$), shorter duration of chronic migraine (27.4 ± 34.9 vs 53.1 ± 63.2 months, $p=0.001$) and a smaller number of days with headache per month (22.0 ± 6.0 vs 25.7 ± 5.1 days, $p<0.001$). Medication overuse (66.2% vs 82.0% , $p=0.018$), and daily headache (54.8% vs 76.8% , $p<0.001$) were predictors of lack of response in our series.

Conclusion: A larger number of days of headache per month and, specifically, the presence of daily headache before initiating OnabotA therapy implied a worst outcome after 2 procedures in our population. These patients might require a longer duration of treatment to achieve improvement.

Disclosure: Nothing to disclose

EPO1158

Diagnostic and therapeutic relevance of headache clinic according to a university hospital experience

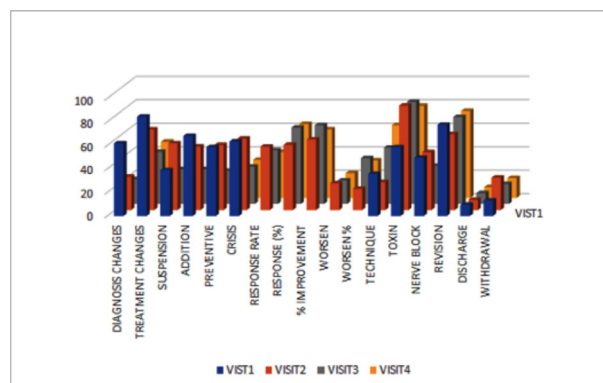
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Background and aims: Our aim was to analyse the impact of referrals to a headache clinic: diagnostic and therapeutic modifications and patients' outcome.

Methods: We included patients attended for 1st time in a headache clinic over 1 year. Data from medical records were retrospectively collected. Response rate was defined as at $\geq 50\%$ reduction on headache frequency.

Results: 283 patients were included: 60% referred from neurologists, 13% from emergency department and 8% from primary. 27.8% had episodic, 26.8% chronic migraine, 31.1% other primary headache and 3.2% secondary headache. 108 patients (38.1%) completed 1 year of follow-up (4 visits). 29.6% had episodic migraine, 36.1% chronic migraine, 29.6% other primary headache and 3.7% secondary headache. At visit 1 22.4% of patients had not received any preventative previously, 25.3% had received 1 preventative, 23.5% 2 preventatives and 28.9% 3 or more preventatives. Definitive diagnosis was done in 175 patients (61.8%) at visit 1. The treatment was modified in 84.5% of patients and 35.7% were treated with OnabotulinumtoxinA and/or anaesthetic injections in the first visit. The response rate was 53.88% at visit 2, 45.77% at visit 3 and 39.05% at visit 4. At visit 4, 62.9% reported a subjective overall improvement from baseline, 58.5% had received OnabotulinumtoxinA and 24.6% had received anaesthetic blockade.



Conclusion: Patients referred to a headache clinic benefitted from a more accurate diagnosis and therapeutic optimization. These results also contribute to increase awareness of the importance of improving management of headaches by general neurologists and primary physicians.

Disclosure: Nothing to disclose

Motor neurone diseases 1

EPO1159

Cutaneous silent period in patients with spinal muscular atrophy type 2 and type 3

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Background and aims: Cutaneous silent period (CSP) is the sudden inhibition of voluntary muscle contraction as a result of a painful stimulus. The aim of this study was to examine CSP changes in the presence of pure lower motoneuron loss. For this purpose, we recorded CSPs in SMA type 2 and type 3 patients

Methods: 14 patients with SMA and 14 healthy individuals were included. CSPs were recorded from thenar muscles after painful stimulation of the index finger while the participant performed slight thumb abduction. Onset latency, duration and magnitude of total CSP, inhibitory phases I1 and I2, and of the long-loop reflex as well as magnitude of post-CSP excitatory period (E3%) were measured. Suppression indices of CSP, I1 and I2 were calculated. The values were compared between SMA patients and healthy subjects, and between ambulatory and non-ambulatory SMA patients

Results: CSP parameters except E3% were not different between SMA patients and healthy individuals. E3% was significantly smaller in patients than healthy subjects. CSP duration and CSP end latency were significantly longer in non-ambulatory vs. ambulatory SMA patients. Hammer-smith scores of SMA patients correlated negatively with CSP duration and positively with E3%

Conclusion: CSP duration is longer in non-ambulatory SMA patients, irrespective of SMA subtype. This finding concurs with a lower motoneuron firing rate in more severely affected SMA patients, otherwise a feature of central lesions. The magnitude of E3 is significantly smaller in SMA patients compared to healthy subjects, in line with motoneuron loss, and hence fewer residual motoneurons available for resynchronization following the CSP.

Disclosure: Nothing to disclose

EPO1160

HDAC4 protein expression and microRNAs in ALS muscle

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Background and aims: MicroRNAs are small non-coding RNAs that regulate the expression of specific genes by binding to the 3' untranslated region of the target mRNA. HDAC4 belongs to the class IIa of HDACs (histone deacetylases) family and plays an important role during the denervation and regulation of miR-206 in ALS pathophysiology.

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by the degeneration of upper and lower motor neuron and the progressive loss of synaptic connection between nerve and muscle. While the majority of ALS cases are sporadic (SALS), about 10% of ALS cases have a familial inheritance (FALS). The most frequent genetic cause of ALS is associated with an expanded repeat in the 3' untranslated region of C9orf72 gene (C9-ALS). Another frequent genetic cause is due to mutation in the gene SOD1, coding for a superoxide dismutase enzyme (SOD1-ALS). A different form of ALS is upper motor neuron disease (UMN).

Methods: We analyzed the expression levels of muscle-specific myomiRNAs (miR-1, miR-133a, miR-133b, miR-206), inflammatory microRNAs (miR-27a, miR-221, miR-155) and HDAC4 protein content by Western Blot in muscle cryostat sections of 18 ALS patients: 8 genetic forms (C9-ALS and SOD1-ALS), 5 SALS and 5 UMN.

Results: Our results show a strong up-regulation of miR-206 in C9-ALS and SOD1-ALS patients, a decreased expression of HDAC4 protein levels. We also observed an increase of inflammatory miRNAs in genetic ALS.

Conclusion: The different expression of miRNAs and HDAC4 in genetic ALS versus SALS and UMN cases might be correlated to different pathogenic mechanisms.

Disclosure: Nothing to disclose

EPO1161

Cyanate could be a plausible toxin contributing to konzo, contrary to thiocyanate: preliminary experimental results

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Background and aims: Cassava-derived cyanide toxicity and protein malnutrition are main risk factors of konzo, a tropical spastic paraparesis of unknown cause. This preliminary study assessed neurotoxic effects of thiocyanate and cyanate, two cyanide metabolites hypothesized to be plausible toxic agents in konzo.

Methods: Cultured mouse neuroblastoma (Neuro-2A) and human neuroblastoma (SH-SY5Y) cell-lines were incubated in MEM-medium containing sodium cyanate (NaOCN) and sodium thiocyanate (NaSCN) in a disease-relevant concentration range. Cells viability was evaluated after 24, 48 and 72 hours using the MTT-assay.

Results: Both NaOCN and NaSCN were toxic in a dose-dependent way, even if NaOCN toxicity appeared at concentrations 100-300 times higher than normal plasmatic levels, contrary to NaOCN (1-3mM). The 2 cell lines tended to exhibit opposite sensitivity to the 2 compounds. Strikingly, Neuro-2A and SH-SY5Y viability dropped drastically between 24 and 48 hours (~60% lowering) and even further between 48 and 72 hours (~80%) in Neuro-2A cells (~65% reduction in SH-SY5Y cells between 24 and 48 hours) under NaOCN (3mM) treatment, whereas no additional viability reduction was observed after 24 hours incubation in NaSCN (30mM) (respectively ~20% and ~21% drop in Neuro-2A and ~4% in SH-SY5Y).

Conclusion: Our results suggest NaOCN as a neurotoxic agent, while NaSCN toxicity could be questioned at such high concentrations. Furthermore, the gradual/delayed NaOCN toxicity and the differential sensitivity of neuronal cell lines are compatible with konzo, especially knowing that cyanate synthesis results from cyanide metabolization only in sulphur amino-acid-deprived conditions (like in konzo patients) and provoked spastic quadriplegia in primate experiments.

Disclosure: This work was supported by the VLIR-UOS Team Project 2017 Ref. No. CD2017TEA439A104

EPO1162

Comprehensive genetic analysis of an italian amyotrophic lateral sclerosis cohort

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Background and aims: 5-10% of patients with amyotrophic lateral sclerosis (ALS) have a positive family history (fALS). More than 25 genes have been identified associated with ALS/Frontotemporal-dementia spectrum disorders. However, mutations in 4 major genes (C9orf72, SOD1, FUS, TARDBP) account for 60%-70% of fALS. Recent studies have highlighted the role of genetic risk factors even in “sporadic” patients (sALS), in which the inheritability component would represent at least 21.0% (Mejzini et al., 2019). We aimed to evaluate the genetic contribution to the pathogenesis of fALS and sALS in an Italian cohort.

Methods: 200 ALS patients (age-of-onset 63±12years) were analyzed. 26% were fALS, of which 10.5% had a positive family history for ALS (fALS-ALS), and 15.5% for other neurodegenerative diseases (fALS-ND). The C9orf72, SOD1, and other genes linked to several ND were analyzed as in Bartoletti-Stella et al., 2018.

Results: We identified 34 mutations in the major ALS genes (C9orf72 n=17; SOD1 n=9; FUS n=4; TARDBP n=4). Considering the double mutants, these variants explain 85.7% of fALS-ALS, 19.35% of fALS-ND, and 6.7% of sALS. Another 43 patients presented likely pathogenic variants in other ALS-related genes (14 genes), or to other ND-related genes (8 genes). As expected, these variants were mainly identified in fALS-ND (38.70%) compared to fALS-ALS (9.5%). Interestingly, 29 carriers were sALS (19.59%).

Conclusion: This study reports a different genes involvement between fALS-ALS and sALS-ND, and the presence of rare causal variants even in sALS. These findings are useful for the development of genetic screening protocols and for counselling strategies for these patients.

Disclosure: Nothing to disclose

EPO1163

Stapedial reflex: a novel biomarker of early bulbar involvement in ALS patients

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a neuromuscular progressive disorder, characterised by limb and bulbar muscle wasting and weakness. 30% present a bulbar onset, while 70% a spinal one, although most of them develop bulbar impairment later, associated with poor prognosis. Due to the lack of early biomarker of bulbar involvement, we wanted to evaluate the role of stapedial reflex (SR) in predicting pre-clinical bulbar impairment in ALS.

Methods: We enrolled 36 ALS patients, 4 excluded for tympanometry alterations, and we assessed revised-ALS functional rating scales and SR, using Amplaid A728 impedance audiometer. Follow-up was performed every 3-4 months for a total of 4 visits. We evaluated presence of SR, ARLT and DECAY. Patients who hadn't developed bulbar signs at 4th visit continued follow-up for maximum 18 months. We analysed data using Mann-Whitney U test, Kruskal-Wallis test and Cox regression analysis.

Results: We observed that DECAY at 500 and 1000Hz is the first parameter of SR to get altered in all ALS before development of bulbar impairment (Fig. 1). 28 patients, developed bulbar impairment during the study. We highlighted a correlation between the progression rate (PR) of disease and both time of decay's alteration and time of bulbar impairment from disease onset (Fig. 2A-B). 4 patients who didn't develop bulbar impairment had a PR lower than the others (p<0.05, Fig. 3).

Patients	Sex	DECAY 500Hz V1	DECAY 500Hz V2	DECAY 500Hz V3	DECAY 500Hz V4	DECAY 1KHz V1	DECAY 1KHz V2	DECAY 1KHz V3	DECAY 1KHz V4	Age disease onset	Progression rate
1	F	Y	Y	Y	Y	Y	Y	Y	A	62,4	0,45
2	M	N	N	N	N	N	N	N	N	71,0	0,77
3	M	Y	Y	A	N	Y	Y	Y	N	62,1	1,24
4	M	Y	N	N	N	Y	N	N	N	78,1	0,26
5	F	Y	Y	A	N	Y	A	A	N	70,8	0,42
6	M	A	A	A	A	A	Y	A	N	69,3	0,34
7	F	Y	N	N	N	Y	N	N	N	70,6	0,82
8	M	N	N	N	N	N	N	N	N	73,2	0,63
9	M	Y	Y	A	N	Y	Y	Y	Y	52,6	0,60
10	M	Y	Y	A	N	Y	A	A	N	38,4	0,61
11	F	N	N	A	A	A	A	N	N	57,5	0,19
12	M	Y	N	N	N	Y	A	N	N	54,0	1,54
13	M	Y	Y	Y	A	Y	Y	Y	A	58,1	0,85
14	M	N	N	N	N	N	N	N	N	61,1	0,41
15	M	Y	Y	A	N	Y	A	A	A	67,6	0,54
16	F	N	N	N	N	N	N	N	N	49,1	0,77
17	M	N	A	A	A	A	A	A	A	75,1	1,02
18	F	N	N	N	N	N	N	N	N	73,0	0,38
19	M	A	A	A	N	A	A	A	A	73,7	0,72
20	F	A	A	A	A	A	A	A	A	66,6	0,34
21	M	A	A	A	A	A	A	A	A	41,3	0,27
22	M	Y	A	A	A	Y	A	A	A	57,0	0,82
23	F	A	A	A	A	Y	A	A	A	63,2	0,66
24	M	N	N	N	N	N	N	N	N	80,6	0,31
25	M	N	N	N	N	N	N	N	N	73,2	0,62
26	M	Y	A	A	A	Y	A	A	A	62,4	1,24
27	M	Y	Y	Y	A	Y	Y	Y	A	55,0	0,14
28	F	Y	Y	A	N	Y	Y	Y	N	64,4	0,16
29	M	Y	A	A	N	Y	Y	A	N	58,3	0,54
30	M	Y	Y	A	A	Y	A	A	A	62,3	0,19

Figure 1: DECAY is the 1st parameter of stapedial reflex (SR) to get altered before development of bulbar impairment. During the progression of disease we observed a gradual alteration and absence of SR at qualitative analysis. V1: first visit; V2: second visit; V3: third visit; V4: fourth visit. Y: SR normal; A: SR altered; N: SR absent.

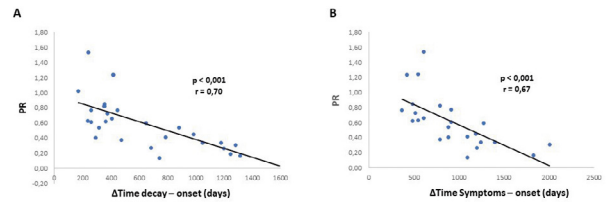


Figure 2: Progression rate inversely correlate with time passed from disease onset and both time of alteration/absence of decay (A) and time of development of bulbar signs (B).

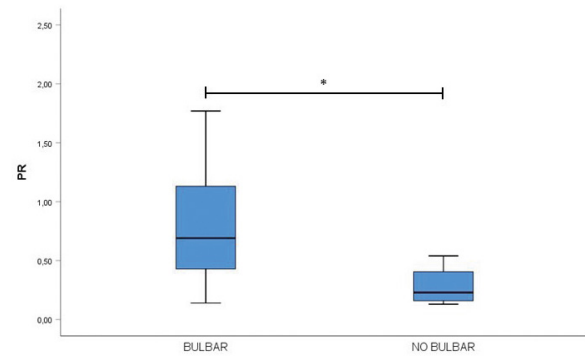


Figure 3: 4 patients who didn't develop bulbar signs before the end of the study present a progression rate to last visit significantly lower than other patients (U-Mann-Whitney; p=0.018).

Conclusion: This study shows that stapedial reflex could be a sensitive measure for detecting pre-symptomatic bulbar involvement in ALS and could represent a simple and useful biomarker of disease progression.

Disclosure: Nothing to disclose

EPO1164

Exosomal angiogenin as a possible biomarker in amyotrophic lateral sclerosis

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Background and aims: It is believed that extracellular vesicles (EVs), particularly exosomes, carry biologically active molecules contributing to disease progression in ALS. Angiogenin (ANG) is suggested to be implicated in the pathogenesis of ALS. This study aimed to analyze the levels of ANG in plasma, CSF and their EV fractions in patients with ALS (PALS).

Methods: The study included 30 PALS and 26 healthy participants (HP). EV fractions were extracted from plasma and CSF with ExoEasy Maxi Kit (Qiagen). Exosomal markers (CD63, CD81, Flotillin1) were detected in obtained EV fractions by western blot. ANG levels were analyzed in plasma, CSF and EVs with ELISA.

Results: Exosomal markers were detected in all EV samples. Levels of ANG in PALS were significantly higher both in plasma (Me 6368.76pg/mg of protein) and CSF (Me 2365.19pg/mg) than in their EV fractions (Me 1869.22 and 223.50pg/mg, respectively) ($p < 0.0002$). Levels of ANG were 1.2 times lower in plasma ($p = 0.0153$) and 1.6 times in its EV fraction ($p < 0.0001$) in PALS compared to HP, which could point to the protective role of ANG. No statistically significant correlations between ANG levels and clinical features were found in PALS. Although, there was a tendency to decreased levels of ANG in patients with lower ALS-FRS-R scores ($p = 0.06$ for plasma EV fraction).

Conclusion: This study confirms previous data on the protective role of ANG in ALS. Data suggest that lowered ANG, especially exosomal, could be a biomarker of disease progression, which should be confirmed in a larger sample.

Disclosure: This study was supported by the Russian Foundation for Basic Research, project no. 18-015-00480 A.

EPO1165

Association between body weight and metabolic function in onset and progression in amyotrophic lateral sclerosis.

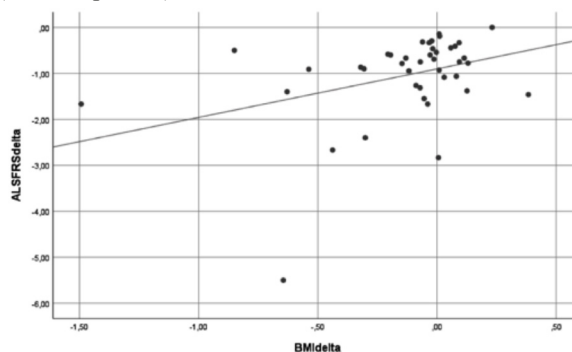
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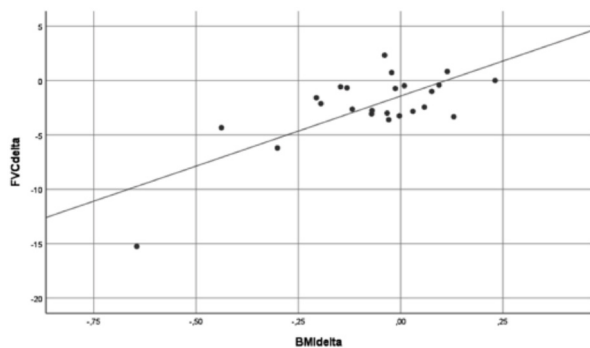
Background and aims: There is growing interest in the role of nutrition in pathogenesis and progression of amyotrophic lateral sclerosis. Indeed, poor prognosis and decreased survival time correlate with worse nutritional status of patients with ALS. Therefore, we sought to evaluate the associations between body weight, metabolic parameters and functional and respiratory markers at diagnosis and over disease course.

Methods: A retrospective/prospective single-center study was conducted between 01/16 and 12/19 at the Tertiary Regional Center for ALS in Novara, Italy. For each patient we collected demographics and clinical features, including metabolic parameters (e.g. weight, height, BMI, arm circumference, triceps skin fold, arm muscle area, type of diet). Patients were followed-up every 3 months after diagnosis, evaluating ALSFRS-R, FVC%, neuropsychological performances.

Results: 235 patients (131M, age at onset 63.3 ± 11.9) were included. 59% had spinal onset, 41% had bulbar one. The mean BMI was $25.57 (\pm 5.3)$. There was a strong positive linear correlation between negative variation in BMI (most recent BMI – baseline BMI/time between measurement) and negative variation in ALSFRS-R ($R = 0.33$, $p = 0.04$). BMI negative variation strongly correlated with FVC% decline ($R = 0.41$, $p = 0.04$).



Correlation between BMI variation (delta BMI) and ALSFRS variation (delta ALSFRS-R)



Correlation between BMI variation (delta BMI) and FVC variation (delta FVC)

Conclusion: A worse metabolic status influence ALS disease course. Starting from these preliminary findings, we established to monitor the diet of ALS patients with a telecare and telemedicine approach, with the aim to prevent/treat malnutrition as soon as it develops. We believe that an early detection of significant changes in food and nutrient intake can be a prompt therapeutic nutritional intervention to improve disease course.

Disclosure: Nothing to disclose

EPO1166

Descriptive analysis of varying real-world treatment patterns and outcomes in patients with spinal muscular atrophy collected from the RESTORE registry

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Background and aims: Spinal muscular atrophy (SMA) is a debilitating disease characterised by muscle weakness, respiratory failure, and early death. While recent advancements have dramatically improved prognosis, real-world data on treatment outcomes remain limited. The RESTORE registry is a comprehensive registry of patients with SMA specifically designed to overcome the recognised limitations of existing single-product registries.

Methods: RESTORE is an ongoing, prospective, multicentre, multinational, observational study, assessing outcomes in SMA patients, informing patients, caregivers, regulatory agencies, and researchers on the effectiveness and safety of approved and emerging treatments; and collecting information on healthcare resource utilisation and caregiver burden. The RESTORE database incorporates data from patients enrolled in partnering registries and the onasemnogene abeparvovec (formerly AVXS-101) managed access programme. Follow-up duration is 15 years from enrolment or until death.

Results: As of 3 January 2020, the RESTORE database comprises information from 64 patients and 25 active sites in the United States. This cohort permits descriptive analyses of patients with a range of baseline characteristics at time of dosing, including individuals who have switched

therapies, and who received treatment under managed/expanded access programmes at a variety of treatment centres. RESTORE is rapidly expanding globally, with 53 sites currently in start-up.

Conclusion: The RESTORE registry represents a pivotal resource for enhancing our understanding of SMA disease course under differing treatment regimens, and off therapy, in a diverse set of patients.

Disclosure: This study was sponsored by AveXis, Inc., a Novartis Company.

EPO1167

ALS plateaus: demographics, disease characteristics, treatments, and co-morbidities

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Objective: To identify differences in demographics, disease characteristics, treatments, and comorbidities between patients with amyotrophic lateral sclerosis (ALS) who experience periods of stability without disease progression (“plateaus”) and patients with typical progression.

Methods: Our retrospective study used data of over 1200 patients followed up at the ALS clinic at Tel-Aviv Sourasky Medical Center during the years 1996-2018. From these ALS plateaus were determined (defined as patients with a drop of 2 points or less on the revised ALS Functional Rating Scale (ALSFRRS-R) within 12 months). Their demographic and clinical data were compared with a group of patients with a classical ALS progression (average 12 points drop in ALSFRS-R within 12 months).

Results: 78 cases and 131 controls were confirmed through chart review. Among the Plateaus, median duration of the plateau period was 18.5 months.

Comparisons between the demographics and disease characteristics of cases and controls did not show any significant differences in family history, past physical activity, occupation, or co-morbidities.

“Plateaus” were more frequently male, had a younger age at onset, lower prevalence of bulbar onset, and smoked more packyears.

The exposure to cannabis was greater for plateaus than for controls. The odds of exposure to Riluzole was significantly lower in plateau patients. The exposures to other medications were not significantly different between groups.

Discussion: Lower age at onset, male sex, smoking and use of cannabis were associated with periods of stability in patients with ALS. Better understanding of the processes leading to disease stability might suggest potential treatment strategies.

Disclosure: Nothing to disclose

EPO1168

Financial Impact of a formal Percutaneous Endoscopic Gastrostomy (PEG) pathway for patients with Motor Neurone Disease (MND) at the Leeds Regional MND Care Centre

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Background and aims: Dysphagia is a major issue in patients with Motor Neuron Disease (MND) and assisted nutrition by percutaneous endoscopic gastrostomy (PEG) is modality of choice at Leeds Regional MND Care Centre. Following a patient death whilst waiting for a PEG in 2014, our centre developed a formal PEG pathway. We conducted this study to assess cost effectiveness of this PEG pathway which is operational since 2015.

Methods: Patients were selected from local MND registry and relevant clinical data was obtained through electronics records. Patient cohorts were defined as '2014' and '2018' (year of PEG insertion) and '2017' (patients died in this year). Financial information was extracted from PLICS (Patient Level Information Costing System).

Results: Average cost of the MND patient journey in the 2014 cohort was £298 while £348 in 2018 cohort. Comparing 2018 to 2014, average cost of the PEG procedure reduced to £2,650 from £4,747, average length of stay (LOS) reduced to 2.5 days from 3.1 days, average LOS for PEG episode has reduced to 5.1 days from 9.3 days. In 2017 cohort, average cost of PEG patient was £272 against £454 in non-PEG patient while average LOS for PEG patients was 2.2 days compared to 3.1 days for non-PEG patients. For the 2017 cohort, total and average costs were £275,652 and £329 respectively.

Conclusion: Formal PEG pathway has proven to be a significant positive impact financially on health care in patients with MND. We suggest that a multidisciplinary dedicated PEG pathway should be a standardised part of MND care.

Disclosure: Nothing to disclose

EPO1169

TDP-43 nucleo-cytoplasmic mislocalization can be rescued by antisense oligonucleotide treatment in ALS cell lines harboring C9Orf72 mutation

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Background and aims: The cytoplasmic accumulation and aggregate formation of hyper-phosphorylated and ubiquitinated TDP-43 is the pathological signature of TDP-43 proteinopathies, including C9Orf72-related fronto-temporal lobe degeneration (FTLD). Impairment in nucleo-cytoplasmic (NC) transport and TDP-43 NC mislocalization have been extensively reported in Amyotrophic lateral sclerosis (ALS), including C9-ALS. We aimed to validate TDP-43 NC mislocalization in cell lines derived from C9-ALS patients, compared to controls, sporadic lines (sALS) and other familial lines (fALS) and to evaluate the therapeutic effect of antisense oligonucleotide (ASOs) administration. Moreover, we aimed to test the role of TDP-43 mitochondrial localization in causing neuronal toxicity in ALS.

Methods: We obtained fibroblasts from ALS patients and controls and we performed immunofluorescence and Western blot for nuclear, cytoplasmic and mitochondrial fractions of TDP-43. Then, we transfected C9 lines with 2 different ASOs with Morpholino chemistry, 1 binding to the expansion motif and the other 1 binding to the promoter and silencing the whole gene.

Results: fALS lines with mutations in TARDP43 and C9Orf72 showed TDP-43 NC mislocalization, compared to controls and other ALS lines. TDP-43 mitochondrial content seemed to be increased in C9-ALS and TDP-43-ALS, and mitochondrial impairment was observed. ASO treatment, particularly with Morpholino-B, was able to revert TDP-43 NC ratio in C9-ALS.

Conclusion: Our results confirm that TDP-43 NC mislocalization is a pathological hallmark in C9-ALS and suggest that ASO may be a promising therapeutic strategy in C9-ALS patients. Further investigations are needed to assess if mitochondrial TDP-43 localization may cause mitochondrial toxicity in C9-ALS, potentially providing new TDP-43-based therapeutical strategies.

Disclosure: Nothing to disclose

EPO1170

The tolerability of non-invasive ventilation in motor neurone disease patients

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Background and aims: Motor neurone disease (MND) is a devastating and fatal neurodegenerative disease. Non-invasive ventilation (NIV) is the gold standard used to treat the respiratory impairment that occurs and is shown to be the most beneficial treatment for increasing survival. Unfortunately, some patients cannot tolerate NIV.

This study aimed to examine MND patients in Manchester who had been referred for NIV to determine if there were factors which correlated with tolerability.

Methods: We retrospectively reviewed MND patients who had been referred for NIV at the University Hospital of South Manchester in 2017. Data was then collected by reviewing the Electronic Patient Record (EPR) at Salford Royal Hospital and the EPR and physical records at the University Hospital of South Manchester.

Results: Tolerability was defined as consistent use of NIV for at least 4 hours a day. Of the 24 patients included, 16 (67%) were tolerant. The only statistically significant result identified was the positive correlation between indoor mobility and tolerability ($p=.004$). Tolerability was also likely correlated with the disease phenotype, psychosocial state, and certain respiratory parameters. See the results table attached.

Median (IQR) / Total frequency (%)	Total n = 24	Tolerant patients n = 16	Intolerant patients n = 8	Statistically significant (p value <0.05)
Age (y)	66.50 (13.25)	66.50 (14)	62.50 (17)	.312
Women	6 (25)	4 (25)	2 (25)	>.999
Deceased	18 (75)	11 (69)	7 (86)	.621
Survival (mo)	27.50 (27)	28.00 (16)	22.00 (37)	.856
Onset				.733
ALS bulbar	6 (25)	5 (31)	1 (13)	
ALS limb	11 (46)	7 (44)	4 (50)	
ALS resp.	1 (4)	1 (6)	0 (0)	
Other	6 (25)	3 (19)	3 (38)	
Cognitive impairment	1 (4)	1 (6)	0 (0)	>.999
Indoor mobility				.004
Independent	14 (58)	13 (81)	1 (13)	
Mobility aid	10 (42)	3 (19)	7 (88)	
Dysphagia				.301
Yes	13 (54)	7 (44)	6 (75)	
No	11 (46)	9 (56)	2 (25)	
Evidence of depression or anxiety	13 (54)	7 (44)	6 (75)	.211
Taking riluzole	18 (67)	12 (75)	6 (75)	>.999
Time (mo) from symptom onset to NIV referral	17.00 (30)	17.00 (21)	25.00 (52)	.602
Patients with respiratory symptoms	n = 23 19 (79)	n = 15 13 (87)	6 (75)	.589
Initiated due to acute decompensation	6 (25)	6 (38)	0 (0)	.066
Reported issues with NIV				.363
Yes	12 (50)	10 (42)	2 (25)	
No	12 (50)	6 (38)	6 (75)	

Results Table

Conclusion: There is a need for further prospective research to make definitive conclusions about what factors influence tolerability. With a better understanding of the impact of the modifiable factors, the rate of NIV tolerability could be improved to allow more patients to benefit from this vital treatment.

Disclosure: This project was done with the support of the University of Manchester, Salford Royal Hospital, and the University Hospital of South Manchester.

EPO1171

Factors affecting survival in patients with motor neuron disease

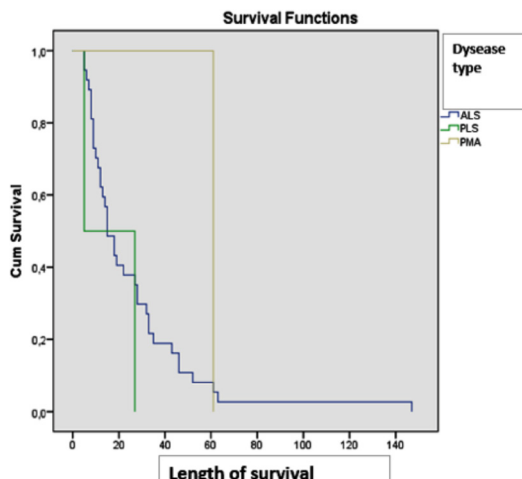
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Background and aims: Motor neuron disease (MND) is a neurodegenerative disorder characterized with upper and lower moton neuron lesion and bulbar symptoms. Etiology is still unknown and prognosis is very poor with short survival period. There are different types of MND depending on involved neurological system (amiotrophic lateral sclerosis, primary lateral sclerosis, progressive bulbar palsy, progressive muscular atrophy) with different survival. The aim was to determine differences in survival depending on the MND type, involved neurological system on beginning, gender, age, duration of symptoms up to and from the beginning of treatment with riluzole.

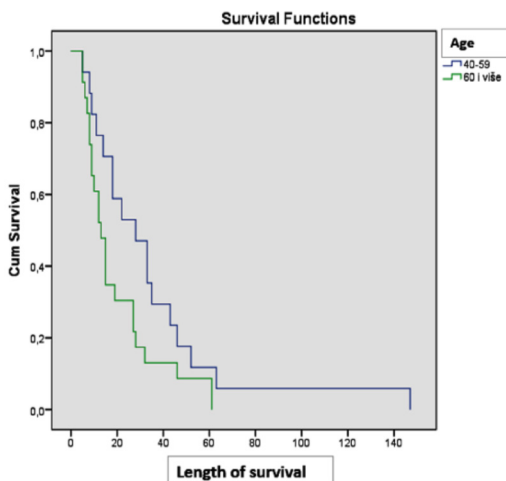
Methods: The study was designed as a retrospective cross sectional, with data extracted from patients medical history. All the patients from 2007 till the end of 2017 were analyzed.

Results: We've analysed 49 patients. Negative correlation was found between the patient's age at the disease onset and the survival ($p < 0.027$) and positive correlation between the length of symptoms duration prior diagnose ($p < 0.001$) and duration of medical treatment with riluzole ($p < 0.020$) and survival. Patients treated more then 1 year with riluzole ($p < 0.013$) and had symptoms more than 1 year before diagnose was made ($p < 0.001$) had better survival. We haven't found difference in survival in respect to the gender, involved neurological system on the begining and type of MND.

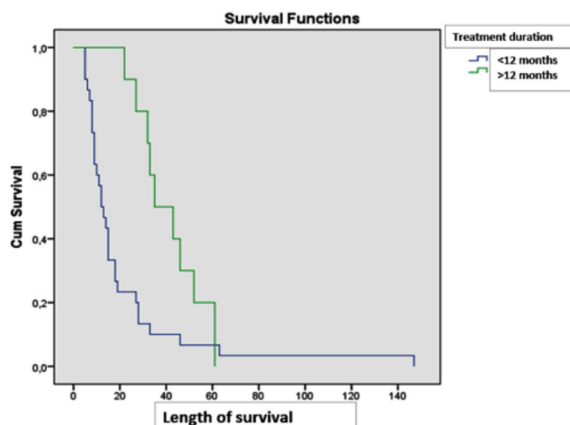
Conclusion: Younger patients, patients with symptoms lasting more than 1 year prior the diagnose and treated with riluzole more than 1 year had better survival. We haven't noticed influence of gender, disease type, neither involved neurological system on begining on survival.



Kaplan Meyer table-disease type



Kaplan Meyer table-age



Kaplan Meyer table-treatment duration

Disclosure: Nothing to disclose

EPO1172

Epidemiological data on ALS in Albania

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Background and aims: The primary objective of this study was to evaluate the hospital incidence of ALS in Albania.

Methods: This is a prospective study. All the patients who were suspected to suffer from ALS from all over the Country were hospitalized at the Department of Neurology, UHC “Mother Teresa”. The diagnosis was made based in the clinical notes, electrophysiological and imaging investigations. All the patients that fulfilled the criteria for ALS were included in our database. The data was retrieved from the patient files database during January 2018 -December 2019. First admission was used to calculate incidences. Age distribution was reported by sex and age group. The study is part of NDAL (Neurodegenerative Diseases in Albania) in collaboration with Center for Neurodegenerative Diseases and the Aging Brain, University of Bari “Aldo Moro”.

Results: A total number of 40 ALS patients, 27 (63%) males and 13 (32%) females were included. The mean age at diagnosis was 56+11.9 years old (max 76, min 21). Males developed ALS more frequently than females on the 5th decade of life. The mean annual incidence of ALS in Albania resulted 0,73 per 100,000 in 2018 and 0,66 per 100,000 in 2019.

Conclusion: ALS affects more frequently males than females in Albanian population. The mean age of 56 years old is almost the same compared to Western countries. ALS incidence in Albania results distinctively low in comparison to other European countries (considering the population in Albania the annual incidence was expected to be approximately 55 cases).

Disclosure: Nothing to disclose

EPO1173

The effect and challenges of nusinersen treatment in adult spinal muscular atrophy patients – preliminary results

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Background and aims: Nusinersen has been approved for all types of SMA, although there are no data from clinical trials in adult SMA type 3 patients. Therefore real-life experiences are essential to show safety and efficacy. We shared our real-life experience in adult patients.

Methods: Nusinersen was administered intrathecally on days 1, 29, 85, and 274. Hammersmith Functional Motor Scale-Expanded (HFMSE) scores were evaluated before the 1st dose and during the follow-ups. The feasibility of lumbar puncture (LP) and side effects of nusinersen were reviewed.

Results: 36 out of 40 patients were SMA type 3, 4 were type 2. The mean age was 34.4 (range:19-60). The mean HFMSE score was 27 (range:0-65), and 42.5% were ambulatory. Conventional LP could not be performed in 6 patients because of scoliosis. After placement of intrathecal catheter, 1 patient completed 3 doses without complications. 1 patient had LP under fluoroscopy-guidance, and 4 have been waiting for surgery. 1 patient discontinued the treatment due to the difficulty of the procedure. So far, 3 patients completed 4 loading doses. Post-LP headache was reported in 2% of LPs. 7 patients developed proteinuria.

Conclusion: Intrathecal administration of nusinersen was generally well-tolerated. Scoliosis was the main challenge that can be overcome by spinal catheter or fluoroscopy-guidance. LP may be the reason for abandoning treatment. The most common side effect was proteinuria that did not cause any discontinuation of treatment. At the time this abstract was written, post-treatment evaluations of patients by HFMSE scores have still been continued and will be presented during the meeting.

Disclosure: Nothing to disclose

EPO1174

Analysis of neuronal loss and pTDP-43 positive neuronal/glial inclusions between bulbar and lower-limb onset ALS phenotypes

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Background and aims: We aimed to see pathological features of bulbar onset and lower-limb onset ALS phenotypes in relation to neuronal loss and pTDP-43 inclusions.

Methods: Brain tissues from 8 bulbar-type ALS patients and 7 classic-type ALS patients with lower limb onset were obtained at autopsy from Toneyama National Hospital. Neuronal loss and gliosis in routine sections were semiquantitatively evaluated. The number of pTDP-43 positive neuronal/glial inclusions were scored in each section using a semiquantitative grading system.

Results: The bulbar-type patients showed neuronal loss: 8/8 (1 mild, 2 moderate, 5 severe) in the hypoglossal nuclei in contrast to the lower-limb onset patients: 6/7 (3 mild, 2 moderate, 1 severe). In the anterior horn of lumbar cords, all patients showed neuronal loss (i.e. bulbar-type patients: 6 mild, 1 moderate, 1 severe; lower-limb onset: 1 mild, 4 moderate, 2 severe). There was a tendency for clinical symptom at onset to affect pathological severity in neuronal degeneration of motor neurons. pTDP-43 staging showed more inclusions in the bulbar-type, Brettschneider stage III and IV (each 4 patients respectively) than in lower-limb type, stage II (2), III (4) and IV (1). We could not find any feature of topographical distribution of inclusions in the supra-tentorial nuclei between bulbar and lower-limb types.

Conclusion: Phenotypes of ALS might affect severity of neuronal loss in motor nuclei. We could not find a clear tendency in pTDP-43 inclusions in either phenotype.

Disclosure: Nothing to disclose

Movement disorders 1

EPO1175

Peripheral silent period in cervical and generalized dystonia

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Background and aims: Dystonia is an involuntary movement disorder in which continuous or intermittent muscle contractions cause abnormal postures or repetitive movements. Abnormalities sensorimotor integration and inhibitory pathways are accused in pathophysiology of dystonia. The aim of this study was to investigate the state of inhibitory pathways in spinal cord in dystonia by recording silent period (SP).

Methods: We included 23 patients with dystonia (12 female, 11 male); 10 patients (44.0%) with cervical dystonia and 13 with generalized dystonia. We also recruited 19 healthy subjects (11 female, 8 male; p=0.711) as a control group. Age was similar between groups (41.4±12.1 vs 36.2±5.2 years, p=0.092). To record SP, surface electrodes were placed over belly of right abductor pollicis brevis (APB) muscle while subject was performing a moderate contraction. For cutaneous stimulation (CuSP), stimulus was 20 times sensory threshold in intensity and applied on right index finger. For mixed nerve stimulation (MnSP), stimulus at 3 times motor threshold was applied on median nerve at wrist.

Results: Regarding onset latency, duration and suppression index of CuSP, the onset and end latencies of MnSP as well as its duration there was no difference between patients with dystonia and healthy subjects. Comparisons of patients with segmental and generalized dystonia showed I2 suppression index was low in patients with generalized dystonia.

Group Statistics					
	grupikili	N	Mean	Std. Deviation	Std. Error Mean
I1onsetlatency	3,00	3	43,6667	3,21455	1,85592
	1,00	20	45,3400	8,18062	1,82924
I2onsetlatency	3,00	18	76,7444	21,87094	5,15503
	1,00	22	76,9364	12,74757	2,71779
LLRonsetlatency	3,00	3	59,6667	2,51661	1,45297
	1,00	18	56,1889	16,10692	3,79644
I2duration	3,00	3	75,6667	11,17915	6,45428
	1,00	21	68,5238	14,19570	3,09776
I121duration	3,00	17	38,2706	10,21419	2,47731
	1,00	20	38,4050	10,59426	2,36895
I2endlatency	3,00	17	119,4588	16,14385	3,91546
	1,00	21	117,2476	14,99452	3,27207
suppindex	3,00	17	98,7294	5,23877	1,27059
	1,00	21	93,6667	15,91645	3,47325

CUSP

Group Statistics					
	grupikili	N	Mean	Std. Deviation	Std. Error Mean
mnspon	3,00	18	25,1222	1,53568	,36196
	1,00	21	25,5667	1,68266	,36719
mnsppoff	3,00	18	110,6500	11,64304	2,74429
	1,00	21	113,2381	19,07036	4,16149
mnsppdur	3,00	18	85,5278	11,50712	2,71225
	1,00	20	87,8050	19,43010	4,34470

MNSP

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
I1onsetlatency	Between Groups	7,304	1	7,304	,119	,734
	Within Groups	1292,195	21	61,533		
	Total	1299,499	22			
I2onsetlatency	Between Groups	,365	1	,365	,001	,973
	Within Groups	11544,255	38	303,796		
	Total	11544,620	39			
LLRonsetlatency	Between Groups	31,101	1	31,101	,134	,719
	Within Groups	4423,024	19	232,791		
	Total	4454,126	20			
I1duration	Between Groups	133,929	1	133,929	,688	,416
	Within Groups	4280,305	22	194,559		
	Total	4414,233	23			
I2duration	Between Groups	,166	1	,166	,002	,969
	Within Groups	3801,805	35	108,623		
	Total	3801,971	36			
I2endlatency	Between Groups	45,935	1	45,935	,191	,665
	Within Groups	8666,694	36	240,741		
	Total	8712,628	37			
suppindex	Between Groups	240,800	1	240,800	1,574	,218
	Within Groups	5505,782	36	152,938		
	Total	5746,582	37			
mnspon	Between Groups	1,915	1	1,915	,732	,398
	Within Groups	96,718	37	2,614		
	Total	98,632	38			
mnsppoff	Between Groups	64,921	1	64,921	,251	,619
	Within Groups	9578,095	37	258,867		
	Total	9643,016	38			
mnsppdur	Between Groups	49,128	1	49,128	,188	,667
	Within Groups	9424,086	36	261,780		
	Total	9473,214	37			

ANOVA

Conclusion: We found no difference regarding spinal inhibitory circuits in patients with cervical or generalized dystonia. However, there was less suppression during CuSP in patients with generalized dystonia whereas it was similar to healthy subjects in patients with cervical dystonia.

Disclosure: Nothing to disclose

EPO1176

Role of increasing levels of the hormone cortisol in cognitive impairment in Parkinson's disease

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Background and aims: Elevated cortisol levels are found in many diseases.

Methods: We studied the level of morning plasma cortisol in Parkinson's disease (PD) in 68 patients who was hospitalized in Department 1 of TMA neurology in the period 2015 to the present. The results of the study were statistically analyzed. Cortisol was determined in all blood samples of patients of the Main and Control groups. The control group consisted of 47 volunteers. The concentration of cortisol was studied by enzyme immunoassay on an automatic analyzer EL808 Ultra Microplate Rider (BIO-TEC Instruments, Inc) using standard sets of reagents "Steroid IFA-cortisol-01" series No. 061P and "Non-extraction IGF-1 ELISA DSL-10-2800". The reference values of the norm of cortisol were 50-250 mg/ml. To assess cognitive status, we evaluated on the MMSE scale, MOCA test.

Results: 50-250mg/ml

250-500mg/ml

500-900mg/ml

Main group n=68

20 (29.4%)

3 (54.4%)

1116.1%)

Control group n=47

32 (68%)

9 (19.1%)

3 (6%)

Spearman's rank correlation coefficient. The relationship of cortisol levels and indicators of cognitive impairment.

Groups

MMSE

MOCA test

Main group

n=68

r=-0.45, p=0.03

r=-0.13, p≥0.05

Control group

n=47, r=0.77, p=0.02

r=0.74, p=0.04

The relationship between the value of cortisol and the assessment of cognitive impairment was determined. In the main group, a statistically significant moderate inverse correlation was determined between plasma cortisol level and cognitive impairment in PD. When studying cortisol levels in PD, its significant increase is noted than in the control (p<0.05).

Conclusion: Increased levels of the hormone cortisol in Parkinson's disease play an important role in cognitive impairment and during the course of the disease and affect the effectiveness of PD therapy.

Disclosure: Nothing to disclose

EPO1177

Non-motor symptoms in a cohort of patients undergoing bilateral subthalamic stimulation

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M. Cánovas Iniesta, L. Fuentes Rumí, E. García Molina,

G. Valero López, A.E. Báidez Guerrero, J. Jimenez Veiga,

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Background and aims: Deep brain stimulation (DBS) of the subthalamic nucleus is an effective therapy in the improvement of motor fluctuations in patients with advanced Parkinson's disease (APD). In recent years, the importance of the presence of non-motor symptoms (NMS) in reducing the quality of life of affected patients has been demonstrated

Methods: Retrospective study of a cohort of patients undergoing DBS in our center, in which the presence of NMS is studied.

Results: 32 patients were interviewed, obtaining a median of 86.5±78 in Parkinson's disease sleep scale, with 31.3% of patients with a score below 86 points, a median of 21±16 in MOCA (Montreal Cognitive Assessment), with 48.1% of patients below 14, and a median of 18.5±13.2 in Beck Depression inventory with 59% of patients within the category of "moderate-severe" depression. 93.7% of the patients presented both hyposmia and pain, and all of them, some dysautonomic symptom. Being a woman [0.072 95% CI (0.007-0.713), p=0.025], and a shorter illness time [0.834, 95% CI (0.692-0.999), p=0.05], protects against a worse quality of sleep. The worst results in MOCA were related with the time of illness [3,741 (95% CI 3.7-12.5), p=0.01], however, in the multivariate analysis the association was lost. The presence of premotor symptoms was associated in the univariate analysis with a worse score in Beck's inventory [OR: 4.81, 95% CI (1,001-25.65), p=0.05], without remaining in the multivariate.

Conclusion: Patients with APD submitted to DBS present significant amount of NMS.

Disclosure: Nothing to disclose

EPO1178

Features of sensory-motor integration between visual perception and the oculomotor system and their MRI correlates in Parkinson's disease

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Background and aims: The eye movements and visual functions are closely interconnected to percept the world properly. Optokinetic reflex (OKN) and saccades reflect visual-motor interaction during the image transferring from the peripheral retina to the fovea. Visual disturbances along with a brain structure degeneration in PD lead to action/perception dissociation. We investigated the relationship between the visual function state, oculomotor parameters and MRI morphometry

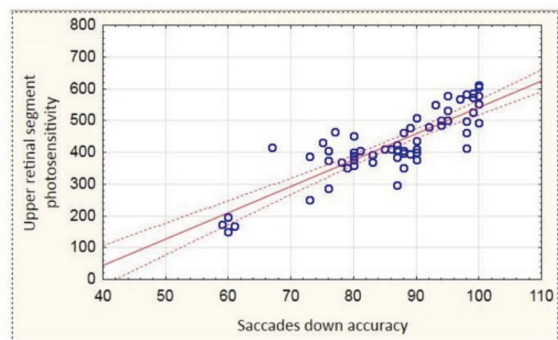
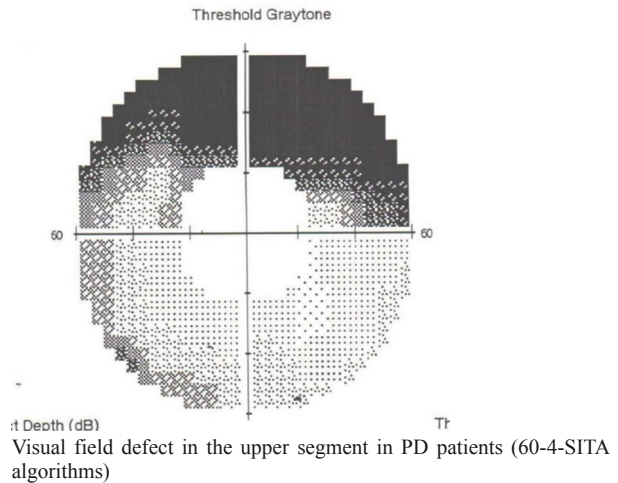
Methods: 42 PDpatients with 2–3 stages and 20 age-matched controls were examined. OKN and saccades were investigated by video-oculography. Threshold perimetry with photosensitivity determination in the central and peripheral retina assessed the visual function. MRI study was performed with voxel-based morphometry analysis.

Results: There was a significant decrease in the vertical saccades accuracy and velocity, vertical OKN velocity with relatively unchanged saccads and OKN in horizontal direction in PDpatients (table). The visual field defect predominately was located in the superior region of the peripheral retina, especially in PDpatients with postural instability. A decrease in the photosensitivity in this retinal region was correlated with a decrease in the downward saccade parametres, and vertical OKN velocity in both directions (figure 1 and 2). Positive correlation was established between reduced in the volume of inferior temporal gyrus, posterior parietal cortex, cuneus and velocity of vertical OKN and saccades, between retinal photosensitivity and volume in posterior parietal cortex and cuneus.

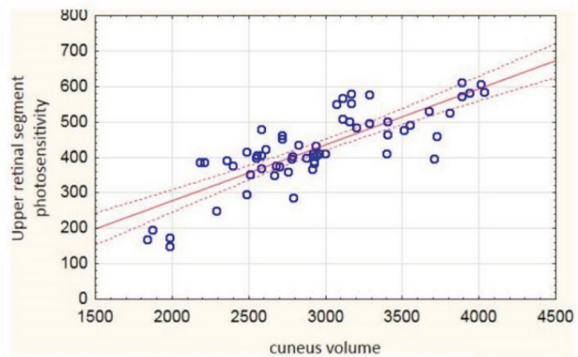
Movement direction	Groups	Saccadic test		OKN	
		Accuracy (%)	Velocity %/c	Stimulus velocity 20°/s	
				Velocity %/c	Gain (%)
Me (Q1, Q3)					
Left	control group	96 (88; 100)	465 (423; 503)	21,3 (20,7; 22,8)	107 (103; 114)
	PD patients	93 (87; 95)	443 (408; 500)	19,7 (17,9; 22,8)	98,8 (94,1; 113)
Right	control group	97 (86; 99)	462 (420; 500)	22 (19,5; 22,9)	110 (107; 115)
	PD patients	91 (85; 94)	443 (414; 484)	19,9 (18,5; 22,3)	99,5 (95,4; 109)
Up	control group	95 (88; 99)	456 (423; 496)	22 (20,7; 23,2)	101 (95; 110)
	PD patients	73 (66; 84)*	346 (266; 393)*	14,8 (10,6; 18,7)*	73 (55; 91)*
Down	control group	96 (87; 98)	450 (424; 502)	21 (20,1; 22,6)	99 (90; 113)
	PD patients	70 (61; 86)*	367 (299; 414)*	14,8 (11,3; 18,3)*	74 (53,1; 93)*

* - Statistically significant difference (p < 0.05) between 1st and control groups (Mann-Whitney test);

Table. Comparative assessment of the saccadic and OKN parameters in PD patients and control group



A. Correlation: r = 0,795



B. Correlation: r = 0,757

An example of a positive correlation between retinal photosensitivity in the upper peripheral segment and saccades down accuracy (A); between retinal photosensitivity in the upper peripheral segment and volume in cuneus

Conclusion: The disturbance of inputs from the superior retina has a great influence on the disturbance of vertical oculomotor reflexes, and is associated with a decrease in the brain structures volume involved in visual perception in PD.

Disclosure: Nothing to disclose

EPO1179

May safinamide have a role in atypical parkinsonism? a retrospective study in clinical practice

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Background and aims: Safinamide (50-100mg) has proved efficacy as an add-on treatment to levodopa in fluctuating Parkinson's disease (PD). Atypical parkinsonian syndromes (AP, progressive supranuclear palsy, PSP, Multiple System Atrophy, MSA, Corticobasal Syndrome, CBS) have a poor prognosis and lack specific treatment. Drugs approved for PD are commonly used off-label for symptomatic treatment in AP.

Methods: Retrospective study (2016-2020) of electronic records of our Movement Disorders Unit: patients with clinical diagnoses of AP with a safinamide prescription were registered. Clinical Global Impression of Improvement (CGI-I) was used for efficacy assessment.

Results: 26 patients, 10 (38%) male, mean 70±10 years, with diagnosis of MSA (14), PSP (11) and CBS (1), and disease duration 7±4 years were prescribed safinamide at 50mg (1), 100mg (21) or 200mg (4). 1 patient was lost to follow-up before reassessment, and the remaining 26 were followed a mean of 8±9 months afterwards. 8 patients (32%) experienced mild adverse events (drowsiness, confusion, feeling unwell, headache). 9 patients (32%) (6 MSA, 3 PSP, 1 CBS) followed 13±11 months improved with safinamide (CGI-I 1 in 1, 2 in 6, 3 in 3), mainly in mobility (6), falls (5), mood (2), pain (2), sleep (1), dyskinesia (1). 14 cases did not improve (11) or minimally worsened (3), leading to discontinuation after 4±4 months.

Conclusion: In our experience with AP, off-label safinamide treatment was overall well tolerated, and had a clinical benefit in a subset of patients. Clinical trials are warranted to establish efficacy and safety of safinamide in this clinical setting.

Disclosure: Nothing to disclose

EPO1180

Cerebral cavernomatosis as a chameleon of Parkinson's disease

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Background and aims: Idiopathic Parkinson's Disease (IPD) is the commonest type of parkinsonian syndromes and has a good response to levodopa. Secondary causes account for 14–16% of the cases, and usually have a poor response to levodopa treatment.

Methods: Clinical case

Results: A 53-year-old-male patient with previous history of cavernomatosis multiple with secondary epilepsy and severe cervical and postural limb tremor, treated with zonisamide 100mg/day, propranolol 120mg/day and carbamazepine 400mg/day, presented with subacute worsening of the gait and tremor and appearance of nocturnal akinesia and slowness in daily activities. The neurological examination revealed a severe akinetic-rigid syndrome with exuberant rest tremor lateralized to the right side, hypomimia and incapacity of gait without pyramidal, autonomic, cerebellar signs or cognitive impairment. Brain MRI demonstrated countless cerebral cavernomas, involving the right pallidocapsular region. Analytic investigation was negative in blood and urine. The patient was started on levodopa trial with gradually increase doses to 300mg per day with improvement of tremor, gait and akinetic-rigid syndrome, being able to walk with a stroller after 2 weeks on treatment. Posterior Datascan revealed a loss of pre-synaptic nigrostriatal neurons in both caudate nucleus, more on the left side.

Conclusion: The uncommon location of pallidal cavernomas could explain the parkinsonian symptomatology, and the stepwise progression is more typical in vascular parkinsonism. However, the good response to levodopa should raise the possibility of IPD. This differentiation between IPD and secondary causes is important not only for the choice of treatment but also for the prognosis of patients.

Disclosure: Nothing to disclose

EPO1181

Peripheral neuropathy in patients with idiopathic Parkinson's disease

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Background and aims: Parkinson's disease (PD) is a neurodegenerative disorder that affects motor system. Peripheral nerves are frequently involved in patients with PD that negatively influences on their quality of life.

Our aim was to assess the frequency and type of peripheral neuropathy (PNP) in PD patients.

Methods: The study comprised 56 patients with PD (31 males, 25 females aged 64-82 years, disease duration was 2-10 years) and 46 age and gender matched controls. Nerve conduction studies were performed in median, ulnar, peroneal, tibial and sural nerves of both limbs. Statistics performed by SPSS -14.0.

Results: Electrophysiological abnormalities consistent with a diagnosis of PNP were found in 30 PD patients (53.6%), who were older (76.3±6.1 vs 70.5±6.3 years) and had a longer duration of PD, compared to 13 healthy controls (28.3%). The most common type of PNP in PD patients was motor demyelinating (30.4%) axonal motor and sensory PNP detected in 23.3%. The most common type of PNP in healthy controls was axonal motor and sensory PNP and in 17.4% and sensory PNP in 10.9% (p<0.01).

Conclusion: PNP is common in PD patients compared to healthy controls. The most common type is the motor demyelinated PNP. Polyneuropathy is rarely found. Our results suggest the correlation between the presence of motor neuropathy in PD and age of patients (p<0.5). No correlation was found between the presence of PNP and gender.

Disclosure: Nothing to disclose

EPO1182

Super-responders to opicapone adjunct treatment to levodopa in parkinson's disease patients with motor fluctuations: combined post-hoc analysis of BIPARK-I and II

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Background and aims: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved to be effective in treating end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2].

Methods: OPC 50-mg data from BIPARK I and II [1,2] were combined to evaluate the efficacy and safety of patients who were considered 'super-responders' (≥2 hours of OFF-time reduction or ≥2 hours of ON-time increase from baseline to double-blind endpoint). Efficacy was assessed by applying Patient and Clinician-Global Impression of Change (PGI-C and CGI-C). Safety was assessed by incidence of at least possibly related treatment-emergent adverse-events (TEAEs).

Results: A total of 265 patients were treated with OPC 50-mg, of whom 100 were super-responders (Safety Set, Table 1). Super-responders had longer duration of daily OFF-time at baseline and were treated with a higher mean daily levodopa amount but had similar Hoehn and Yahr stage, disease duration and onset of motor fluctuations. The percentages of patients rated as showing improvement on both PGI-C and CGI-C were approximately 15% higher for super-responders than for total study population treated with OPC 50-mg (Figure 1). The incidence of at least possibly related TEAEs was similar, with higher dyskinesia rates in super-responders (most likely due to the higher mean daily levodopa at baseline) but low overall and dyskinesia-related discontinuations (Table 2).

Table 1. Baseline characteristics (Safety Set)

Characteristic	Total study population	Super-responders
	OPC 50 mg N=265	OPC 50 mg N=100
Male gender, n [%]	160 (60.4)	60 (60.0)
Age, mean (SD) years	64.5 (8.8)	64.7 (8.8)
Disease duration, mean (SD) years	7.6 (4.3)	7.5 (3.8)
Onset motor fluctuations (SD) years	2.7 (2.9)	2.4 (1.8)
Hoehn & Yahr staging at ON state	2.4 (0.5)	2.3 (0.5)
Daily OFF-time, mean (SD) hours	6.2 (2.0)	6.9 (2.1)
Levodopa dose, mean (SD) mg/day	698.1 (322.8)	751.3 (337.6)

OPC, opicapone; SD, standard deviation

Table 1

Figure 1. Proportions of patients who were rated as improved* (assessed by PGI-C and CGI-C) in total study population (n=262) and super-responders (n=100) at study endpoint following treatment with OPC 50-mg (Full Analysis Set). *Improvement was defined as being rated as 'very much improved', 'much improved' or 'minimally improved'. CGI-C, Clinical Global Impression of Change; OPC, opicapone; PGI-C, Patient Global Impression of Change

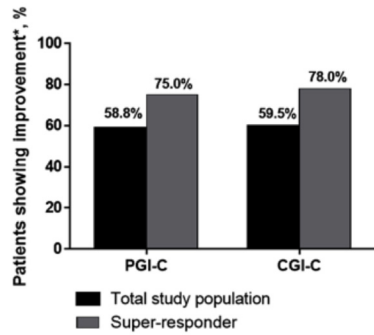


Figure 1

Table 2. Summary of TEAEs (Safety Set)

	Total study population	Super-responders
	OPC 50 mg N=265	OPC 50 mg N=100
At least possibly related* TEAEs, n (%)	113 (42.6)	46 (46.0)
Most frequently reported ^b at least possibly related* TEAEs, n (%)		
Dyskinesia	52 (19.6)	25 (25.0)
Constipation	10 (3.8)	4 (4.0)
Insomnia	8 (3.0)	3 (3.0)
Nausea	9 (2.6)	1 (1.0)
At least possibly related* TEAEs leading to discontinuation, ^b n (%)	20 (7.5)	3 (3.0)
Dyskinesia	8 (3.0)	1 (1.0)

*Relationship to study medication reported as 'possible', 'probable', 'definite' or missing; ^b≥2% of patients in total study population (n=265). OPC, opicapone; TEAE, treatment-emergent adverse event

Table 2

Conclusion: Super-responders to OPC 50-mg showed a high patient and clinician global impression of change and favourable tolerability.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.
2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPO1183

MiR-146 as a potential biomarker for Parkinson's disease

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Background and aims: Parkinson's disease (PD) is the most common movement disorder worldwide. In some cases it develops due to genetic mutations, but in most cases it is multifactorial. In the last few years there is an increasing interest on epigenetic mechanisms in the development of PD. 1 of the most important epigenetic regulators is microRNA. Previously the difference in expression of microRNA in PD and control groups has been shown in various brain regions, blood, iPSC. The aim of this study is to analyze a role of microRNA as a potential biomarker of PD.

Methods: 20 patients with PD and 10 healthy volunteers were included in the study. Expression of miR-132, miR-7, miR-146 was explored. Total RNA was extracted from blood leukocytes using RNeasy Mini Kit (Qiagen), then specific reverse transcription for each microRNA was performed with a kit for reverse transcription with stem-loop primers, followed by real-time PCR with fluorescent probes. MiR-191 was used as a housekeeping gene. Expression has been measured using ΔC_t method. Data analyses was performed with Statistica 10.0.

Results: There was significant overexpression of miR-146 in leucocytes of patients with PD compared to healthy controls ($p=0.03$, Mann-Witney U test). MiR-146 expression negatively correlated with UPDRS total score ($R=-0.47$, $p=0.025$, Spearman's rank correlation).

Conclusion: MiR-146 should be considered as a potential biomarker for PD. Further investigation is needed to confirm the diagnostic role of this microRNA.

Disclosure: This work is supported with Russian Science foundation grant №17-75-20211

EPO1184

Effectiveness, tolerability and safety of opicapone in fluctuating Parkinson's disease

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Background and aims: To evaluate the effectiveness, tolerability and safety of opicapone as an add-on to levodopa in fluctuating Parkinson's disease (PD) patients.

Methods: Observational, retrospective, cohort study that included fluctuating PD patients who started opicapone 50mg/day as add-on to levodopa. Demographic and clinical data were recollected. Clinical effectiveness was assessed by the Clinical Global Impression of Change (CGI-C) at the follow-up visit. The effect on dyskinesia and the presence of adverse events (AEs) were also reported.

Results: We included 35 fluctuating PD patients. The clinical characteristics of patients are shown in table 1. 18 patients showed non-troublesome dyskinesia at baseline (mostly mild). At the follow-up visit, 65.7% of patients showed a clinical improvement (CGI 1-3) and 17.2% a worsening (CGI 5-7) (Figure 1). 42.9% of patients referred at least one AE ($n=12$ one AE/patient, $n=3$ 2 AEs/patient) of mild to moderate intensity. Dyskinesia was the most frequent AE reported. The frequency of AEs is described in Table 2. 7 patients withdrew prematurely from opicapone because of AEs and/or lack of benefit, 17 patients maintained the treatment, 6 patients reduced the Levodopa Equivalent Daily Dose (LEDD) mainly because of AEs and 5 increased the LEDD because of an insufficient benefit. There were no differences between LEDD in baseline and follow-up visit ($p=0.3941$). We neither found predictive clinical variables associated with clinical improvement.

Table 2: Adverse Events at follow-up visit

Dyskinesia (n (%))	9 (25.7%)
Intensity:	
-Mild worsening	4
-Moderate worsening	5
History of dyskinesia at baseline visit:	
-Dyskinesia-naïve PD	4
-Dyskinesia history	5
Hallucinations (n (%))	2 (5.7%)
Insomnia (n (%))	2 (5.7%)
Dizziness (n (%))	2 (5.7%)
Worsening of a pre-existing impulse control disorder (n (%))	2 (5.7%)
Constipation (n (%))	1 (2.9%)

*None of our patients developed nausea/vomiting, somnolence, dry mouth, cramps, muscle pain nor blood CPK increased

Table 2. Adverse Events at follow-up visit

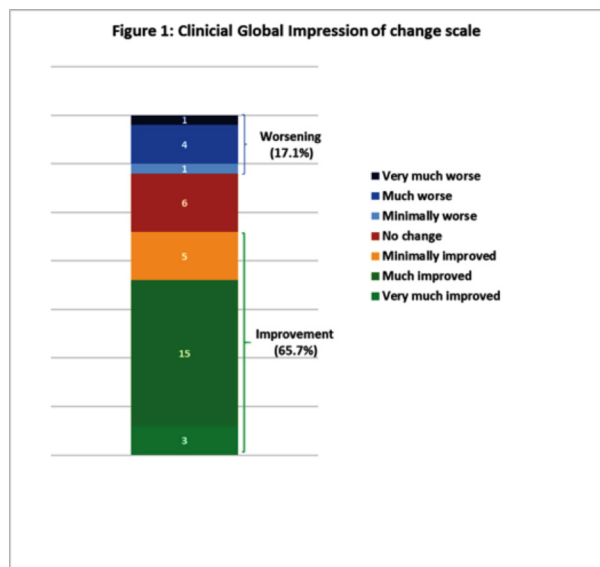


Figure 1. CGI-C scale

Table 1: Demographic and clinical data at baseline visit

Total PD patients (n)	35
Sex (female; n(%))	17 (48.6%)
Age (years)*	72.9 [62.1-77.1]
Disease duration (years)*	9.4 [6.3-13.5]
mH&Y score*	2.5 [2-3]
History of falls (n (%))	4 (11.4%)
Cognitive impairment (n (%)):	
-Mild Cognitive Impairment	3 (8.6%)
-Dementia	2 (5.7%)
History of Impulse Control Disorders (n (%))	7 (20%)
History of non-troublesome dyskinesia (n (%)):	
-Mild dyskinesia	17 (48.6%)
-Moderate dyskinesia	1 (2.9%)
LEDD (mg/day)*	880 [710-1230]
Follow-up visit (months after Baseline-visit)*	4.7 [3-7]

*Median [Interquartile range], mH&Y= modified Hoehn &Yahr scale, LEDD = Levodopa Equivalent Daily Dose

Table 1. Demographic and clinical data at baseline visit

Conclusion: Our results indicate that opicapone provides a significant motor improvement in fluctuating PD. Dyskinesia is the most common complaint that might be ameliorated adjusting the concomitant dopaminergic treatment.

Disclosure: Nothing to disclose

EPO1185

Distinctive blood alpha-synuclein profile and lysosomal alterations in Parkinson's Disease patients bearing GBA1 mutations

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Background and aims: Mutations in the GBA1 gene, encoding the lysosomal enzyme glucocerebrosidase (GCase), are the most frequent risk factor for Parkinson's disease (PD). The aim of this study is to characterize the blood profile of alpha-synuclein and the main lysosomal proteins of PD subjects carrying GBA1 mutations (GBA-PD), as well as their clinical features.

Methods: In this study we recruited 14 GBA-PD, 25 PD subjects without GBA1 mutations (iPD) and 31 healthy subjects (HC). We evaluated alpha-synuclein levels in peripheral blood lymphocytes, plasma exosomes and whole plasma and lysosomal alterations in lymphocytes by analyzing the expression of the main GCase-related proteins (cathepsin D, LAMP1, LIMP2, Saposin C). Moreover, we assessed motor and non-motor signs in all subjects by means of clinical questionnaires and scales (MoCA, UPSIT, RBDsq, UPDRS-III, SCOPA-AUT and BDI).

Results: In GBA-PD, both the alpha-synuclein expression in lymphocytes and the total plasma alpha-synuclein levels were significantly increased than iPD and HC. Furthermore, a significantly higher concentration of alpha-synuclein was detected in the exosomal vesicles in iPD than GBA-PD. The GBA-PD group also displayed lower Saposin C levels and higher LIMP-2 levels compared to iPD. A prevalence of non-motor features were observed in GBA-PD group compared to iPD.

Conclusion: This study confirms the presence of distinctive lysosomal alterations related to GCase enzyme deficiency in GBA-PD group compared to iPD and highlights that differences also exist in the blood alpha-synuclein profile between patient's group.

Disclosure: Nothing to disclose

EPO1186

Coexistence of Klinefelter's syndrome and essential tremor: a case report

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Background and aims: Klinefelter's syndrome is the most common sex chromosomal anomaly among males and the most common cause of male infertility. Typical clinical features are long stature and disproportionately long extremities, gynecomastia, small testes, azoospermia and infertility. It is also frequently associated with developmental delay, mood problems, and behavioral issues. There are also controlled and uncontrolled studies in the literature that patients with Klinefelter syndrome have a higher prevalence of essential tremor than the general population.

Methods: A 41-year-old male patient was admitted to our clinic with tremor in both hands. The patient whose complaints started in 2000 was followed in our clinic with the diagnosis of essential tremor for 19 years. In last 6 months right hand resting tremor was added to the clinical findings. The patient's last neurological examination revealed bilateral upper extremity postural and actional tremor with resting tremor in the right thumb, without rigidity and bradykinesia. As the patient was tall and he had gynecomastia, we studied a karyotype genome analysis. The analyse revealed that 47 XXY was consistent with Klinefelter syndrome.

Results: Our patient was resistant to medical treatment and some treatment options could not be used because of comorbid diseases of the patient and finally we planned to evaluate the patient for deep brain stimulation (DBS).

Conclusion: Our case will be discussed together with Klinefelter syndrome and essential tremor or essential tremor-like clinical cases reported in the literature.

Disclosure: Nothing to disclose

EPO1187

Long-term efficacy of botulinum toxin in facial movement disorders

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Background: Botulinum toxin type A injections is known as the best treatment for facial movement disorders. **Aim:** To examine the long-term effect of 2 botulinum toxin A products, Botox (Allergan) and Dysport (Madison) in patients with hemifacial spasm, facial synkinesis and benign essential blepharospasm

Methods: Registry analysis of 87 consecutive patients (51 women, 36 men) who had undergone treatment for ≥ 6 years. The long term effects, as well as side effects of Botox or Dysport local injection were evaluated.

Results: The mean treatment duration was 9.9 (range 6-11, SD 1.0) years. A total of 2441 treatments were given, 1162 with Botox and 1279 with Dysport. Good to full improvement was seen in 89% of treatments both with Botox and with Dysport. Treatment responses were consistent during the study with both drugs. Side effects were relatively few, mainly ptosis and lacrimation (6.1% in visits 1-3, and 3.9% in visits 4 thru study end).

Conclusion: A good long-term effect for local injection of botulinum toxin A (BTX-A) was observed in patients with hemifacial spasm, facial synkinesis and benign essential blepharospasm. Both BTX-A, Botox[®] (Allergan) and Dysport[®] (Madison) were effective. The two botulinum toxin A brands were interchanged as needed

Disclosure: Nothing to disclose

EPO1188

Wilson and Parkinson's disease: beyond copper metabolism

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Background and aims: Parkinsonism is evident in approximately 40% of patients with Wilson's disease and responds favourably to metabolism control. Single photon emission computed tomography (SPECT) studies suggest both presynaptic and postsynaptic nigrostriatal dopaminergic damage, although not universally. Anecdotal case reports communicated favourable response to levodopa. Transcranial sonography (TCS) findings include mostly lenticular nucleus hyperechogenicity, while substantia nigra hyperechogenicity (SN+) is rare.

Methods: Case report.

Results: A 35 year-old woman was referred to our clinic 15 years after Wilson's disease diagnosis. Clinical onset was at the age of 20 with cognitive impairment, upper limb tremor and dystonia, all successfully controlled with D-penicillamine, zinc and trihexyphenidyl. 10 years after she presented bilateral feet dystonia and dysarthria, partially responsive to trientine and botulinum toxin injections. Treatment was suspended for 3 months without clinical changes, and zinc was restarted due to liver enzymes increase. 4 years later, she complained of slowness and gait problems leading to several falls, and bradykinesia and freezing of gait were evident on examination. A SPECT-DaTscan showed presynaptic damage and TCS hyperechogenic substantia nigra without abnormalities in lenticular nucleus. Levodopa 300mg daily improved symptoms, and a marked clinical worsening was noted after discontinuation.

Conclusion: We present a case of Wilson's disease with late onset parkinsonism unrelated to copper balance, with positive DaTscan and TCS similar to sporadic PD, as well as favourable response to levodopa. While a very unusual presentation of Wilson's disease is the most likely diagnosis, the possibility of an independent disorder such as a juvenile Parkinson's disease needs to be considered.

Disclosure: Nothing to disclose

EPO1189

Substantia nigra echogenicity as a predictor of drug withdrawal response in suspected drug-induced parkinsonism: a five year follow-up study

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Background and aims: Differential diagnosis between drug-induced parkinsonism (DIP) and Parkinson's disease (PD) is challenging, as 15% of suspected DIP are actually PD unmasked by drug exposure. Substantia nigra hyperechogenicity (SN+) as detected with transcranial sonography (TCS) has proved useful for PD diagnosis. In a previous study (n=60), we assessed the role of TCS in suspected DIP, obtaining a positive predictive value (PPV) of SN+ of 49.9% for underlying PD. We hypothesized a longer follow-up could increase the PPV if more incidental PD cases were registered.

Methods: At the end of the previous study 16 patients had PD diagnosis, and 44 DIP (7 SN+, 37 SN-), being clinical resolution after drug withdrawal the diagnostic gold standard. 44 DIP patient's records were analysed 5 years after the completion of the study.

Results: After a mean follow up of 2.1 years (0-5), incidental PD diagnosis occurred in 2 SN+ patients (28.6%) and 1 (2.7%) SN-. 10 patients died (1 SN+, 9 SN-). Accuracy of SN+ to distinguish PD from DIP improved in terms of sensitivity 88% (82.4%), specificity 88% (previous 85.4%) and PPV 54.5% (49.9%); with similar negative predictive value 96.2% (96.5%), area-under-the-curve 0.83. The hazard ratio for final PD diagnosis in SN+ subjects with suspected DIP was 11.4 (95% confidence interval 3.7-34.8, p<0.0002).

Conclusion: This study strengthens the role of TCS in the assessment of suspected DIP, not only for differential diagnosis but also as a prognostic tool. In our study, PPV of SN+ improved by 5%, even if follow-up was potentially insufficient in some patients.

Disclosure: Nothing to disclose

EPO1190

The potential of asymmetric stimulation frequency in subthalamic stimulation for Parkinson's disease

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Background and aims: Subthalamic deep brain stimulation (STN-DBS) is the best treatment for motor fluctuations in Parkinson's disease (PD). High-frequency stimulation (HFS) (i.e. from 130Hz) is classically the best choice to control the segmental PD symptoms. Higher frequencies (i.e. 130-180Hz) can further improve the tremor. However, HFS may also have slight differential effect on akinesia and tremor, but can also worsen some symptoms as gait. Cartesia-Boston[®] system for STN-DBS (Vercise Cartesia[™] Directional Lead, Boston Scientific, Valencia, CA, USA) allows configuring different frequency stimulation between left and right sides. As the motor symptoms of the PD are asymmetrical, we aimed to display if differentiated frequency can improve the tremor in patients with STN-DBS.

Methods: Postoperatively, after 1 year, 17 PD patients with STN-DBS were assessed in 4 conditions (stimulation on/medication off, stimulation off/medication off, stimulation off/medication on, stimulation on/medication on). 4 (age between 56 and 68 years old; H/F=3/1; disease duration between 12 and 25 years old) were not satisfied because of a persistent asymmetrical tremor. Differentiated frequency was proposed with higher frequency to control the tremor.

Results: Differentiated HFS (185Hz vs 140Hz for 3 patients, 174Hz vs 130Hz for the last 1) reduced the tremor subscore and clinical global impression for 3 patients in comparison with symmetrical HFS (130Hz bilaterally). No worsening of the total MDS-UPDRS III was highlighted.

Conclusion: Differentiated HFS is an option to reduce tremor in STN-DBS patients. More studies are needed to assess which profile of PD patients could benefit from it.

Disclosure: Nothing to disclose

EPO1191

Prevalence of depression in Parkinson's disease patients in Albania and the relationship with gender and stage of disease

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Background and aims: Depression is 1 of the most common non-motor symptoms in PD with a large negative impact on patient's quality of life. It is largely unrecognized by neurologists, emphasizing the need of an approach to psychiatric symptoms by non-psychiatrists in order to ensure an early diagnosis of depression in PD.

Methods: We include in this study 76 PD patients, range age 42-79 age range, diagnosed from neurologists in Department of Neurosciences in UHC "Mother Teresa", Tirana Albania. They were presented in out patient service in our department, from december 2018 to june 2019. All of them was underwent neurological examination with UPDRS test, MMSE, HAM-D.

Results: In this study are included 76 PD patients, range age 42-79 years, 77% of PD patients were presented with depression symptoms. 43% of patients were male and 57% female. 76% of patient with depression had a Hoehn&Yahr stage ≥ 3 ($p=0.001$). There was no statistically significant difference in the prevalence of depression between man and women ($p=0.279$). Later stages of PD patients had higher prevalence and gravity of depression ($p<0.001$). Patients with depression that had long years with PD had higher scores in HAM-D ($p<0.001$)

Conclusion: High prevalence of depression in our PD patients with an important correlation with stage and years of disease. There wasn't any important difference between man and woman.

Disclosure: Nothing to disclose

EPO1192

Diplopia in Parkinson's disease, a possible role of dopaminergic treatment

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Background: Diplopia could be present in 10-30% of Parkinson's Disease (PD) patients. Its pathophysiology is discussed; associations with dementia and visual hallucinations have been proposed. Diplopia is also reported as a non-common side effect of dopamine-agonist (DA).

Objective: Aim of our study was to explore the role of dopaminergic treatment in PD patients with diplopia.

Method: PD non-demented patients with diplopia were retrospectively recruited and matched with PD patients without diplopia for age and disease duration. Motor and cognitive assessment was evaluated at baseline (T0) and after 1 year (T1) from diplopia onset. In diplopic patients DA was reduced or withdrawn. For each patient we evaluated Daily Levo-Dopa Dose Equivalent Total (LEDD-T) and for DA (LEDD-DA). Presence of other side effects of DA was assessed.

Results: 40 PD were recruited, 20 with diplopia and 20 without (age 58.8 ± 12.4 vs 59.7 ± 11.2 years, disease duration 13.25 ± 8.3 vs 13.7 ± 7.2 years respectively), all patients were assuming DAs. LEDD-T and LEDD-DA were significantly higher in diplopic patients than in those without diplopia ($p=0.044$, $p=0.003$ respectively); mean disease time before diplopia onset was 7.3 ± 7.0 years. At T1 ten patients reported reduction or disappearance of diplopia. At both T0 and T1 no significant differences were found in motor evaluation, cognitive assessment, presence of hallucinations, somnolence and impulsive control disorder between groups.

Conclusion: Dopaminergic treatment, in particular DA, seems to have a role in the pathogenesis of diplopia in non-demented PD patients; however longer follow up is needed to validate the PD psychosis spectrum hypothesis for this symptom.

Disclosure: Nothing to disclose

Movement disorders 2

EPO1193

Refractory cervical dystonia: is the infiltration of the obliquus capitis inferior muscle a game changer?

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Background and aims: Cervical dystonia is occasionally refractory to botulinum toxin (BT) therapy. The obliquus capitis inferior (OCI) muscle contributes to head rotation and is active in most patients with torticollis, being its infiltration potentially useful. However, a specific training for ultrasound-guided injections is required.

Methods: Retrospective analysis of electronic records of patients with cervical dystonia of our movement disorders unit who underwent ultrasound-guided OCI infiltration.

Results: 11 patients (4 males) with an average duration of disease (DOD) of 7.6 ± 6.9 years were included. All had torticollis and 7 had tremor. Most had undergone several cycles (8.8 ± 5.9) of BT infiltration with poor response. After 2.6 ± 1.5 OCI infiltration cycles (5 patients with 57 ± 16 U of onabotulinum toxin, 3 with 71 ± 19 U of incobotulinum toxin and 3 with 131 ± 23 U of abobotulinum toxin) and a follow-up of 13.1 ± 7.8 months, 8 notably improved, while 3 did not (all males, with significantly longer DOD – $p=0.02$). A non-significant trend to improvement was observed regarding pain, tremor, position and functional capacity (Clinical Global Impression-Improvement scale scores 2.0 ± 1.2 ; 2.2 ± 1.3 ; 2.0 ± 1.2 ; 2.1 ± 1.4 respectively), although women showed significant improvement in pain and position ($p<0.05$). There were no differences concerning duration of BT effect (2.5-3 months) nor either adverse events.

Conclusion: The infiltration of OCI is safe and feasible with specific training and expertise, and may offer a clinical benefit to patients refractory to conventional patterns of infiltration.

Disclosure: Nothing to disclose

EPO1194

Falls needing specialist care in the 10 years preceding the initial diagnosis of Parkinson's disease

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Background and aims: The 1st motor symptoms of Parkinson's Disease (PD) become obvious after a significant (30-80%) cell-loss in the substantia nigra. Postural instability is considered a sign appearing in the late stage of PD. We assume that postural instability might occur earlier in the course of PD.

Methods: In the framework of the National Brain Research Program we used the database of the National Health Insurance Fund (NHIF) in Hungary, a country with a single-payer health insurance system. We evaluated falls as the cause of trauma (ICD-10 W00-W19) in the 10-year history preceding the 1st diagnosis of PD (ICD-10 G20) or cerebral infarction (CI, ICD-10 I63) in those who had the initial diagnosis of PD or CI in 2015 and 2016. Record linkage by the anonymized unique patient identifiers was used to identify falls needing specialist visits.

Results: In 2015-2016 there were 16403 and 93278 new cases of PD (mean age: 74.3 ± 10.1 years) and CI (mean age: 70.3 ± 13.0 years) in Hungary. Falls as the cause of trauma were recorded in 47% of PD and in 44% of cerebral infarctions in the 10 years history (chi-squared test, $p<0.001$). Those with a history of falls were 2 years younger in both groups. In logistic regression age ($p<0.001$) and diagnosis type (G20 or I63; $p=0.007$) were independent predictors of falls in the 10-year history.

Conclusion: Based on these initial results we suggest that signs of postural instability – reflected by falls needing specialist care – may appear earlier in the course of PD than assumed previously.

Disclosure: Nothing to disclose

EPO1195

Characteristics and outcomes in a 12-month follow-up case series of advanced parkinson's disease patients on stable 24-hour/day levodopa-carbidopa intestinal gel from the DUOGLOBE study

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Background and aims: Stable 24-hour/day levodopa-carbidopa intestinal gel (LCIG) has the potential to extend the benefit of Parkinson's disease (PD) symptomatic control through nighttime, compared to a 16-hour regimen. Here we present a case series summary on the effectiveness of stable 24-hour/day LCIG therapy on motor fluctuations and non-motor symptoms (NMS) including sleep during routine clinical practice.

Methods: In this interim case series analysis from the ongoing DUOGLOBE study, "Off" time, dyskinesia (UDysRS total score), NMS (NMSS total and sleep subdomain scores), and sleep symptoms (PDSS-2 and ESS) were assessed in patients on stable 24-hour/day LCIG infusion at baseline (BL) and month (M) 12. Serious Adverse Events (SAEs) were monitored.

Results: As of December 2018, 7 patients were on stable 24-hour/day LCIG; 5 patients had M12 follow-up. From BL to M12, improvements were observed in median values for "Off" time (5.0h/day to 0.0 h/day; range at M12: 0 to 3.5h/day; n/n=7/5) and median cores on the UDysRS (44.5 to 14.0; n/n=6/3), NMSS (84.0 to 22.0; n/n=7/4), NMSS sleep subdomain (27.0 to 6.0; n/n=7/4), PDSS-2 (42.0 to 14.0; n/n=7/5), and ESS (10.0 to 5.0; n/n=7/5). SAEs occurred in 42.9% of patients (n/n=3/7); 1 patient discontinued LCIG due to AEs (pulmonary embolism and acute psychosis) and another withdrew consent.

Conclusion: These limited case series summary data suggest that stable 24-hour/day LCIG may provide benefits in motor complications and NMS including sleep. In this small sample, the safety events were consistent with the established safety profile of LCIG but needs confirmation in larger studies.

Disclosure: AbbVie funded the research for this study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission. All authors had access to the data; participated in the development, review, and approval of the abstract, and agreed to submit.

EPO1196

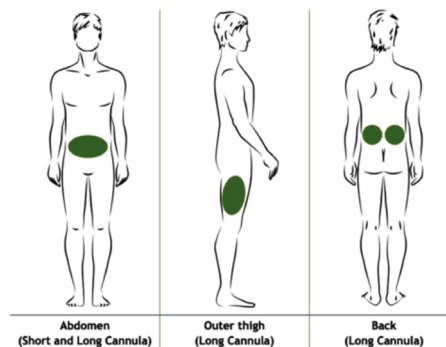
Pharmacokinetics of ND0612 administered at different infusion sites and with different cannula lengths: an open-label, randomised, cross-over study in healthy volunteers

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Background and aims: This phase 1 study aimed to evaluate the impact of subcutaneous (SC) infusion site location and cannula length on levodopa and carbidopa pharmacokinetics administered as a single 16-hour infusion of ND0612 in healthy volunteers. ND0612 is a drug-device combination designed to deliver liquid levodopa/carbidopa (60/7.5mg/mL) via SC-infusion to reduce motor complications in patients with Parkinson's disease.

Methods: Single-centre, open-label, randomised, single-dose, 4-period, crossover study in 24 healthy subjects (16M/8F). Subjects were randomised 1:1:1:1 into one of four sequences. Each subject sequentially received ND0612 at three different infusion sites (32h washout time), with the abdomen infused twice, once with a long cannula (reference route of administration) and once with a short cannula. The outer thigh and back sites were assessed with long cannula [Figure].



Infusion approaches tested

Results: Mean plasma drug concentration-vs.-time profiles (for levodopa and carbidopa) were similar for ND0612 infused with long cannulas at the abdomen and the other infusion locations, or with short cannulas. The 90% confidence intervals for the C_{max} and the AUC parameters were within the pre-defined limits of 80-125% among all tests and the reference, indicating bioequivalence. The most common adverse events were infusion-site reactions; none led to study discontinuation and none were classified as serious/severe.

Conclusion: There were no differences in the rate or extent of absorption of levodopa or carbidopa independent of infusion site location or cannula length. Furthermore, infusion to the back and outer thighs did not affect the safety of ND0612, offering patients alternative infusion locations for long-term ND0612 use.

Disclosure: Funded by NeuroDerm

EPO1197

The effect of medical xenon on affective disorders in patients with advanced stages of the Parkinson's disease

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Background and aims: Affective disorders of the anxiety-depressive spectrum are quite common in the advanced stages of Parkinson's disease (PD), significantly reducing the patient's quality of life. The purpose of this research was to evaluate the possibility of correction of affective disorders in patients with advanced stages of PD using medical xenon.

Methods: We examined 15 patients having complaints of affective disorders and suffering from PD, stage III according to Hoehn-Yahr (average age 63.0±2.9 years), as well taking stable dopaminergic therapy for at least 3 months and not receiving any psychotropic drugs. Evaluation of the severity of the affective disorders was carried out on HADS, MADRS, STAI and WAN scales. For the treatment of affective disorders was used a therapeutic course of inhalation of an oxygen-xenon mixture in a ratio with a mass fraction of xenon of 30%.

Results: After the course of therapy with the usage of medical xenon was noted a decrease in the severity of anxiety disorders (on the HADS-A scale -30%, on the STAI scale, the severity of situational anxiety decreased by 15%, personal anxiety by 6%), depressive disorders (on the HADS-D scale -20%, MADRS -35%), according to the WAN scales overall health improvement was noted by 34%, activity by 30%, mood by 24%.

Conclusion: According to the obtained pilot results, the use of medical xenon therapy in the complex treatment of advanced stages of PD reduces the severity of both anxiety and depressive disorders, which improves the overall quality of patients' life.

Disclosure: Nothing to disclose

EPO1198

Genetic characterization of Parkinson's disease in a selected population from North-eastern Italy

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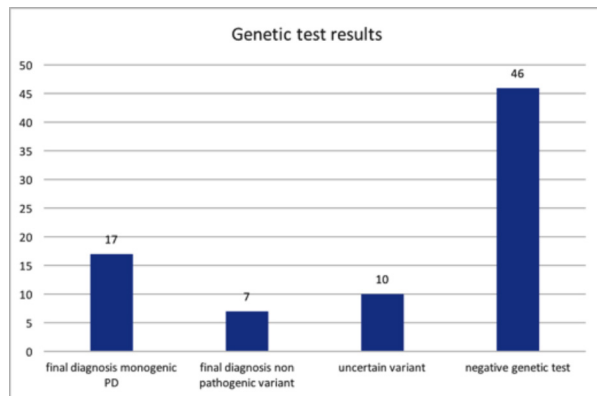
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Background and aims: Monogenic forms of PD account for 5-10% of all patients, being genetically heterogeneous and with potential additional genes still unknown. The use of Next-Generation Sequencing Techniques and patients' selection will increase our knowledge in this field. We assessed the prevalence of pathogenic variants in PD-related genes and clinical phenotype in a selected cohort of PD patients.

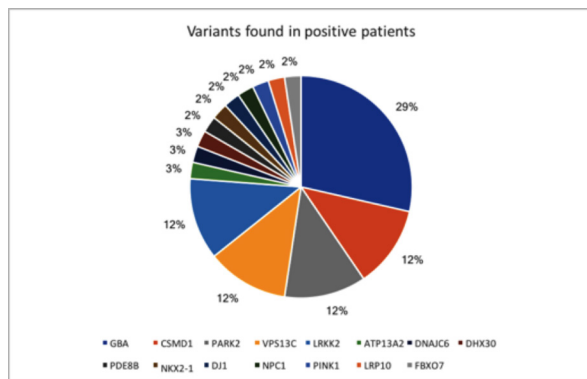
Methods: We selected 80 patients from 2 specialized centers (Padua and Vicenza) with onset under 50 years and/or positive family history and/or early cognitive decline. Genetic analysis by NGS with a customized gene panel including 80 genes related to movement disorders was carried out. Bioinformatic data-analysis, literature revision and database search were performed to determine pathogenicity. Clinical and neuropsychological assessment was performed.

Results: 34 out of 80 patients (42%) carried at least 1 variant in one PD-related gene, for a total of 42 different mutations in 14 genes (GBA, PARK2, LRRK2, CSMD1, VPS13C, ATP13A2, DNAJC6, NPC1, PDE8B, DHX30, NKX2-1, PINK1, DJ1, LRP10). 43% variants had evidence of pathogenicity, whereas 26% had an uncertain significance. A definite genetic diagnosis was formulated in 22% of patients. 12 patients carried a pathogenic variant in GBA gene and 6 of them underwent DBS.

Conclusion: Pathogenic variants in PD-related genes were common in our cohort and our screening criteria were useful predictors of an underlying genetic etiology. Testing patients with specific clinical manifestations allows better resource allocation and increases the probability of finding pathogenic variants. Clinical use of genetic panels broadens the spectrum of PD-related genes and may lead to targeted treatments.



genetic test results in entire cohort



gene variants in positive patients

Disclosure: Nothing to disclose

EPO1199

“Dozing off” in the car and Excessive Daytime Sleepiness (EDS) in Parkinson’s disease

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Background and aims: EDS is a key non-motor symptom (NMS) of Parkinson’s disease (PD), disease-related and iatrogenic. Phenotypic correlations of PD with EDS have been of recent interest in relation to personalised medicine and PD.1

Objectives: To explore the risk of dozing off and possibility of road traffic accidents in PD patients with EDS. Neuropsychiatric symptoms, quality of life and pattern of medication in PD patients will also be considered.

Methods: From the Non-motor International Longitudinal Study database of 630 patients assessed holistically for motor and NMS at baseline, a high EDS group was selected defined by scores ≥ 10 on the Epworth Sleepiness Scale (ESS).

Results: The high EDS group consisted of 125 patients (mean age at assessment= 65 ± 9.68 , mean age of PD onset= 58 ± 10.79 , mean disease duration= 7 ± 6.40). 42.48% of high EDS patients reported a likelihood of dozing off in a car whilst in traffic, posing a risk for car accidents; 50% were taking Dopamine Agonists (DAs) including ropinirole (21.2%), pramipexole (1.9%) and rotigotine (25%). Ropinirole is a DA with high affinity to D3 receptors; D3 receptor agonists are known to induce sleepiness. Patients scored in the clinically significant range on the Hospital Anxiety and Depression Scale (81.6%) and on the PD Sleep Scale (64.8%). Patients scored on average 11.42 ± 6.63 points on the PD Questionnaire-8.

Conclusion: ESS may predict a risk for work-related somnolence which may cause road traffic accidents. DAs are confirmed as a risk factor and depression and anxiety are commonly comorbid.

Disclosure: Nothing to disclose

EPO1200

Differences in performance on clock drawing tasks as predictive measurements for disease classification among patients with Parkinson's disease and essential tremor

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Background and aims: Non motor symptoms are widely being recognized in both Parkinson's disease (PD) and Essential Tremor (ET). Although visuospatial dysfunction is common in PD, data on ET are lacking. Our aim was to examine whether clock-drawing test as a quick test could predict visuospatial deficits in patients with ET.

Methods: Visuospatial performance was assessed in 58 consecutive patients with ET and 75 with PD and 22 healthy controls (HC) who visited 2 specialized memory clinics of Athens in Greece. The clock-drawing (CD) and copy (CC) items of the Parkinson's Disease-Cognitive Rating Scale were used as a test of visuospatial function.

Results: Both CD and CC scores were lower for ET compared to PD patients and HC ($p < 0.001$ for both comparisons). A binomial logistic regression showed that both CD and CC items predict if participants had ET or PD with high sensitivity 94.7% and specificity 87.9% and an area under the curve (AUC) 0.980 (95% confidence interval, 0.962- 0.997). The model explained 86.1% (Nagelkerke R²) of the variance in the disease variable (ET/PD) and correctly classified 91.7% of the cases.

Conclusion: Patients with ET have more visuospatial deficits compared to PD. Clock-drawing test is a robust predictor of ET after adjust for age and education. These findings suggest that the clock-drawing task may be an easy useful tool to track cognitive changes in nondemented patients with ET in clinical practice.

Disclosure: Nothing to disclose

EPO1201

Combining device-aided treatments in advanced Parkinson's disease patients: a 10 years experience from the Cretan PD cohort.

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Background: Continuous delivery of levodopa-carbidopa intestinal gel (LCIG), deep brain stimulation (DBS) and apomorphine subcutaneous infusion (ASI) are device-aided therapies for motor complications of advanced Parkinson's disease (PD). Studies addressing the effect of combining such treatments are lacking. We present a series of patients from the Cretan PD cohort (CPDC) who required 2 device-aided treatments for optimal management of their disease.

Methods: The CPDC includes PD patients followed prospectively over the course of 10 years. We identified advanced PD patients who received a device-aided treatment and later experienced problems that required implementation of a 2nd interventional treatment. We present their clinical characteristics and the indications of combining treatments.

Results: 63 patients on device-aided treatments were followed prospectively from 2009 to 2019. 8 patients (13%) experienced problems that required implementation of a 2nd interventional treatment. 5 of them were treated with STN-DBS and later received LCIG, 1 STN-DBS patient received later ASI, and 2 patients on LCIG received later STN-DBS. The main reason for adding infusion therapies on DBS was the re-appearance of motor fluctuations. Adding DBS on LCIG treatment improved intractable drug-induced symptoms (i.e psychosis) by allowing reduction of levodopa dose.

Conclusions: Advanced PD patients treated with 1 device-aided treatment may experience additional benefit from a 2nd interventional therapy. While infusion therapies can optimize dopaminergic drug delivery in DBS treated patients, DBS added to LCIG can be levodopa sparing. In the era of precision medicine, combining interventional treatments can maximize their effectiveness and tailor therapy to match patient's needs.

Disclosure: Nothing to disclose

EPO1202

Effective long-term treatment with inco-botulinum toxin after immuno-resistance to abo- or ona-botulinum toxin in patients with cervical dystonia

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Background and aims: Botulinum toxin type A (BoNT/A) is a 150kDa large molecule, embedded in a fivefold larger protein complex. Antibody formation can hardly be avoided in BoNT/A therapy with different forms of injection. This cross-sectional study aimed to investigate the effectiveness of switching to inco-BoNT/A in partially resistant patients with cervical dystonia (CD) to abo- or ona-BoNT/A.

Methods: In 51 CD-patients with clinical signs of partial secondary treatment failure (PSTF) who had been switched to inco-BoNT/A, mouse hemidiaphragm assay (MHDA) was performed to detect the presence of neutralizing antibodies (NABs), and the TSUI-score and the dose per treatment session were extracted from their charts.

Results: NABs were detected in almost 28% of all patients (=14) (ABPOS-group), and MHDA was negative in 37 patients (ABNEG-group). In both ABPOS- and ABNEG-group clinically and statistically significant worsening ($p < 0.05$) was found before switching to inco-BoNT/A. When the course of BoNT/A treatment was synchronized to the time of the switch to BoNT/A, significant response to inco-BoNT/A was found which was more pronounced in the ABNEG-group ($p < 0.001$) than in the ABPOS-group ($p < 0.05$). After several years of inco-BoNT/A treatment, the severity of CD in the ABPOS-group approached the level of improvement in the ABNEG-group.

Conclusion: In CD-patients with a PSTF after abo- or ona-BoNT/A therapy, switch to inco-BoNT/A can play a prominent role in the level of improvement and should have higher priority over deep brain stimulation in the treatment plan.

Disclosure: Nothing to disclose

EPO1203

First Belgian case of myoclonus-dystonia caused by a mutation in KCTD17

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Background and aims: Myoclonus-dystonia is a rare movement disorder, in which familial cases are most commonly caused by genetic mutations in SGCE. More recently, in 2015, Mencacci et al. reported a missense mutation in KCTD17 in a British family with a myoclonus-dystonia phenotype, and described a similar German family. Since then, the pathogenic role of KCTD17 mutations has been confirmed by 2 independent groups describing an Argentinian and Italian patient.

Methods: A 50-year-old man presented with problems of increasing dysarthria, clumsiness and fatigue. Since childhood there were mild involuntary jerky movements of the arms and hands. There was no response to alcohol or psychiatric comorbidities. At the time of presentation both parents were already deceased, however similar symptoms were reported in his father according to the family.

Results: Clinical examination revealed non-epileptic myoclonic jerks of the upper limbs combined with a cranio-cervical dystonia involving the right shoulder. In addition, the patient exhibited a general slowness, hypomimia, hypokinetic dysarthria and a mild unsteady gait. DaTscan and MRI scan of the brain revealed no clear abnormalities. Whole exome sequencing revealed an Arg145His mutation in the KCTD17 gene, which is the same variant as reported previously in literature.

Conclusion: The clinical presentation in our patient (5th reported family) is strikingly similar to the 1 reported in literature and further confirms the phenotype associated to KCTD17 related myoclonus-dystonia. Moreover, our patient exhibits bradykinesia which potentially broadens the clinical spectrum further.

Disclosure: Nothing to disclose

EPO1204

The influence of deep brain stimulation on sweet liking and taste preferences in Parkinson's disease

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Background and aims: Weight gain is 1 of potential adverse effects of deep brain stimulation (DBS) in patients with Parkinson's disease (PD). It has been suggested, that DBS-induced weight changes has a multifactorial nature, with the role of impulsivity and reflects the complex functional organization of the STN. Aim. The present study aimed to investigate sweet liking and taste preferences in PD patients with a specific focus on the effects of DBS in the subthalamic nucleus.

Methods: Basic demographic and clinical data were collected from 12 patients (9 males and 3 females), mean age 61.25 ± 7.69 , with disease duration of 9.91 ± 3.99 years. The study participants were free of severe neuropsychiatric disorders, including depression and dementia. Pleasantness ratings of sucrose solutions (1-30%, w/w) and sweet liking/disliking status were assessed as well as basic sensory aspects of gustation (intensity ratings, electrogustometric thresholds).

Results: 7 patients declared olfactory deficits and 6 patients reported subjective taste problems. Decrease and increase of about 2.2% and 4.4% of initial weight was noted in 3 and 9 patients, respectively. We did not observe significant changes in electrogustometric threshold and intensity and pleasantness ratings of sucrose solutions. However, 50% of patients declared increase in sugar craving.

Conclusion: The results of the present study may suggest that post-DBS weight alterations are not associated with significant changes in basic gustatory function, including taste reactivity to sweet stimuli.

Disclosure: Nothing to disclose

EPO1205

Neurophysiological evaluation of voluntary postural control in PD patients on selection for stereotactic treatment and during deep brain stimulation

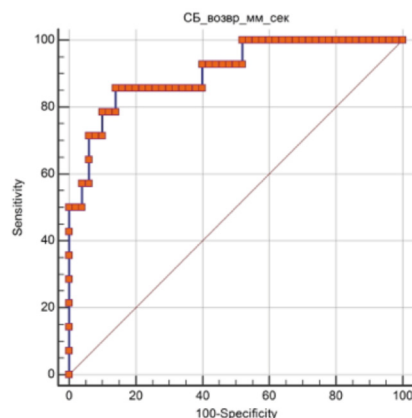
A. Buniak¹, I. Maryenko¹, S. Likchachev²

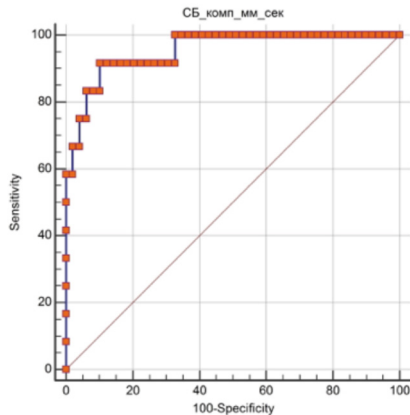
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Background and aims: 1 of the contraindications for DBS in PD patients is a disturbance of voluntary postural control (VPC) does not respond to levodopa. Stabilometry with biofeedback is used to objectify of VPC at the selection stage and postural disturbances on DBS. The impairments of VPC in PD patients at the selection and on DBS using the speed characteristics of the statokinesiogram during voluntary movements will be evaluated.

Methods: We examined 106 PD patients on selection and 52 on DBS. 28 male and 24 female, mean age 55.98 ± 7.04 , 32 patients—II stage of H&Y, 20—III. 40 patient with DBS STN, 9 – DBS GPi, 3 – DBS Vim. We used computer stabiloanalizator with biofeedback. Test was carried out with a stepped exposure. Patients moved the pressure center forward (I stage), then returned (II stage). The speed of throw (ST), mm/s was evaluated at the I and II stage.

Results: The optimal ST at the I stage 13.72mm/s, AUC 0.86 (95% CI 0.73-0.95), $p < .0001$. The sensitivity 76.9 (95% CI 46.2-95.0), specificity 87.5 (95% CI 71.0-96.5). The optimal ST at the II stage 11.95mm/s, AUC 0.91 (95% CI 0.81-0.96), $p < .0001$. The sensitivity 85.7 (95% CI 57.2-98.2), specificity 86.0 (95% CI 73.3-94.2). Statistically significant difference by W-test of ST indicators revealed after 1m ($p=0.0004$), 1y ($p=0.018$), 2y of DBS ($p=0.028$).





Conclusion: The results revealed diagnostic markers of VPC in PD patients at the selection stage. Excess markers indicate the presence of postural disorders. The selected indicators help to evaluate changes of VPC in PD patients on DBS.

Disclosure: Nothing to disclose

EPO1206

CERS1 deficiency causes a rare progressive myoclonic epilepsy: two new familial cases

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Background and aims: Progressive myoclonic epilepsy (PME) comprises a heterogeneous group of disorders characterized by myoclonus, tonic-clonic seizures, and progressive neurological dysfunction, including ataxia, neuropathy and myopathy. Despite the advent of genomic sequencing, the genetic cause is unknown in the majority of PME patients. Extremely rare mutations in CERS1, so far reported in one family and in an isolated single case, define PME type 8. CERS1 is the gene encoding ceramide synthase 1, precursor of sphingolipids, critical components for normal brain functions. We report 2 new cases with PME carrying mutations in CERS1.

Methods: Diagnostic work-up consisted in: Neuropsychological evaluation, MRIs, EEGs, ENoG, EMG, SSEP, plasma oxysterols, molecular testing (CSTB, EPM1, EPM2, MERRF), genetic panel (ADCK3, AFG3L2, APTX, CYP27A1, FXN, KCND3, NPC1, NPC2, PDYN, PEX7, PHYH, PNPLA6, POLG, PRAKCG, SACS, SETX, SLC52A2 and TTPa), skin biopsy and whole-exome sequencing.

Results: 2 brothers, aged 44 and 34, firstly presented generalized tonic-clonic seizures and myoclonus at the age of 11 and 12 respectively. They acquired slowly progressive ataxia and cognitive impairment, affecting the younger brother more severely. Neurological examination revealed truncal and limb ataxia, dysarthria and myoclonus. At neuropsychological evaluation the patients presented from mild to moderate cognitive impairment. EEG showed multifocal discharges. After an extensive metabolic and genetic diagnostic work-up, whole-exome sequencing revealed the H183Q homozygous mutation in the CERS1.

Conclusion: These 2 new cases strengthen the genotype-clinical phenotype association between mutant CERS1 and PME. However, while the clinical features are broadly similar to the previously reported cases, there is phenotypical variability and different grades of severity exist.

Disclosure: Nothing to disclose

EPO1207

Adult onset craniocervical dystonia with uncommon mutations: report of two cases

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Background and aims: Adult onset primary dystonia commonly begins in the craniocervical region and tends to remain focal or spread to a segmental distribution (generalisation is rare). Most cases are sporadic, being the genetic cause less common.

Methods: We present 2 patients without family history of dystonia, diagnosed of adult craniocervical onset dystonia caused by uncommon mutations.

Results: 48-year-old female diagnosed of spasmodic dysphonia since she was 33 treated with botulinum toxin with mild response. At the age of 45 she developed right torticollis, blepharospasm and trunk stiffness. Genetic study showed an heterozygous mutation in the ANO3 gene, responsible for the autosomal dominant DYT24 dystonia. 52-year-old female, with a 14-year history of progressive craniocervical dystonia. Initially she developed a head shake that progressed to a severe right laterocollis and right upper limb dystonia. Symptoms were severe and refractory to medical treatment and botulinum neurotoxin, so she was treated with deep brain stimulation (DBS) targeting bilaterally globus pallidus interna (GPi), with clinical improvement. Years later she developed left hemidystonia. Genetic study was performed, revealing an heterozygous mutation in the GNAL gene, responsible for the autosomal dominant DYT25 dystonia. There is no previous report in literature of DYT25 dystonia treated with DBS.

Conclusion: Primary genetic dystonia is an uncommon disease, specially if the symptoms have an adult onset. In addition, the cases described above are caused by mutations rarely described in literature. DBS could be a treatment option in craniocervical dystonia refractory to conventional medical therapy.

Disclosure: Nothing to disclose

EPO1208

Phenotypic characterization of a cohort of patients affected by laryngeal dystonia: a monocentric study

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Background and aims: Laryngeal dystonia (LD) is characterized by involuntary spasms of the vocal cords during phonation. Botulinum toxin (BTX) is considered the preferable treatment. Aims of this study were: describing a cohort of patients with LD; comparing findings with available literature; evaluating patients' quality of life and the effectiveness of BTX; investigating non-motor symptoms.

Methods: 43 patients (33 F, 10 M) affected by LD were consecutively recruited at the ENT Department of Padua University. Demographical and clinical data were collected by direct interview and a thorough neurological examination was performed. The following questionnaires were used to better characterize patients' phenomenology and comorbidities: VPQ, VHI-30, BDI and PSQI.

Results: 76.7% patients were females; mean age at examination was 58.4±11.4 years and mean age at onset was 50.3±12.3 years. Mean disease duration was 9 years. 19/40 (15 F, 4 M) patients presented extra-laryngeal dystonia/tremor on examination (Table 1). Difference between VHI-30 scores at the time of greatest benefit given by BTX (23.8±24.1) vs scores during BTX wearing-off (87.1±27) was statistically significant (p<0.01) (Table 2). Psychiatric comorbidities and sleep disorders were present in 10/43 and 6/43 patients respectively (Table 3). Considering preliminary data, BDI and PSQI scores did not differ significantly (Mann-Whitney U test) from healthy age- and sex-matched population.

Table 1. Demographical and clinical data			
N° and Sex of patients	43	F 33 (77%)	M 10 (23%)
Age at examination (y)	58.4	F 59.7	M 54.3
Age at onset (y)	49.5	F 50.3	M 47
Years of illness (y)	9.25		
Years of illness at diagnosis (y)	2.6		
Profession (at onset time)			
	Office worker/assistant	14/43 (32.6%)	
	Teacher/Professor/instructor	9/43 (18.6%)	
	Salesman/shop assistant	4/43 (9.3%)	
	Social and health worker	3/43 (7.0%)	
	Physician	2/43 (4.7%)	
	Lawyer	2/43 (4.7%)	
	Farmer	2/43 (4.7%)	
	Housewife	2/43 (4.7%)	
	Singer	2/43 (4.7%)	
	Baker	1/43 (2.3%)	
	Butcher	1/43 (2.3%)	
	Plumber	1/43 (2.3%)	
	Cashier	1/43 (2.3%)	
	Priest	1/43 (2.3%)	
	Chief police inspector	1/43 (2.3%)	
	University Researcher	1/43 (2.3%)	
Singers	Amateur	10/43 (23.3%)	
	TOT	12/43 (28.0%)	
Type of LD	Adductor (ADLD)	40/43 (93.0%)	30 F (75%) 10 M (25%)
	Abductor (ABLD)	0/43 (0.0%)	
	Mixed	1/43 (2.3%)	1 F (100%)
	Breathing (ALBD)	2/43 (4.7%)	2 F (100%)
Referred Trigger	Emotional Stress	23/43 (53.5%)	
	Airways infection	4/43 (9.3%)	
	Quit singing	1/43 (2.3%)	
	Rhinoplasty	1/43 (2.3%)	
	No trigger	13/43 (30.2%)	
	Unknown	2/43 (4.7%)	
Other dystonias/tremor	Upper limb tremor	15/43 (34.9%)	
	Head tremor	5/43 (11.6%)	
	Torticollis	3/43 (7.0%)	
	Oromandibular dystonia	3/43 (7.0%)	
	Blepharospasm	6/43 (14.0%)	
	TOT	19/43 (44.2%)	
Positive family history		11/43 (25.6%)	

Table1. Demographical and clinical data.

Table 2. Quality of Life (QoL)			
2A. BTX treatment and QoL scores			
Years treatment in our ENT clinic (y)	3.0		
N° of injections	7.3		
TOI years of treatment (y)	3.7		
Frequency of treatment	5.4 ± 2		
Complaints of aphonia/breathing voice	22/43		
Duration of aphonia (w)	3.0 ± 1.8		
Complaints of dysphagia	15/43		
Duration of dysphagia (d)	9.8 ± 5.7		
Efficacy duration (m)	3.7 ± 2.0		
VPQ	(33 ± 10)/60	F (34 ± 10.5)/60	M (28.5 ± 3)/60
VHI-30 OFF BTX	(87 ± 27)/120	F (88 ± 27.5)/120	M (97 ± 8)/120
VHI-30 ON BTX	(24 ± 24)/120	F (25 ± 25)/120	M (15 ± 13)/120
Δ VHI OFF-ON	(65 ± 27)/120	F (63 ± 27.5)/120	M (82 ± 14)/120
Personal efficacy (%)	(81.3 ± 15.5)	F (80.8 ± 17)	M (82.8 ± 12)
2B. Ameliorating and Worsening Situations or Gestures			
	Phone speaking	20	
	Stress/Negative emotivity	12	
	Reading out loud	7	
	Evening	6	
Worsening (n° of cases)	Morning	4	
	Crouded places/Noise	4	
	Talking a lot	3	
	Physical activity	2	
	Head/Neck Flexion	2	
	Shouting	11	

Table 3. Non-motor symptoms and scores			
Sleep disturbances (N° of cases)	6	6	0
On Medication (N° of cases)	4	4	0
Family history (N° of cases)	3		
RSQI score (Partial data)	(7 ± 5)/21	F (8.7 ± 3.0)/21	M (3.0 ± 1.7)/21
Depression (N° of cases)	5	5	0
On Medication (N° of cases)	5	5	0
Family history (N° of cases)	4		
BDI score (Partial data)	(7.8 ± 7.0)/63	F (12 ± 8)/21	M (2.3 ± 3.2)/21
Anxiety disorders (N° of cases)	7	6	1
On Medication (N° of cases)	7	6	1
Family history (N° of cases)	4		
Other psychiatric disturbances	1 (Stress eating)	1	0
Further Family History	1 (Bipolar disorder)		

Table3. Non-motor symptoms.

Conclusion: LD prevalence was higher in females and in some professional groups. Dystonic involvement of extra-laryngeal anatomic regions was frequent. We confirm the efficacy of treatment with BTX injections.

Disclosure: Nothing to disclose

EPO1209

Acute freezing of gait: a rare presentation of ischemic stroke

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Background and aims: Freezing of gait (FOG) is defined as an aberrant pattern of brief episodes of inability to step or by short steps that typically occur on initiating/turning while walking.

Methods: Case report and literature review.

Results: A healthy 80-year-old woman was admitted to the emergency department due to sudden-onset gait impairment which had started 2 days prior. Her past medical and pharmacological histories were unremarkable. Her neurological examination was striking for FOG, sensitive to visual cues, when turning and initiating gait but otherwise normal. Brain CT revealed subacute right cortico-subcortical parietooccipital stroke. Brain MRI performed a week later showed hemorrhagic transformation. Stroke etiology workup was unremarkable. The patient was started on levodopa and referred to physical rehabilitation. Although she first noticed no improvement with medication, its suspension led to acute deterioration and hence medication was restored. While morphometric studies in PD patients and FOG show posterior parietal lobe atrophy, possibly implying this region in the generation of FOG, post-lesional FOG is seldom reported. Lesions are topographically heterogeneous, and, in functional connectivity maps, most lesions overlap the dorsal medial cerebellum network. Although the posterior parietal is extensively connected with the cerebellum, the structural disconnectome analysis showed only disconnection to the ventral striatum.

Conclusion: Lesion-induced FOG is seldom reported in the literature, and these cases can potentially shed some insight into the neuroanatomical substrate of this phenomenon, which in turn might have implications for identifying possible treatments. Our case highlights that other pathways or different lesions in the same patient might contribute to the genesis of FOG.

Disclosure: Nothing to disclose

EPO1210

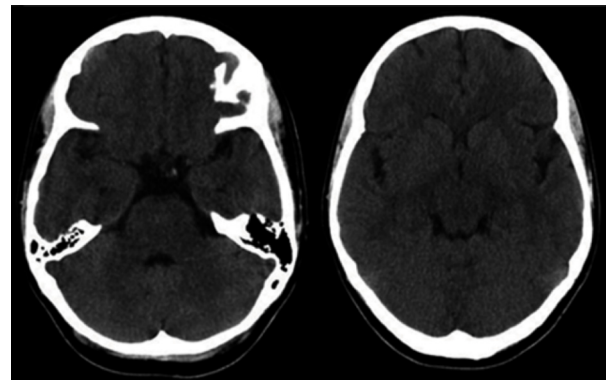
Unusual cause of Chorea acquired secondary to Cannabinoids consuming

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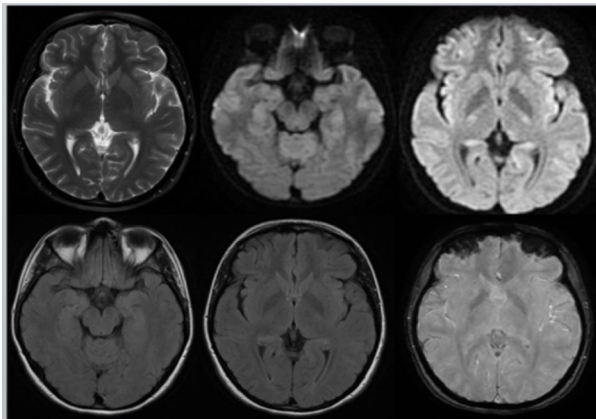
Background and aims: There is evidence that cannabinoids may play a role in the neurotransmission systems within the basal ganglia by increasing GABAergic transmission in internal Globus Pallidum, inhibiting the release of glutamate in the substantia nigra pars reticulata and affecting dopaminergic uptake which could induce chorea. Some drugs such as oral contraceptives may cause chorea as an acute phenomenon or as a result of long-term therapy but may require pre-existing basal ganglia dysfunction (neurodegenerative disease or Sydenham chorea). We present an unusual case of chorea secondary to toxic/drugs by combination of oral contraceptives and cannabis use.

Methods: Case report presentation



Cranial TC Chorea

Results: A 23-year-old woman was admitted to the emergency department because she abruptly presented an episode of involuntary hyperkinetic movements, brief and irregular, predominantly on the right hemibody, but flowed from 1 side to the other with mild involvement of the trunk and head, not inhibited with distraction maneuvers. These movements occurred after consuming cannabis use for the 1st time, resolved spontaneously in 2 hours. She was taking oral contraceptives for 4 years. There was no history of previous infections, Sydenham chorea, neurological or family history. Brain CT and MRI, biochemistry, blood count, autoimmunity, echocardiography, throat culture and ceruloplasmin were normal. There was a positive cannabinoid analysis in urine and ASLO was also positive.



Brain MRI

Conclusion: Cannabinoids consuming may produce chorea, in our case, oral contraceptives and ASLO might be susceptibility factors.

Disclosure: Nothing to disclose

EPO1211

Advanced Parkinson's disease treatment eligibility in France: the EpiPark cross-sectional study

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Background and aims: Epidemiological data on French patients with advanced Parkinson's disease (aPD) are limited. We aimed to estimate the size of the French population of aPD patients, describe aPD patients' characteristics, and assess eligibility for deep brain stimulation (DBS), apomorphine pump (APO) and levodopa/carbidopa intestinal gel (LCIG).

Methods: The epidemiological, cross-sectional and observational EpiPark study, proposed to 2,841 neurologists (hospital, mixed or private), was conducted with 38 neurologists, representative of the territory and stratified according to their type of practice and geographic location. 2 complementary parts were simultaneously introduced: CENSUS part to count aPD patients seen consecutively in outpatient consultation over six months (N=688) and extrapolate to all aPD patients; CORE part to collect patients' characteristics and identify populations eligible for LCIG according to the Market Authorization and the National Authority for Health criteria, for DBS and APO. aPD criteria were: duration of levodopa-treatment ≥ 3 years, motor complications, and insufficient control by antiparkinsonian conventional treatment. An independent Expert Committee validated the patients' selection criteria.

Results: The 410 patients who entered the CORE analysis had aPD (Table 1). Eligibilities for LCIG, DBS and APO are shown in Table 2. After extrapolation to the total French population of PD patients, 55,258 were aPD patients, including 14,732 patients eligible for LCIG according to the Market Authorization, 2,767 to 14,801 for DBS, and 20,633 to 24,524 for APO.

Disclosure: This study was funded by AbbVie.

Table 1. Demographic and clinical characteristics of patients in the CORE part of the study (N=410)

Characteristics	All (N=410)
Gender, N (% male)	239 (58.3%)
Age ^a , years	71.05 ± 9.44
Time since initial Parkinson's disease diagnosis ^a , years	12.46 ± 5.86
Time since onset of motor complications ^a , years	5.85 ± 4.49
Time between initial diagnosis and onset of motor complications ^a , years	6.60 ± 3.59
General health status	
Excellent	63 (15.4%)
Good	226 (55.1%)
Medium	109 (26.6%)
Bad	12 (2.9%)
Current motor fluctuations	
Presence of troublesome 'off' phases for more than 25% of waking time	236 (57.6%)
Current dyskinesia	
Presence of dyskinesia for more than 25% of waking time	308 (75.1%)
Presence of severe dyskinesia during 'on' time response	188 (45.9%)
Impact at least minimal on functional activities	109 (26.5%)
	242 (59.0%)
Dystonia	
Severe dystonia during 'on' phase	121 (29.5%)
	35 (8.5%)
At least one ongoing antiparkinsonian treatment, N (%)	
History of levodopa per os, N (%)	408 (99.5%)
Levodopa treatment ongoing, N (%)	410 (100%)
Time since levodopa's treatment start date ^a , years	394 (96.1%)
Other antiparkinsonian treatments, N (%)	12.21 ± 9.67
	394 (96.1%)
Levodopa challenge test, N (%)	
Excellent response	56 (13.7%)
Good response	24 (5.9%)
Moderate response	24 (5.9%)
	8 (1.9%)

Table 2: Individual endpoints for complete eligibility to LCIG according to the Transparency Committee's opinion (primary objective) and to its market authorization (first secondary objective) – analysis on raw datasets and on weighted population

		Main analysis (Scenario 1) ^a	Complementary analysis (Scenario 2) ^b
Overall analysis population	N	410	410
Endpoint 1:	N (%)	117 (28.5%)	117 (28.5%)
Severe motor fluctuations and hyper/dyskinesia	[95% CI]	[24.38; 33.09]	[24.38; 33.09]
Endpoint 2:	N (%)	389 (94.9%)	389 (94.9%)
Levodopa-responsiveness	[95% CI]	[92.30; 96.63]	[92.30; 96.63]
Endpoint 3:	N (%)	402 (98.0%)	334 (81.5%)
Non-eligibility to DBS	[95% CI]	[96.20; 99.01]	[77.42; 84.93]
Endpoint 4:	N (%)	240 (58.5%)	217 (52.9%)
Contra-indication, intolerance or failure to APO	[95% CI]	[53.71; 63.20]	[48.09; 57.71]
Endpoint 5:	N (%)	369 (90.0%)	369 (90.0%)
No contra-indication to LCIG	[95% CI]	[86.71; 92.54]	[86.71; 92.54]
Eligibility to LCIG according to the French National Authority for Health (endpoints 1,2,3,4 and 5)	N (%)	71 (17.3%)	60 (14.6%)
	[95% CI]	[13.96; 21.28]	[11.54; 18.38]
Eligibility to LCIG according to its French market authorization (endpoints 1,2 and 5)	N (%)	98 (23.9%)	98 (23.9%)
	[95% CI]	[20.0; 28.3]	[16.2; 25.2]

^a Scenario 1 (overestimation): Regarding the eligibility to DBS and the contra-indication, intolerance or failure to APO, the missing data handling planned in the first version of the statistical analysis plan were in favor of eligibility to LCIG rather than to DBS or APO.

Conclusion: EpiPark provides epidemiological data on French aPD patients in a real-life setting, describing their characteristics and quantifying populations eligible for DBS, APO and LCIG.

Disclosure: This study was funded by AbbVie.

Movement disorders 3

EPO1212

Biological markers of neurodegeneration in patients with Idiopathic Parkinson's Disease (IPD), Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP)

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Background and aims: Parkinsonian syndromes can be classified according to the predominant type of protein in cell inclusions to intracellular synucleinopathy (IPD), extracellular synucleinopathy (MSA) and tauopathy (progressive supranuclear paralysis-PSP). Our study aimed to find a panel of CSF and serum biomarkers to differentiate patients with MSA and PSP from IPD.

Methods: CSF and blood samples were obtained from patients with clinical diagnoses of IPD (n=28), PSP (n=19), MSA (n=21) and from healthy patients as a control group without neurodegenerative disease. Levels of chromogranin-A, phosphorylated neurofilament heavy chain, phosphorylated τ protein, total τ protein, β -amyloid 42, tau/ β ratio, α -synuclein, cystatin C were measured in CSF.

Results: We found a statistically significant difference in the levels of pNF-H, β -amyloid 42, tau/ β ratio, serum α -synuclein and the difference in serum and CSF α -synuclein concentrations. The tau/ β ratio is significantly different between IPD and MSA (p=0.023). Serum α -synuclein concentration in IPD or MSA was significantly higher than in PSP (p=0.001). In patients with IPD was significantly higher compared to control (p=0.032) and PSP (p=0.002), in patients with MSA was marginally higher compared to PSP (p=0.07)

Tab. 1 Statistical values of monitored markers in individual ND groups

	IPD (n = 28)			PSP (n = 19)			MSA (n = 21)			Control group (n = 9)			P
	Median	Min	Max	Median	Min	Max	Median	Min	Max	Median	Min	Max	
chromogranin A [μ g/l]	90.55	30	433.21	110.4	302	339.82	113.34	303	500	114.5	52.71	228.99	0.72
pNF-H [ng/l]	293	3.19	1102	342	185	2444	511	120	739	585	185	2595	0.04
phosphorylated τ [ng/l]	36.85	15.6	75.7	29.7	19.2	58.5	37.45	15.6	86.1	37.55	33.7	76.5	0.343
total τ [ng/l]	237	62	647	215	48	644	273	145	758	290	197	574	0.005
β -amyloid 42 [ng/l]	837.72	253.8	1305.44	867	558.07	1179.4	622.11	408.75	1340	1176.5	1030	1327	0.001
tau/ β ratio	0.25	0.07	2.38	0.25	0.12	0.68	0.44	0.2	1.39	0.23	0.16	0.51	0.019
α -syn CSF [ng/l]	165.95	25.6	872.6	185.8	131	566.4	149.9	25.6	786.6	268.35	161.9	604.5	0.339
α -syn S [ng/l]	1126.05	362.4	1833.8	510.4	340.5	1628.8	1216.4	240.9	1631.1	583.75	376.2	1069.2	0.001
cyst C [mg/l]	3.45	1.91	6.97	3.81	1.7	5.6	4.05	1.79	6.25	4.25	3.25	5.89	0.444
total α -syn CSF α -syn S	892.8	-257	1716.1	325.8	-200.4	1179.1	740.8	138.8	1303.3	328.3	183.7	484.6	0.004

Tab. 2 Statistical values of serum α -synuclein in synucleinopathies and PSP

	IPD & MSA (n = 49)			PSP (n = 19)			P				
	Median	Percentile 25	Percentile 75	Min	Max	Median		Percentile 25	Percentile 75	Min	Max
α -syn S [ng/l]	1150.1	804	1392.1	240.9	1833.8	510.4	398.4	835.7	340.5	1620.8	0.001

Statistical values of monitored markers in individual ND groups

Conclusion: The tau/ β ratio could serve to differentiate intracellular and extracellular synucleinopathies, i.e. IPD and MSA. Serum α -synuclein, or the difference between serum and CSF α -synuclein concentrations, could be used to differentiate synucleinopathies and tauopathies. Thus, the determination of α -synuclein concentrations and the resulting differential diagnosis of synucleinopathies and tauopathies could be limited to biochemical blood testing.

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EPO1213

Assessment of motor and non-motor symptoms in patients with Parkinson's disease in the early post-transplant period

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Background and aims: Treatment of patients with Parkinson's disease (PD) using autologous mesenchymal stem cells (MSCs) is a perspective method to influence on the pathogenesis of the disease. At the same time, this is a complex and still insufficiently explored process. On January 17, 2019, in the 5th Minsk City Clinical Hospital, the 1st implantation of MSCs in the Republic of Belarus was performed to a patient with PD. Currently, the number of patients in the post-transplant period has increased to 12.

Objective: To evaluate the immediate results of the effectiveness of the introduction of MSCs on motor and non-motor symptoms in patients with PD.

Methods: The therapy of MSCs in patients with PD was performed using 2 methods developed by us: systemic (intravenous) administration method and method of tandem (intranasal + intravenous) administration

Effectiveness of the therapy was evaluated before the transplantation (Day 0) and after the introduction of MSCs (Month 1 and Month 3) according to the dynamics of non-motor symptoms when scoring the following scales: The Montreal Cognitive Assessment, Hamilton Depression Rating Scale, The Pittsburgh Sleep Quality Index, The Epworth Sleepiness Scale, Non-Motor Symptoms Scale. The severity of motor symptoms of PD was evaluated on the basis of Section III of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS).

Results: A decrease of the severity of motor and non-motor symptoms in the post-transplant period was revealed.

Conclusion: Positive results allow us to consider the usage of MSCs in PD as a therapy modifying the course of the disease.

Disclosure: The research was carried out from the task "Development and implement a Parkinson disease therapy method using cellular technologies" (the subprogram "Transplantation of cells, organs and tissues" of the State scientific-technical program "New methods of medical care" (state registration number 20171292))

EPO1214

Application of the AT(N) biomarker classification system in corticobasal syndrome

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Background and aims: Corticobasal syndrome (CBS) is a rare clinical phenotype comprising symptoms and signs of higher cortical as well as basal ganglionic dysfunction. Diverse pathologies may underlie CBS, including corticobasal degeneration (CBD) and Alzheimer's disease (AD). A decrease in cerebrospinal fluid (CSF) beta-amyloid (A β 42), with an increase of total tau (τ T) and phosphorylated tau at threonine 181 (τ P-181) are established biomarkers of an underlying AD pathology. The AT(N) classification system groups biomarkers into those indicative of β amyloid deposition (A), pathologic tau (T) and neurodegeneration (N). This results in 5 biomarker groups: a) normal AD biomarkers; b) AD pathologic change; c) AD; d) AD and concomitant suspected non-AD pathologic change; e) non-AD pathologic change. The aim of this study was to classify CBS patients according to the AT(N) system.

Methods: All patients with a diagnosis of probable or possible CBS and available classical CSF biomarker data, which were examined at our clinic from 2011 to 2019, were included. All CSF analyses were performed by commercially available enzyme-linked immunosorbent assay kits (ELISAs).

Results: A total of 27 patients with CBS were included. 12 patients (44.4%) had an AD CSF profile and 3 patients an "Alzheimer's pathologic change" profile (11.1%). 7 patients (25.9%) had normal CSF biomarkers and 5 patients (18.5%) had a "non-AD pathologic change" CSF profile.

Conclusion: About 40% of CBS patients had an AD-CSF profile. More than 50% of CBS patients had decreased CSF A β 42 levels. The AT(N) system can be helpful in investigating the underlying pathology in CBS.

Disclosure: Nothing to disclose

EPO1215

STW5 (Iberogast®) for constipation in Parkinson's disease

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Background and aims: Chronic constipation is a frequent non-motor symptoms in Parkinson's disease (PD), and impairs patients' quality of life.

The aim of this pilot study was to assess the efficacy and tolerability of STW5, a phytotherapeutic agent composed of nine extract plants, for the treatment of constipation in PD patients.

Methods: We carried out an open-label monocentric study of STW5 for treating constipation in PD patients. 44 PD patients with a mean age of 66.4±7.3 years (range, 35-78), a mean disease duration of 12.6±5.4 years (range, 3-27) and with constipation defined by Rome III criteria for functional constipation were included. Following a 2 weeks laxative-free baseline period, all the patients were treated with 20 drops STW5 t.i.d for 28 days, after a 7 days titration period. Treatment efficacy was defined as a marked improvement of the stool frequency with an increase of 3 exonerations on the last week of treatment when compared to the week before treatment initiation. The treatment would be considered to be of clinical interest if a success response rate was obtained at least in 29/45 patients.

Results: An increase of stool frequency ≥ 3 eliminations/week was observed in 4 out of 44 patients (9,0%) at the end of the study. The only significant difference observed before and after treatment was a decrease of stool consistency ($p=0.0272$).

Conclusion: Our results suggest that STW5 is safe but is not effective as a phytotherapeutic agent to treat constipation in PD.

Disclosure: The research was supported by a researcher grant from C.H.U. Nantes.

EPO1216

Enteric LRRK2 as potential link between Parkinson's and Crohn's diseases

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Background and aims: An accumulating body of literature has emerged over recent years to show that Parkinson's disease (PD) is not only disorder of the brain but also of the gut-brain axis. Recent reports have shown that, aside from enteric synuclein neuropathology and gastrointestinal dysfunction, PD patients also exhibit some degree of gastrointestinal inflammation. The possible link between gastrointestinal inflammation and PD is further reinforced by genetic observations showing that the Leucine-rich repeat kinase 2 (LRRK2) gene, which has emerged as the gene most commonly associated with both familial and sporadic PD, is also a major susceptibility gene for Crohn's disease (CD).

This suggests that LRRK2 could be a link between gastrointestinal inflammation, PD and CD and therefore we set out to examine the expression levels of LRRK2 in the gastrointestinal tract of sporadic PD and CD patients.

Methods: Colonic biopsies of 14 controls, 6 CD and 9 PD subjects were analyzed by Western Blot and qPCR.

Results: We found that the expression levels of LRRK2 were increased in the colonic samples of CD patients when compared to controls. By contrast, no changes in the expression levels of LRRK2 were observed in colonic biopsies of sporadic PD patients.

Conclusion: Our results show that, despite the genetic and molecular links between the 2 disorders, the gastrointestinal inflammation in PD and CD follows different molecular mechanisms. Further research is nevertheless needed to determine if the expression levels of LRRK2 is increased in PD patients with a short disease duration or with LRRK2 mutations.

Disclosure: Nothing to disclose

EPO1217

A novel CCM2 mutation associated with choreoathetosis in family with Cerebral Cavernous Malformations

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Background and aims: Cerebral Cavernous Malformations (CCM) are vascular malformations occurring in the central nervous system. These abnormalities can present incidentally or manifest as hemorrhagic stroke, seizures and focal neurological deficits. CCMs are present in both sporadic and familial forms. The pathologic mutations of KRIT1/CCM1, MGC4607/CCM2 and PDCD10/CCM3 are responsible for familial cases of CCMs, inherited in an autosomal dominant manner. We report 2 family members presenting both with choreoathetosis, with a novel CCM2 mutation.

Methods: Case report.

Results: A 52-year-old woman, without personal or familiar history of stroke or epilepsy, was diagnosed with CCM at age 28. 10 years ago, she presented choreoathetoid movements of the right hand which evolved progressively until functional limitation. The proband's 23-year-old son reported since his 16 years old a tremor in both hands, with a right predominance. At the neurological evaluation he presented also choreoathetoid movements of the right hand. Subsequent MRI evaluation of both patients revealed multiple CCMs, with the largest lesion located in the left thalamic region. Genetic testing was performed and identified a c.514G>T p.(Glu172*) heterozygous mutation in the MGC4607/CCM2 gene, consisted in a premature terminated codon. To our knowledge, this mutation was not yet reported in the literature or population databases.

Conclusion: The anatomic location of the CCM is directly associated with the patient's symptoms. Choreoathetosis is an uncommon manifestation of CCM and in this family is most probably related with the thalamic lesion. Since both patients had a similar presentation, their mutation might be correlated with this specific phenotypic variation.

Disclosure: Nothing to disclose

EPO1218

Cardiac Innervation in Huntington's disease

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Background and aims: Huntington's disease (HD) patients often present abnormal modulation of blood pressure and heart rate. Arrhythmias and sudden cardiac death occur more frequently in HD subjects than in controls. We aimed to investigate whether cardiac autonomic innervation assessed by 123I- metaiodobenzylguanidine (MIBG) imaging is impaired in HD patients, in comparison with controls (Ctrl).

Methods: 14 patients (6 F and 8 M) were assessed by the Unified HD Rating Scale (UHDRS) and the Total Function Capacity (TFC). All patients and x Ctrl (5 F and 5 M) subjects underwent 123I-MIBG imaging. From planar images, the early and late heart-to-mediastinum (H/M) ratios were computed. Moreover, myocardial washout rates (WR) were also calculated.

Results: Demographic and clinical data are shown in Table 1, MIBG scintigraphy results in Table 2. We did not find a significant difference in early and late H/M ratios and WR between HD patients and Ctrl. There were no significant correlations between 123I-MIBG imaging data, clinical features and CAG expansion.

	Early H/M*	Late H/M*	Wash Out rate (%)*
Cases	2.03±0.28	2.06±0.36	14.6±17.9
Ctrl**	2.2±0.12	2.1±0.20	19.9±9.6

Table 2: MIBG scintigraphy results. Values below or above 2SD the mean of Ctrl were considered abnormal.

*: mean±SD; ** Ctrl: control subjects

Table 2: MIBG scintigraphy results. Values below or above 2SD the mean of Ctrl were considered abnormal. *: mean±SD; ** Ctrl: control subjects

Subjects	Gender	Age	DD*	UHDRS [§]	TFC [^]
1	F	50	10	20	13
2	M	51	1	27	11
3	M	65	3	25	11
4	F	68	5	33	9
5	M	47	5	34	10
6	F	64	8	35	11
7	F	41	4	15	10
8	F	39	3	11	13
9	M	46	2	4	13
10	M	66	11	42	7
11	F	74	3	11	13
12	M	35	1	8	13
13	M	47	6	12	12
14	M	42	7	45	8

Table 1: demographic and clinical data

*DD: disease duration; [§]UHDRS: section III of Unified Huntington's Disease Rating Scale; [^]TFC: Total Functional Capacity

Table 1: demographic and clinical data *DD: disease duration; [§]UHDRS: section III of Unified Huntington's Disease Rating Scale; [^]TFC: Total Functional Capacity

Conclusion: Our study results suggest that myocardial postganglionic sympathetic innervation is preserved in HD and the cardiovascular dysfunction may due to the impairment of brain areas, as the prefrontal cortex, the bilateral insular cortex, the anterior cingulate gyrus, the amygdala and the hypothalamus, associated with the regulation and modulation of the heart function and shown to be altered in HD. Furthermore, decreased levels of brain-derived neurotrophic factor, known to play a role in the neuro-mediated regulation of the heart rate and blood pressure, are reported in HD.

Disclosure: Nothing to disclose

EPO1219

Dopamine transporter imaging in Progressive Supranuclear Palsy subtypes

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Background: Recently new criteria for Progressive Supranuclear Palsy (PSP), which includes different phenotypes, have been proposed. In PSP patients a reduced tracer uptake in 123FP-CIT dopamine transporter single photon emission computed tomography (SPECT-DAT) is present. Nowadays there is an increasing interest in identifying neuroimaging biomarkers to support differential diagnosis among different PSP phenotypes.

Aim: The aim of our study was to investigate the role of SPECT-DAT imaging in differentiating between PSP-Richardson (PSP-RS) and PSP non-RS phenotypes.

Methods: Patients with diagnosis of PSP were included in the study. Patients performed SPECT-DAT imaging at disease onset; caudate and putamen binding specific indices and caudate to putamen ratio were evaluated for each side. Clinical features including motor assessment, performed using Progressive Supranuclear Palsy Rating Scale (PSPrs), were considered.

Results: 29 PSP patients were enrolled in the study, 22 PSP-RS and 7 PSP non-RS. No significant differences were found in caudate, putamen indices or caudate to putamen ratio for each side between PSP-RS and nonRS in SPECT-DAT imaging. SPECT imaging shows low sensitivity and specificity in differentiating PSP-RS and non-RS. No significant differences were found in age, disease duration or PSPrs between groups.

Conclusion: SPECT-DAT imaging does not show an adequate diagnostic accuracy to differentiate PSP-RS and PSP non-RS phenotypes in our samples, however such data need to be confirmed in larger samples of patients.

Disclosure: Nothing to disclose

EPO1220

Quantitative EEG analysis and neuropsychological testing in de novo PD patients

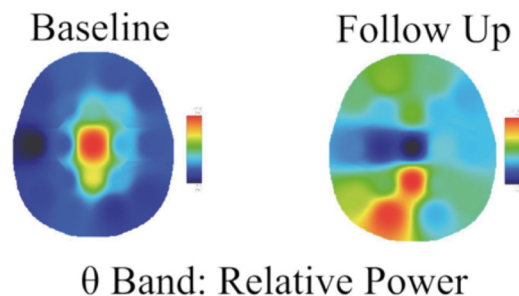
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Background and aims: Search for disease biomarkers is essential to improve our knowledge on pathophysiology and treatment for Parkinson's Disease (PD). Quantitative EEG analysis may reflect the cognitive status of patients affected by PD. The aim of our study was to evaluate quantitative EEG (qEEG) and neuropsychological testing in patients with PD.

Methods: 16 de novo cognitive preserved PD patients underwent motor symptoms examination (UPDRS-III), neuropsychological assessment and qEEG during the diagnostic work-up and after 18 months. EEG was performed at rest. As reference parameter of spectral analysis, relative power of EEG bands (delta, theta, alpha and beta) was considered. In the neuropsychological evaluation we used a validated multi-domain neuropsychological battery for PD.

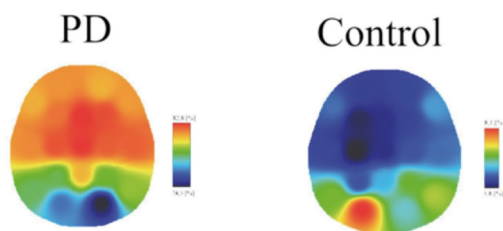
Results: We noticed a greater representation of slow rhythms in PD de novo patients compared to healthy controls, already at the baseline. Conversely, at follow-up the slowdown of the scalp activity was not homogeneous in all the derivations considered. We also observed a decrease in the UPDRS-III scores and an increase (that is, an improvement of performance) in RAVLT, Recognition, MFTC, Stroop test. Finally, the greater was the representation of the theta rhythms, the lower was the improvement in motor performances obtained after therapy (L-dopa, dopamine agonists, iMAO-B).



Spectral maps. Modifications of theta band in PD patient between t0 and t1.

Conclusion: qEEG analysis may represent an useful neurophysiological approach in patients with de novo Parkinson's disease to observe cognitive performance and disease progression. Longer follow-up and more patients are needed to confirm this preliminary impression. Finally, is to be elucidated if it was the disease itself or therapy that influenced the qEEG parameters among time.

Disclosure: Nothing to disclose



θ Band: Relative Power

Spectral maps. Representation of theta band in PD vs controls.

EPO1221

Perampanel and Essential Tremor

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Objectives: To assess the safety of Perampanel in patient with essential tremor and to clarify the efficacy of the aforementioned medication in this population.

Background: Essential Tremor (ET) is the most frequent movement disorders. Medical treatment for ET is often unsatisfactory with 1st-line drugs only achieving 50-60% improvement. Over the last year, distribution problems of primidone led to rapid change of treatment for some ET patients in Spain. Since perampanel has been suggested to be effective for ET we have tried perampanel in those ET patients previously treated with primidone

Methods: We have evaluated patients from our movement disorders clinic with the diagnosis of ET, who were refractory to 1st-line drug (primidone and propranolol). Assessments were done in base line condition (without any other medication for ET) and after 1 month of 4mg perampanel a day. Details about tolerance and effectiveness were collected. Clinical evaluation included Tolosa scale (paired non-parametric test). Specially in those patients to not tolerated perampanel.

Results: We have found positive results in some, not all patients. We will report our final results of our patients treated with perampanel.

Conclusion: Our preliminary study suggests that perampanel may be an option for ET patients.

Disclosure: Nothing to disclose

EPO1222

Skin biopsy may help to distinguish Multiple System Atrophy-parkinsonism type from Parkinson's disease with orthostatic hypotension

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Background and aims: Multiple System Atrophy parkinsonism type (MSA-P) shows a similar clinical but a different prognosis compared to Parkinson disease with orthostatic hypotension (PD+OH). No established diagnostic test is available to help the differential diagnosis of these 2 conditions. This study aimed to distinguish MSA-P from PD+OH by means of the search of phosphorylated α -synuclein (p-syn) in skin nerves.

Methods: 20 patients fulfilling clinical diagnostic criteria for MSA-P and 20 patients with clinical diagnostic criteria for PD+OH with similar disease duration were recruited for this study. Clinical diagnosis was supported by brain MR typical findings in all patients with MSA-P and abnormal cardiac MIBG in the majority of patients with PD+OH. Patients underwent skin biopsy from cervical, thigh and leg to search for p-syn deposits in skin nerves

Results: All PD+OH patients were positive for p-syn in autonomic skin fibers; scarce somatic fibers were positive for p-syn in 2 patients. The intraneural p-syn positivity was found in 75% of MSA-P patients, mainly in distal skin sites. Importantly, p-syn deposits differ from PD+OH since they were mainly found in somatic fibers of subepidermal plexuses and in scant sympathetic fibers of 2 patients.

Conclusion: The main conclusions of our study are: 1) skin biopsy allows to differentiate PD+OH from MSA-P since p-syn deposits are mainly found in different skin nerve fibers which may help the clinical differentiation of these 2 disorders; 2) the site of autonomic failure is likely different mainly affecting postganglionic sympathetic fibers in PD+OH and pre-ganglionic fibers in MSA-P.

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EPO1223

A case of dystonia gravidarum

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Background and aims: We describe a case of cervical dystonia in a 36 year-old, secundigravid, Caucasian woman at 8 weeks gestation, which responded to treatment with procyclidine and clonazepam with reduction in severity of dystonia, but not complete resolution of symptoms. Pregnancy is known to cause extrapyramidal syndromes, including chorea, ballismus and restless leg syndrome. The mechanism is poorly understood, but oestrogen likely plays a role in modulating nigrostriatal dopaminergic activity. Drug induced dystonic reactions are common in pregnancy, but there has only been 4 cases of new onset dystonia of pregnancy reported in the literature.

Methods: Patient clinical notes were reviewed along with results of ancillary investigations.

Results: Investigations were unremarkable for secondary causes of dystonia, including wilson's disease, autoimmune disease and thyrotoxicosis.

Conclusion: Pregnancy is known to both exacerbate existing movement disorders and precipitate de novo movement disorders. Based on a small number of case studies, dystonia gravidarum is an emerging clinical entity with a distinct clinical phenotype. Low dose benzodiazepines and anticholinergics can provide symptomatic relief, but symptoms appear to resolved spontaneously in the 3rd trimester or soon after delivery with or without treatment.

Disclosure: Nothing to disclose

EPO1224

Efficacy and safety of opicapone in Parkinson's disease patients according to duration of motor fluctuations: post-hoc analysis of BIPARK-I and II

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Background and aims: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved effective in the treatment of end-of-dose motor fluctuations in Parkinson's disease (PD) patients in 2 large multinational trials (BIPARK-I and II) [1,2]. This exploratory post-hoc analysis evaluated the efficacy and safety of OPC in levodopa-treated PD patients with duration of motor fluctuations of up to 1 year ('early motor fluctuators' [EMF]) or more than 1 year ('long-standing MF' [LMF]).

Methods: Patient-level data from matching treatment arms in BIPARK-I and II were combined in placebo (PLC) and OPC 50mg groups. Studies had similar designs and eligibility criteria [1,2]. Outcomes were compared for PLC versus OPC for EMF and LMF. Statistical analysis of efficacy was performed using analysis of covariance.

Results: Overall, 71 PLC and 85 OPC patients were EMF whereas 174 PLC and 162 OPC patients were LMF (Safety Set; Table 1). Changes from baseline in absolute OFF- and ON-time were significantly greater for OPC versus PLC in both EMF and LMF (Table 2). Dyskinesia was the most frequently reported at least possibly related treatment-emergent adverse event, with approximately 2-fold increase in incidence in LMF versus EMF in the OPC groups (23.5% vs. 11.8%), which might be due to longer disease duration and higher daily levodopa dose.

Table 1. Baseline characteristics (Safety Set)

Characteristic	EMF (<=1 year)		LMF (>1 year)	
	PLC N=71	OPC 50 mg N=85	PLC N=174	OPC 50 mg N=162
Age, mean (SD) years	63.9 (9.4)	63.7 (9.4)	62.3 (9.1)	65.1 (8.6)
Disease duration, mean (SD) years	5.8 (2.6)	5.9 (2.8)	8.5 (4.1)	8.6 (4.7)
Daily OFF-time, mean (SD) hours	5.8 (1.8)	6.0 (1.7)	6.3 (2.2)	6.4 (2.1)
Levodopa dose, mean mg/day	585.4 (274.6)	616.6 (301.5)	742.3 (324.6)	739.3 (323.3)

EMF, early motor fluctuators; LMF, long-standing motor fluctuators; OPC, opicapone; PLC, placebo; SD, standard deviation

Table 1

Table 2. Changes from baseline in absolute OFF- and ON-time (Full Analysis Set)

Characteristic	EMF (</=1 year)		LMF (>1 year)	
	PLC N=71	OPC 50 mg N=85	PLC N=172	OPC 50 mg N=161
Absolute OFF-time				
LS mean (SE; 95% CI)	-74.4 (19.2);	-139.6 (18.1);	-51.9 (13.5);	-112.4 (13.2);
change from baseline, min	-112.1, -36.7)	-175.1, -104.1)	-78.3, -25.5)	-138.3, -86.5)
LS mean (SE; 95% CI)	-65.2 (26.3; -116.9, -13.5)		-60.5 (18.9; -97.5, -23.5)	
absolute difference, min	0.0135		0.0014	
p-value	0.0135		0.0014	
Absolute ON-time				
LS mean (SE; 95% CI)	52.9 (19.1);	140.4 (18.0);	48.2 (13.4);	115.3 (13.2);
change from baseline, min	15.4, 90.4)	105.1; 175.7)	21.9, 74.6)	89.5, 141.1)
LS mean (SE; 95% CI)	87.5 (26.3; 35.9, 139.0)		67.1 (18.8; 30.2, 104.0)	
absolute difference, min	0.0009		0.0004	
p-value	0.0009		0.0004	

CI, confidence interval; EMF, early motor fluctuators; LMF, long-standing motor fluctuators; LS, least squares; OPC, opicapone; PLC, placebo; SE, standard error

Table 2

Conclusion: OPC 50mg demonstrated efficacy in both EMF and LMF, with a lower incidence of dyskinesia in EMF. This reinforces the usage of OPC regardless of duration of motor fluctuations.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.
2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPO1225

Subacute parkinsonism due to bilateral subdural hematoma

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Background and aims: To illustrate a non-common presentation of subacute parkinsonism.

Methods: A 92-year-old male patient with non relevant neurological background.

Results: The patient suffered a traffic accident 4 months before the start of the symptoms. The clinic begins one month before the entry to hospital with progressive deterioration that intensified in the two previous weeks in which his family saw him more standing, with slower walking and slow activity. More inexpressive and depressed mood as well as unexpected falls. In neurological examination stood out hypophonia, bilateral bradykinesia of right predominance with stiffness of the 4 limbs and the gait with short passage, anterocoli and decrease in bracing stood out. Cranial CT is performed showing bilateral subdural hematoma, being evacuated the day after with great improvement of bradykinesia and gait.

Conclusion: We present an unusual cause of subacute parkinsonism in order to emphasize the relevance that can take this form of presentation in order to raise a correct management.

Disclosure: Nothing to disclose

EPO1226

Olfactory dysfunction in restless legs syndrome

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Background and aims: Dopaminergic dysfunction has been implicated in the pathogenesis of restless legs syndrome as in Parkinson's disease (PD). Because PD is associated with a loss of olfactory function, we aimed to investigate olfactory functions in patients with restless leg syndrome (RLS).

Methods: 54 with RLS and 50 healthy controls were included in the study. Olfaction was tested using the Connecticut Chemosensory Clinical Research Center (CCCRC) olfactory test.

Results: The mean age (50.9 ± 8.5 vs 50.7 ± 8.7 years, $p=0.893$) and gender distribution (female/male, 37/17 vs 31/19, $p=0.485$) were similar between patient and control groups. In the patient group, the olfactory threshold, discrimination and total scores were significantly higher than the control group ($p<0.01$). There was a significant negative correlation between age ($p=0.16/r=-0.196$) and olfactory domains in contrast to disease duration, drug use duration and RLS severity scale.

Conclusion: Our results confirm that decreased olfaction in patients with RLS. This supports the similarity of pathogenesis of PD and RLS.

Disclosure: Nothing to disclose

EPO1227

Efficacy of continuous subcutaneous infusion of ABBV-951 on early morning symptoms in advanced Parkinson's disease patients from a phase 1b study

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Background and aims: ABBV-951 (foslevodopa/foscarbidopa) is a new soluble formulation of carbidopa and levodopa prodrugs designed for 24h/day delivery via continuous subcutaneous infusion (CSCI). Early morning symptoms (e.g. akinesia, delayed-on) are a significant burden for Parkinson's disease (PD) patients. The 24h/day CSCI of foslevodopa/foscarbidopa may improve early morning symptoms.

Methods: Individually optimized therapeutic doses of foslevodopa/foscarbidopa were delivered as CSCI for 28 days in advanced PD patients (Study M15-739, NCT03374917). Differences in daily hours of "Off" and "On" time, with or without dyskinesia, and changes in the 1st symptom reported upon awakening after ≥ 2 h of continuous sleep (from midnight to noon), were assessed via PD diaries from baseline (BL, before switching from oral levodopa to foslevodopa) through study end (D28). Safety endpoints were monitored.

Results: 21 patients (62% male, mean age 61.6, 43% ≥ 10 years PD duration) were included in this analysis. The overall mean (SD) change from BL to D28 in normalized daily "Off" time was significantly reduced (-4.6 [2.5], $p<0.001$). Comparing BL to D28, the percentage of patients reporting "Off" time as the first symptom upon awakening decreased from 86.7% to 10.8%, "On" without dyskinesia increased from 10.0% to 84.2%, "On" with non-troublesome dyskinesia increased from 0% to 4.9%, and "On" with troublesome dyskinesia decreased from 3.3% to 0%. 19 patients (90.5%) experienced at least one adverse event, with most rated mild to moderate in severity.

Conclusion: In advanced PD patients, tested doses of foslevodopa/foscarbidopa were generally well-tolerated when delivered 24h/day via CSCI, reduced overall daily "Off" time and improved early morning symptoms.

Disclosure: AbbVie funded the research for this study and participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission. All authors had access to the data; participated in the development, review, and approval of the abstract, and agreed to submit this abstract.

EPO1228

Foslevodopa/foscarbidopa maintains stable levodopa and carbidopa exposure following subcutaneous infusion in Parkinson's disease patients

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Background and aims: As Parkinson's disease (PD) progresses, symptoms can no longer be well controlled by oral medication presumably due to large fluctuations in levodopa concentrations and a narrow therapeutic window. Foslevodopa/foscarbidopa, also known as ABBV-951, is a new investigational drug being developed for the treatment of PD that provides continuous therapeutic levels of levodopa (LD) and carbidopa (CD). The current work characterizes the LD and CD pharmacokinetics (PK) in PD patients following subcutaneous (SC) infusions of foslevodopa/foscarbidopa delivered at 4 different rates.

Methods: Foslevodopa/foscarbidopa was administered via abdominal SC infusion of PD patients over 72 hours. Patients were stratified in 4 dose groups and received a fixed dose of ABBV-951 based on their oral daily LD intake. Serial plasma PK samples were collected to assay for LD and CD concentrations. Safety and tolerability were assessed throughout the study.

Results: Preliminary results from 14 subjects who completed the study showed that following foslevodopa/foscarbidopa SC infusion, LD and CD exposure quickly reached a steady state and remained stable with minimal fluctuations. In this study, LD exposure from foslevodopa/foscarbidopa was consistent with that from oral LD medications, covering the broad range expected to control motor symptoms in PD patients. 4 subjects reported adverse events that were considered possibly related to treatment. The only adverse event which occurred in more than 1 subject was infusion site pain which occurred in 2 subjects.

Conclusion: Foslevodopa/foscarbidopa was able to deliver stable LD and CD exposures in PD patients.

Disclosure: This study was funded by AbbVie and AbbVie contributed to the study design, research and interpretation of data, writing, reviewing and approving the publication, all authors are AbbVie employees and may hold AbbVie stocks or options.

EPO1229

Improvements in motor symptoms in patients with advanced Parkinson's disease on long-term LCIG monotherapy or combination therapy: an analysis of the COSMOS observational study

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Background and aims: Advanced Parkinson's disease (PD) patients may experience insufficient symptom control with oral medication over time and may be candidates for device-aided therapies such as levodopa-carbidopa intestinal gel (LCIG) delivered continuously via percutaneous endoscopy gastrostomy with a jejunal extension tube. The COSMOS study is the 1st assessment of real-world usability of LCIG as monotherapy or in combination with add-on PD medications.

Methods: In this multicountry, retrospective and cross-sectional, post-marketing observational study (NCT03362879), advanced PD patients treated with LCIG for ≥ 12 months were stratified into 3 groups: LCIG monotherapy, LCIG monotherapy with oral or transdermal PD medication at nighttime only (ie, LCIG daytime monotherapy), and LCIG plus add-on PD medications. Assessments included motor symptom frequency/severity, and evaluation of "Off" time and "On" time with dyskinesia before starting LCIG and at study visit.

Results: Of 378 patients, 120 (32%) were treated with LCIG monotherapy at the 12-month visit, 94 (25%) received LCIG daytime monotherapy with adjunctive nighttime oral/transdermal PD medication, and 164 (43%) received LCIG plus add-on PD medication. Patient characteristics were similar between groups (Table). Patients treated with LCIG monotherapy tended to have slightly lower baseline "Off" time and dyskinesia duration than other treatment groups. All treatment groups experienced significant ($p < 0.0001$) reductions from baseline in "Off" time and dyskinesia duration, with no significant between-group differences (Figure). Most motor symptoms showed improvements in frequency and severity after LCIG initiation.

Table 1. Patient Demographics and Characteristics at Patient Visit

Characteristic	LCIG Monotherapy (n = 120)	LCIG Daytime Monotherapy (n = 94)	LCIG + Add-on PD Medication (n = 164)
Male, n (%)	75 (62.5)	66 (70.2)	104 (63.4)
Age, y	69.6 (8.1)	70.4 (7.1)	68.8 (7.9)
Time since PD diagnosis, y	15.2 (5.5)	15.3 (5.5)	16.3 (6.3)
Time from PD diagnosis to Motor fluctuation onset, y	7.3 (3.4)	7.1 (3.6)	7.5 (4.1)
LCIG initiation, y	12.0 (5.1)	12.7 (4.8)	13.5 (6.8) ^a
LCIG treatment duration, months	39.3 (25.6) ^b	31.8 (22.3) ^c	35.7 (21.9)
"Off" time before LCIG initiation, hours	5.7 (3.3)	6.7 (4.4)	6.1 (3.3)
Dyskinesia duration, hours/day	3.3 (2.9)	4.6 (3.5) ^d	3.8 (3.4)
	(n = 85)	(n = 59)	(n = 110)

^aP = 0.0211 compared with LCIG monotherapy group.

^bn = 118.

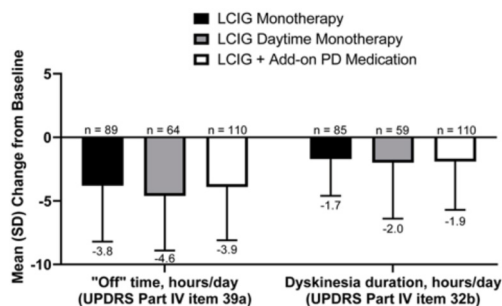
^cP = 0.0328 compared with LCIG monotherapy group.

^dP = 0.0337 compared with LCIG monotherapy group.

Data are presented as mean (SD), unless otherwise noted.

LCIG, levodopa-carbidopa intestinal gel; PD, Parkinson's disease; SD, standard deviation.

Figure. Change from Baseline in "Off" Time and Duration of Dyskinesia After 12 Months of LCIG Treatment



LCIG, levodopa-carbidopa intestinal gel; PD, Parkinson's disease; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale.

Conclusion: Patients with advanced PD treated with LCIG monotherapy or combination therapy experienced similar reductions in "Off" time and duration of dyskinesia.

Disclosure: AbbVie funded the research for this study and provided writing support for this abstract. Medical writing assistance, funded by AbbVie, was provided by Kelly M Cameron, PhD, CMPPTM, of JB Ashtin.

EPO1230

Characterizing intercountry differences in patients with Parkinson's disease controlled vs uncontrolled with current treatment: a subgroup analysis of the OBSERVE-PD observational study

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Background and aims: As Parkinson's disease (PD) progresses, oral levodopa often becomes insufficient for symptom control. Classification of advanced PD (APD) is not distinct, making it challenging to determine the need for advanced therapies. This analysis focused on characterization of PD patients with/without controlled PD symptoms and intercountry differences.

Methods: OBSERVE-PD is a multicountry, cross-sectional, observational study conducted in 2615 PD patients across 128 movement disorder centers in 18 countries. This post hoc analysis stratified patients into 4 groups: APD or non-APD with controlled or uncontrolled symptoms. Patients were diagnosed as APD vs non-APD by investigator judgment. Whether patients were controlled on current therapy was determined by specific Delphi criteria (any of the following: taking oral levodopa ≥ 5 times/day, having ≥ 2 hours/day "Off" time, unpredictable fluctuations of motor symptoms, troublesome dyskinesias, or limitations in ≥ 1 activity of daily living). Intercountry differences were analyzed with descriptive statistics.

Results: Based on the Delphi criteria, 78% of patients were uncontrolled on their current therapy, although the intercountry range was varied (4% to 96%). More APD vs non-APD patients had uncontrolled symptoms (Table). The mean age range across countries was similar. APD patients generally had a longer time since PD diagnosis than did non-APD patients, with some intercountry variability, regardless of patients' symptom control.

Table. Patient Baseline Characteristics

Characteristic	Mean (SD)			
	Overall population (N = 2615) ^a	Intercountry Range		Non-APD (n = 679)
		Controlled (n = 47)	Uncontrolled (n = 1353)	
Age, years	67.0 (9.9) (n = 2610)	54.3 (6.35) – 70.0 (0.00)	63.9 (8.92) – 71.3 (10.39)	69.5 (6.19) – 77.5 (2.12)
Time since PD diagnosis, years	7.7 (5.9) (n = 2553)	5.0 (3.57) – 30.5 (N/A) ^b	7.8 (4.61) – 14.0 (6.06)	1.8 (1.70) – 7.2 (1.77)
Duration of motor fluctuations, years	4.4 (3.7) (n = 1423)	2.0 (N/A) ^b – 15.0 (N/A) ^b	3.3 (2.14) – 8.6 (5.73)	1.0 (N/A) ^b – 2.0 (N/A) ^b
Time since referral, years	3.5 (4.2) (n = 1902)	0.1 (N/A) ^b – 10.4 (N/A) ^b	0.5 (1.26) – 7.3 (4.83)	0.3 (0.22) – 3.8 (5.09)

^aOnly available data are presented.

^bOnly 1 patient was in the specified group with available data, so the standard deviation could not be calculated.
APD, advanced Parkinson's disease; SD, standard deviation.

Conclusion: Most patients with APD were uncontrolled on current therapy and >50% of non-APD patients did not have controlled PD symptoms, although this was varied between countries. Criteria-based assessment of sufficient symptom control may help inform the need for further treatment optimization.

Disclosure: AbbVie funded the research for this study and provided writing support for this abstract. Medical writing assistance, funded by AbbVie, was provided by Kelly M Cameron, PhD, CMPP™, of JB Ashtin.

MS and related disorders 1

EPO1231

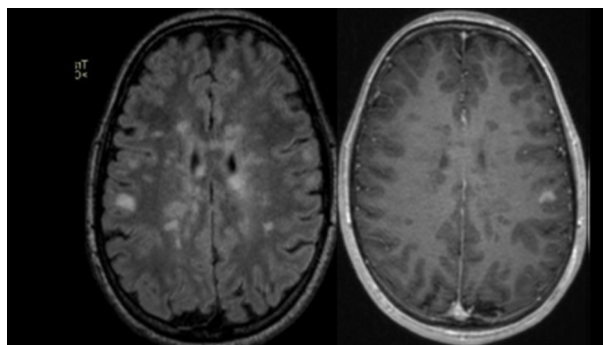
MOG-IgG positivity in pediatric-onset multiple sclerosis: a diagnostic and therapeutic challenge

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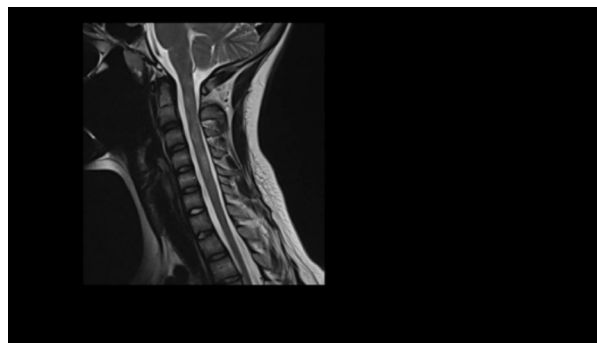
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Background and aims: Myelin oligodendrocytes glycoprotein (MOG)-IgG are found in children with acquired demyelinating syndromes with a distinct phenotype from multiple sclerosis (MS). Interpretation of positive MOG-IgG in pediatric-onset MS and treatment implication are unclear. We present the case of a typical MS patient with positive MOG-IgG and discuss our treatment approach.

Methods: A 15-year-old girl with congenital aortic stenosis developed subacute right hand tingling, weakness, and gait instability. Physical examination showed right-sided proprioceptive ataxia and brisk deep tendon reflexes in the lower extremities (per-attack EDSS of 1.5). Brain MRI showed numerous juxtacortical, periventricular, and infratentorial lesions, with at least 8 enhancing lesions. Cervical and thoracic cord MRI showed multiple short-segment contiguous lesions extending along the cervical cord, with 2 enhancing lesions, and 2 non-enhancing short-segment lesions in the mid-thoracic cord. CSF studies showed positive oligoclonal bands. Aquaporin4-IgG were negative. Anti-MOG-IgG were positive (titer 1:20). She received high-dose intravenous methylprednisolone for 5 days followed by an oral prednisolone taper with near-complete resolution of symptoms. She was started on intravenous Rituximab 1000mg.



Brain MRI (left: axial T2 FLAIR, right: axial T1 with gadolinium) showing multiple lesions typical of multiple sclerosis, with some but not all lesions with contrast enhancement.



Cervical cord MRI (sagittal T2 sequence) showing numerous short-segment contiguous lesions, suggestive of multiple sclerosis.

Results: This patient has a clinical and radiological presentation consistent with pediatric-onset MS rather than acute demyelinating encephalomyelitis (ADEM), which is known to be associated with MOG-IgG in children. Transient MOG-IgG positivity is described in monophasic ADEM but not clearly reported in MS relapses. We elected to treat her with Rituximab as a highly-effective disease modifying therapy for MS and for its efficacy in MOG-related disorder.

Conclusion: MOG-IgG positivity in typical pediatric-onset MS poses a diagnostic and therapeutic challenge and should be further investigated.

Disclosure: Nothing to disclose

EPO1232

Disability, cognition and double inversion recovery magnetic resonance imaging brain sequence in a sample of egyptian patients with multiple sclerosis

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Background and aims: In Multiple Sclerosis (MS) cortical pathology recently returned to the spotlight of research as a result of specialized magnetic resonance imaging (MRI) sequences, double inversion recovery (DIR) which allows better detection of cortical lesions (CLs). Cognitive impairment occurs in 40-65% of MS patients, typically involving complex attention, information processing speed, episodic memory and executive functions. The aim of this study is to investigate the association between the presence of CLs, the clinical disability and psychological features of MS.

Methods: 30 Egyptian patients of RRMS underwent MRI for the assessment presence of cortical lesions using DIR sequences on 1.5 tesla. Disability was assessed using the Expanded Disability Status Scale (EDSS). Cognitive functions were assessed using the Brief International Cognitive Assessment for Multiple Sclerosis patients (BICAMS) Arabic version

Results: 27 out of 30 patients had cortical lesions detected by DIR and not detected by FLAIR. Patients were cognitively impaired mainly in Visual processing speed detected by Symbol Digit Modality Test (SDMT) which is highly sensitive in the assessment of cognitive impairment, and verbal memory detected by California verbal fluency test, with significant negative correlation with disability ($r=-0.381$, $p=0.038$, $r=-0.548$, $p=0.002$) respectively. There was a significant negative correlation between numbers of cortical lesions and verbal memory especially in right hemisphere lesions ($r=-0.431$, $p=0.018$), but not with the disability

Conclusion: Cortical lesions are better to be assessed with the DIR sequence compared to FLAIR. Cortical lesions correlated with verbal memory but not with disability in MS patients

Disclosure: Nothing to disclose

EPO1233

The effect of pelvic floor exercise program on incontinence and sexual dysfunction in multiple sclerosis patients

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Background and aims: Patients with multiple sclerosis (MS) may present with urological symptoms and sexual dysfunction or may develop such symptoms at any time. Besides, incontinence and sexual dysfunction may persist in the remission phase after the attack. Therefore, patients may experience a significant decrease in their quality of life. This study aimed to investigate the effect of pelvic floor exercise program on incontinence and sexual dysfunction in MS patients.

Methods: Patients with RRMS admitted to the outpatient clinic between January 2018 and September 2018 were included in the study. Pre-exercise bladder and post-void residual volumes (PVR) of the patients were measured by ultrasonography. Patients completed Incontinence Questionnaire Short Form (ICIQ-SF), Beck Depression Inventory (BDI), Multiple Sclerosis Quality of Life-54 (MSQOL-54), Female Sexual Function Index (FSFI), Sexual Health Inventory for Men (SHIM). In the control examination of the patients who completed the program regularly for 3 months, questionnaires and measurements with ultrasound were repeated. Data from 26 patients were analyzed.

Results: There was a statistically significant increase in bladder volume when pre- and post-exercise measurements were compared, but there was no difference in PVR ($p=0.004$, $p=0.4$, respectively). There was a significant reduction in post-exercise values of ICIQ-SF ($p=0.026$). There was no difference in depression scales, quality of lives, and sexual functions in the pre- and post-pelvic floor examinations.

Conclusion: According to this study, while pelvic floor exercise had no effect on sexual dysfunction in MS patients, it can be thought that incontinence may decrease by causing increased bladder volume.

Disclosure: Nothing to disclose

EPO1234

Presence of brainstem lesions is associated with diffuse spinal cord abnormalities in patients with early multiple sclerosis

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Background and aims: The presence of early spinal cord (SC) and infratentorial lesions has been associated with higher risk of long-term disability in multiple sclerosis (MS). Little is known about significance of early diffuse SC abnormalities. We aimed to examine the association of intracranial lesion distribution and SC pathology in patients with early-stage MS (PweMS; disease duration ≤ 5 years).

with ScanView. Diffuse SC pathology was estimated by 2 raters on T2WFS/PDW images. Volume and lesion parameters of PweMS with- and without diffuse SC abnormalities were compared by (non)parametric tests. Risk of having diffuse SC abnormalities was determined by logistic regression.

Results: Table 1 summarizes the results. PweMS with diffuse SC abnormalities had higher brainstem and cerebellar LV than PweMS without ($p=0.007$ and $p=0.024$), whereas they did not differ in total intracranial LV ($p=0.249$), brain- and SC-volume ($p=0.975$, $p=0.716$). Early brainstem lesions showed a 6-fold increased risk of diffuse SC abnormalities (OR 6.04, 95% CI 1.56–23.39, $p=0.009$).

Conclusion: Early brainstem lesions are associated with higher risk of SC diffuse abnormalities, that are not associated with relative SC volume loss. Early diffuse SC abnormalities might therefore i.) precede spinal cord atrophy and ii.) present a link between infratentorial lesions and risk of long-term disability.

Disclosure: The Project was Supported by: RVO-VFN64165, AZV grant NV18-04-00168. Michaela Andelova received financial support for conference travel from Novartis, Genzyme, Merck Serono, Biogen Idec and Roche. The complete disclosures from my coauthors exceed the limit of 100 words and if they are required for the abstract submission, I can send them in a separate email. Thank you in advance for letting me know.

Table 1. Demographic and MRI data of early MS patients with- and without diffuse spinal cord abnormalities.

	diffuse SC abnormalities absent	diffuse SC abnormalities present	p value
n	38	21	
Age	33.0 \pm 8.2	30.1 \pm 6.3	0.165
Disease duration	0.73 \pm 1.04	1.1 \pm 1.4	0.276
Brain tissue	1133.89 \pm 125.1	1132.94 \pm 135.8	0.975
Corpus callosum	4.90 \pm 0.64	5.08 \pm 0.99	0.407
MUCCA	89.25 \pm 8.0	88.36 \pm 10.28	0.716
Lesion volume	6.06 \pm 7.74	8.94 \pm 11.0	0.249
Frontal lesions	1.01 \pm 1.61	1.85 \pm 3.0	0.387
Temporal lesions	0.53 \pm 1.07	0.89 \pm 1.58	0.423
Parietal lesions	1.11 \pm 1.91	2.09 \pm 3.70	0.369
Occipital lesions	0.43 \pm 0.41	0.62 \pm 0.72	0.414
Deep hemispheric les.	2.94 \pm 3.44	3.31 \pm 2.18	0.177
Cerebellar lesions	0.01 \pm 1.61	0.07 \pm 0.01	0.024
Brainstem lesions	0.02 \pm 0.04	0.11 \pm 0.18	0.007
EDSS	1.5 (0 – 4.0)	2.0 (0 – 4.0)	0.086

Data are displayed as means \pm standard deviations except EDSS for that median (min. – max.) is shown; age and disease duration are measured in years; volumetric data are shown in millilitres except of the area of corpus callosum and MUCCA which are measured in mm². Normalized data are not shown.

EDSS = expanded disability status scale, MUCCA = mean upper cervical cord area, TIV = total intracranial volume.

Table 1. Demographic and MRI data of early MS patients with- and without diffuse spinal cord abnormalities.

Methods: Brain volumes were assessed in 59 PweMS on T1-w images using the MorphoBox prototype. Intracranial lesion volumes (LV) and location (frontal, temporal, parietal, occipital, deep hemispheric, cerebellar, brainstem) were automatically assessed using T1-w and FLAIR images using the LeManPV-prototype. SC volume was measured

EPO1235

Influence of some non-HLA SNPs on the severity of disability in multiple sclerosis during the interferon-beta and glatiramer acetate therapy

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Background and aims: It is known that lots of non-HLA single nucleotide polymorphisms (SNPs) contribute to the multiple sclerosis (MS) risk. The aim was to evaluate the influence of some non-HLA SNPs on MS severity and progression.

Methods: The study included 151 MS patients (46 male/105 female). The median age was 39 [32;48] years. The level of disability (EDSS median=4,0 [3.0;5.5]) and progression rate (0.42 [0.28;0.67]) were moderate. All patient received disease modifying therapy at least 6 months (76.8%-interferon-beta (IFN-beta), 23.2%-glatiramer acetate (GA). The genetic analysis of rs10492972 (KIF1B), rs11787532 (ZFHX4), rs9527281 (STARD13), rs7308076 (CIT), rs733254 (ZFAT) SNPs was conducted with real-time PCR using TaqMan probes. Multiple analysis of the alleles frequency was done by SNPstats software (Institut Català d'Oncologia, Spain).

Results: The allele combination TGTCa (alleles are arranged in order of SNPs mention) was associated with the high rate of MS progression in patients taking IFN-beta (OR=1.07, 95% CI 0.62-1.52, p=0.004). In the same group the TGGTC combination was significantly associated with a higher EDSS score (OR=1.53, 95% CI 0.28-2.79, p=0.046) and TGTCC with a lower one (OR=-2.12, 95% CI -4.0-0.23, p=0.046). In the group of GA the EDSS score was depended on TGGCA (OR=3.14, 95% CI 0.81-5.47, p=0.046) and CGTCA (OR=4.01, 95% CI 1.79-6.23, p=0.046) combinations.

Conclusion: The results might be used as additional criteria for disease modifying therapy selection (Priority of the invention №2019108392, 03.22.19).

Disclosure: The research was supported by the regional grant U.M.N.I.K. №13195GU/2018 (FSBI «Innovation promotion fund», Russia).

EPO1236

Clinical and neuroradiological characterization of a MS-plus population with low frequency of perivenular lesions identified with central vein sign: is there an underlying disease other from MS?

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Background and aims: Central vein sign (CVS) is a multiple sclerosis (MS) specific MRI-biomarker defined as a perivenular white matter lesions frequency (PVL-f)>50% ("50%-rule"). CVS distinguishes MS from its mimics, in which PVL-f is steadily<50%. Thus far CVS has never been evaluated in MS-plus (MS-patients with red flags of better explanation of disease). Aim of this study are to 1) identify with CVS a proportion of MS-plus patient with PVL<50% 2) characterize MS-plus subgroups in terms of clinical, laboratory and MRI features.

Methods: Definite relapsing-remitting (RR)MS and RRMS patients with MRI, laboratory or clinical red-flags of better explanation (MS-plus), were included. Patients underwent one brain-MRI scan including FLAIR and T2*sequences, and were stratified according to the 50%-rule. Clinical-demographic, laboratory and additional MRI features were collected and analyzed.

Results: 50%-rule was fulfilled by 28/28 (100%) MS-patients (median PVL-f 90.5%, range 68-100%) and by 32/60 (53%) MS-plus patients (median PVL-f 70.5%, range 55-100%), whereas 28/60 (47%) MS-plus patients showed PVL<50% (median PVL-f 23.5% range 10-48%), identifying a separate subset of patients (Fig. 1).

MS-plus with PVL<50% compared to the PVL>50% subgroup showed a higher proportion (p<0.001) of cardiovascular risk factors, MRI red flags (p=0.02), small (<3mm) white matter lesions (p=0.005), subcortical lesions (p<10-7). Moreover, while receiving less disease-modifying-therapy (p<0.001) they didn't exhibit higher annualized relapse rate nor worse disability progression (further details:tables 1-2).

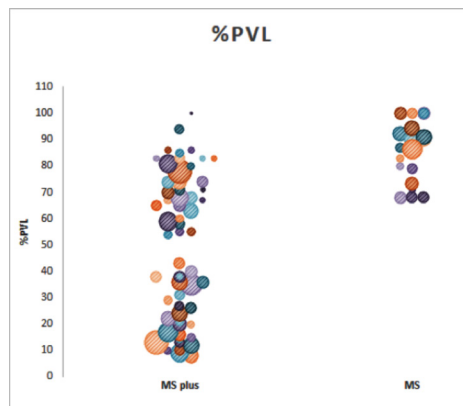


Figure 1. Frequency of perivenular (PVL) lesions in MS and MS plus

patients. The size of each circle is proportional to the total number of white matter lesions considered for central vein sign analysis. The MS plus population shows a bimodal distribution with two subgroups according to the 50%-rule: 47% of patients do not fulfill the rule.

Lesion Characteristics	MS	Patient group		Statistics (Mann Whitney U test)		
		MS plus >50% PVL	MS plus <50%PVL	MS plus <50%PVL vs >50%PVL	MS plus <50%PVL vs MS	MS plus >50%PVL vs MS
Total lesion load (mm ³)	4619 (1118-19892)	2432 (539-26781)	1926 (486-8667)	p=0,20510	p=0,0022	p=0,0463
lesion size (mm ³)	301,5(124-873)	131 (54-477)	70 (20-160)	p<10 ⁻⁷	p<10 ⁻⁷	p=0,0000
% Juxtacortical lesions	30 (11-66)	43 (1-100)	14(0-50)	p<10 ⁻⁷	p=0,0000	p=0,030
% Subcortical/deep white matter lesions	38(0-75)	44 (0-80)	81 (16-100)	p<10 ⁻⁷	p<10 ⁻⁷	p=0,64
% Juxtacortical/Leukocortical lesions	16 (0-61)	0 (0-48)	0 (0-65)	p=0,43152	p=0,0000	p=0,0000
% Infratentorial lesions	0 (0-30)	4 (0-100)	0 (0-11)	p=0,0002	p=0,0261	p=0,813
%Juxtaleukocortical, juxtacortical and infratentorial lesions	63 (25-100)	50 (20-100)	20(0-84)	p<10 ⁻⁷	p<10 ⁻⁷	p=0,573
Total lesion count (No.)	605	882	1107	-	-	-
Lesion/patient, n. median (range)	22 (15)	28 (22)	40 (29)	p=0,056*	p=0,0053*	p=0,382*
Perivenular lesion/patient, n. median (range)	19(13)	16(16)	7(6)	p=0,0002*	p=0,0000*	p=0,215*

Table 2: Characteristics of brain white matter lesions in MS patients, in MS plus patients and in MS plus subgroups stratified according to the 50% rule).

		MS+ PVL<50% n=28	MS+ PVL>50% n=32	test
Clinical-demographic				
Female	n (%)	26 (93%)	25 (78%)	p=0,15*
Age at MRI ¹ , years	median (range) mean (SE)	48,5 (34-62)	43,5 (20-65)	p=0,07*
Age at disease onset, years	median,(range) mean (SE)	37,8 (23,6-58)	38,2(14,9-62,4)	p=0,23**
Patients with onset age >50 years	n(%)	5 (18%)	5(16%)	p=1,00*
Patients aged > 50y at MRI scan,	n(%)	13 (46%)	10 (31%)	p=0,29*
Disease duration at MRI, years	median (range)	7,4 (0,4-2 8,4)	3,75 (0,2-24,8)	p=0,18*
EDSS ² score at onset	median (range)	0 (0-2,5)	1(0-1,5)	p=0,43*
Time to EDSS worsening, years	median (range)	4,05 (0-20,8)	2,55 (0-20,8)	p=0,31*
Time to DMFT ³ start, years	median (range)	1,64(0-28,4)	0,3 (0-24,8)	p=0,0006*
Time to First Relapse, years	median (range)	2,05 (0,5-18,1)	1,55 (0,5-20,8)	p=0,3204**
AAR ⁴ over 10 ys...	median (range)	0,1 (0-0,5)	0,1(0-0,4)	p=0,8328**
Red flags				
Red flags/patient,	median (range)	2 (1-3)	1,5 (1-3)	p=0,54*
Patients with clinical red flags	n(%)	14 (50%)	18 (56%)	p=0,79*
Patients with serological red flags	n(%)	9 (31%)	14 (44%)	p=0,43*
Patients with CSF ⁵ red flags	n(%)	9 (32%)	10 (31%)	p=1,00*
Patients with MRI red flags	n(%)	19(68%)	12 (36%)	p=0,02*
Cardiovascular risk factors				
All CVRF ⁶ n(%)		14 (50%)	6 (19%)	p=0,01*
History of Arterial Hypertension n(%)		8(29%)	1(3%)	p=0,009*
Other* n(%)		11(39%)	6(19%)	p=0,09*

* Fisher exact χ^2 test; ** Mann-Whitney U test;
1 MRI Magnetic Resonance Imaging **2** EDSS expanded disability status scale **3** DMFT disease modifying therapy **4** AAR annualized relapse rate; **5** CSF cerebrospinal fluid **6** CVRF cardiovascular risk factors * Diabetes, dyslipidemia, hypertension, hypercholesterolemia, polymorphism of coagulation factors, smoking, patent foramen ova

Table 1: Demographic, clinical, laboratory and MRI characteristics in MS plus subgroups, identified according to the 50% rule.

Conclusion: CVS identified a proportion of MS-plus patients with PVL<50%. In these patients, distinctive MRI and clinical features suggest a possible alternative pathogenic mechanism and therefore an alternative diagnosis to MS that should be investigated.

Disclosure: Nothing to disclose

EPO1237

Fulminant Marburg’s variant of multiple sclerosis: six months follow-up after high dose cyclophosphamide treatment.

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Background and aims: Marburg’s variant of multiple sclerosis (MS) is considered fulminant, leading to deterioration or death within weeks even with treatment. We present a 6 month follow-up of a patient diagnosed of Marburg disease, with favorable evolution after treatment with high dose cyclophosphamide (HiCy).

Methods: A 21-year-old male, with no prior illnesses or relevant epidemiological background, showed rapidly progressive gait impairment over the course of a week, with right-side hemiparesis, impaired bilateral proprioception, marked hyperreflexia, dysarthria and moderate cognitive decline (EDSS:6.5) on examination. MRI showed coalescent T2-hyperintense supratentorial, subependymal, splenial and anterior pontine plaques, some with gadolinium enhancement in open-ring pattern (Figures 1, 2). Lumbar puncture revealed slight leukocytosis and negative IgG oligoclonal bands. Five 1g intravenous methylprednisolone pulses (IVMP) were administered without improvement. As the clinical situation worsened (EDSS:8.0), a new MRI was obtained, and brain biopsy was performed to rule out other diagnoses in order to intensify immunosuppression.

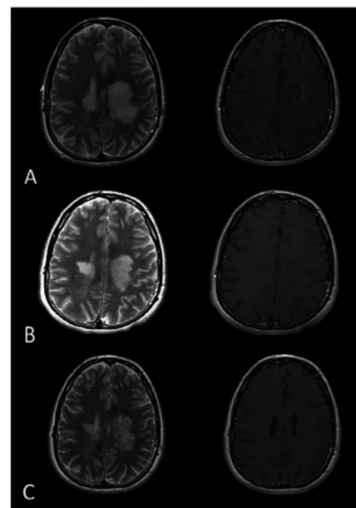


Figure 1. Supratentorial evolution of lesions, hyperintense in T2 with open-ring enhancement (T1-Gd) in July (A), October (B) and December (C).

Figure 1. MRI, supratentorial evolution.

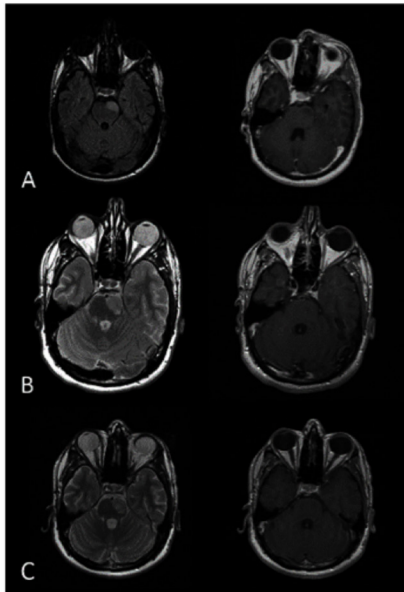


Figure 2. Evolution of the anterior pontine lesion, hyperintense in FLAIR/T2, with no clear enhancement in July (A), October (B) and December (C).

Figure 2. MRI, pontine evolution.

Results: The brain biopsy confirmed the diagnosis of Marburg's MS displaying intense demyelination with numerous macrophages. He had received 2 cycles of IVMP and 10 plasma exchange sessions with insignificant response. Monthly HiCy was started.

After 5 doses of HiCy the patient has had a remarkable clinical and radiological improvement. 6 months after diagnosis the patient walks with one aid and has milder cognitive impairment.

Conclusion: Marburg's disease is considered fatal, but with aggressive and combined immunosuppressive treatment it is possible to prolong survival and ameliorate disability. Our findings suggest that HiCy may be a therapeutic alternative to induce clinical and radiological improvement.

Disclosure: Nothing to disclose

EPO1238

Bereitschaftspotential and event related desynchronization – A glimpse at motor preparation in multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is 1 of the most common diseases of the central nervous system. A triad of demyelination, neurodegeneration and inflammation characterizes its pathophysiology. MS related lesions would alter several cognitive, motor and sensory functions. Motor preparation - a cognitive ability of utmost importance for an appropriate execution of daily tasks - has been rarely studied in this population. The aim of this work was to assess this ability in MS patients through the exploration of Bereitschaftspotential (BP) and event related desynchronization (ERD).

Methods: 12 MS patients and 10 healthy subjects were recruited for this purpose. Patients sociodemographic and clinical data were collected. All participants were asked to perform series of 30 finger extension movements. EEG signals were collected from 18 central electrodes, and an offline analysis was done to assess BP (early and late BP (i.e., BP1 and BP2)) and alpha/mu ERD.

Results: BP and alpha/mu ERD had longer latency (i.e., earlier onset) in MS patients compared to their healthy counterparts. BP amplitude and percentage of desynchronization of ERD did not significantly differ between groups. In addition, a direct correlation was found between BP latency and disability scores.

Conclusion: These findings reflect a prolonged motor preparation process, thus an altered premotor scheme in MS patients. Based on the cognitive reserve theory, activity of preexisting circuits seems to be strengthened and alternative networks appear to be recruited in order to ensure a proper, yet longer, motor preparation process.

Disclosure: Nothing to disclose

EPO1239

Alemtuzumab in the treatment of active relapsing-remitting multiple sclerosis: Croatian multicenter, observational study

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Background and aims: We aimed to analyse the efficacy and safety of alemtuzumab in a multi-centre cohort of people with relapsing-remitting multiple sclerosis (pwRRMS).

Methods: Data on all pwRRMS who received 2 cycles of alemtuzumab in 7 neurological departments across Croatia were retrospectively analysed. Annualized relapse rate (ARR) and ARR reduction were calculated.

Results: 49 pwRRMS (mean age 33.2 years, 36 females) were identified. Number of relapses in the previous year was 2 (0-6) with an ARR for the group 1.86. ARR in the 1st 2nd and 3rd year after treatment was 0.08 (ARR reduction 95.6%), 0.07 (ARR reduction 96.2%), and 0.24 (ARR reduction 86.9%), respectively. There was statistically significant reduction in total number of relapses in the first year, the 2nd year and the 3rd year, all in comparison with the year previous to treatment (all $p < 0.001$). In a multivariable regression model including age, sex, and EDSS, EDSS at the time of treatment initiation was identified as an independent predictor of a relapse (OR 2.203, 95%CI 1.067-4.549, $p = 0.033$). Sustained NEDA was achieved in 18 (52.9%) patients who had completed 3-year follow-up. Confirmed disability progression was identified in 7 (14.3%) pwRRMS. Six patients received 3rd cycle of alemtuzumab and one was switched to ocrelizumab. Seven (14.2%) patients developed hypothyreosis and 2 (4.1%) hyperthyreosis. 1 case of pulmonary embolism was observed during the 3rd cycle.

Conclusion: This study confirmed clinical and MRI efficacy of alemtuzumab in a real life setting.

Disclosure: Nothing to disclose

EPO1240

A Real World Data of Ocrelizumab in Multiple Sclerosis

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Background and aims: Ocrelizumab has been recently approved for the treatment of relapsing remitting MS (RRMS) and primary progressive MS (PPMS). This study aims to describe the effectiveness, safety outcomes, treatment satisfaction and quality of life of MS patients on ocrelizumab.

Methods: This is an observational, prospective, single-center study of 102 patients with MS treated with ocrelizumab for minimum 12 months. Demographics, clinical and neuroimaging characteristics, including annualized relapse rate (ARR), Expanded Disability Status Score, previous treatment, adverse events, and MS related quality of life (MSQoL) were analyzed.

Results: A total of 102 patients were included: 52% female, 48% male; mean age 43 years (18-75); mean disease duration 10 years (1-26); mean ocrelizumab use 18 months. Patients were classified as RRMS (52%), SPMS (30%), or PPMS (17%). In this study 38% of patients received prior 1st-line disease-modifying therapies (26% enjectables or 12% oral), 48% of patients were previously treated with second-line disease-modifying therapies (43% fingolimod or 5% natalizumab), and 14% were treatment naive. The annualised relapse rate decreased by 92.3 % for the total population at the end of the 1st year of treatment and all patients were free from EDSS progression. All patients had no radiological activity. Only 10% of patients had mild infusion reactions during the initial dose of ocrelizumab and none discontinued treatment. At the end of 12 months with ocrelizumab, health-related quality of life and fatigue scores improved significantly in 88% of patients.

Conclusion: In this real-world data, ocrelizumab appeared to be significantly effective, safe and well tolerated.

Disclosure: Nothing to disclose

EPO1241

Oxidative Stress in Highly Active Multiple Sclerosis

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Background and aims: investigation of free toxic radicals and antioxidative enzymes in HAMS and their relation with Cognitive status of patients.

Methods: Totally 52 patients aged 21- 52 years, 18- with HAMS, 34 -with RRMS investigated. Control comprised age matched 15 healthy volunteers. Disease onset age, duration, number of relapses, EDSS scores collected. Cognition screened by Symbol Digit Modalities Test (SDMT). MRI (1.5-T) Gadolinium enhanced lesions calculated. Blood free toxic radicals and antioxidant enzymes detected by Electron Paramagnetic Resonance Method (EPR). Statistics performed by SPSS-20.

Results: Blood EPR specters of Lypoperoxiradical (LOO-) and superoxide anion (O₂-) increased in HAMS compared to RRMS and control (12.4±0.4 versus 7.6 ±0.5 versus 2.4 ±0.4; p<0.05) respectively (9.4±0.4 versus 4.4±0.5 versus 1.7±0.2; p<0.05). Blood EPR specters of Superoxidismutase (SOD), Catalase (CAT) found elevated in RRMS and control against HAMS, while between RRMS and Control the significant differences were not found(p<0.5). Positive correlation established between LOO- and O₂- with EDSS (r=+0.27 and r=+0.18 respectively, p<0.05). Negative correlation found between SOD, CAT and SDMT standardized scores (r=-0.32 and r=-0.24 respectively, p<0.01). Multivariate logistic regression showed the significance of HAMS duration in conjunction of SOD levels for cognitive status of patients (p<0.01).

Conclusion: Present study showed that antioxidation defensive system is relatively weak in HAMS and plays the pivotal role in detrimental consequences of the disease.

Disclosure: it was not granted.

EPO1242

A new perspective on sex-related differences in multiple sclerosis: the impact of fetal-maternal microchimerism on clinical and imaging features in women with multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) is a chronic autoimmune disorder characterised by inflammation and neurodegeneration. It has been hypothesized that persisting fetal microchimeric cells could contribute to autoimmune diseases pathogenesis. The aim of the study is to investigate the impact of microchimerism on the clinical, radiological, and laboratory features of MS.

Methods: We recruited 51 MS patients: 25 patients were nulliparous (mean age: 35.6±8.8 years, median EDSS: 2.0), 19 patients had at least one male son (mean age: 41.2±8.1 years, median EDSS: 2.0), and 8 patients had only daughters (mean age: 44.6±12.5 years, median EDSS: 3.75). Demographic, clinical, radiological, and paraclinical data at baseline and follow-up were collected. MRI protocol included 3D-T2w FLAIR FatSat and 3D-T1w FSPGR.

Results: Patients with at least a male son had a significantly lower age at onset (p=0.0002, p=0.0308) and a not-significant lower number of relapses over the 1st 3 years (2.60±2.22 vs 5.34±2.52 in women with daughters and 3.31±2.21 in nulliparous; p>0.05). The same group had a not-significant lower time-gap onset-EDSS4 (98.9±75.5 vs 192.2±154.1 and 159.0±155.3; p>0.05) and onset-EDSS6 (66.0±75.2 vs 66.0±75.2 and 235.0±193.3; p>0.05). Finally, this group showed a lower lesion volume (17.53±10.11 vs 18.25±9.25 and 18.82±10.45; p>0.05) and a more severe atrophy of the chiasma (p=0.0234, p=0.0185).

Conclusion: Our data suggest that, in a multifactorial background, the microchimeric XY fetal cells could modulate the inflammatory and neurodegenerative mechanisms underlying the MS, influencing the disease features.

Disclosure: Nothing to disclose

EPO1243

Prevalence of bowel and bladder dysfunctions in multiple sclerosis: an italian multicenter study

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Background and aims: Bladder and bowel dysfunctions are reported as common and disabling symptoms in multiple sclerosis (MS) patients, affecting severely their quality of life. To date, no studies have explored the prevalence of these symptoms in a multicenter setting. Aims of the present study are to assess: i) the prevalence of bladder and bowel symptoms in a large multicenter Italian MS population and ii) the correlation between the severity of these symptoms and clinico-demographic variables.

Methods: Each participating center screened prospectively MS patients: 1100 patients were enrolled. All subjects completed the following questionnaires exploring bowel and bladder dysfunction: the Neurogenic Bowel Dysfunction (NBD) score and the International Prostatic Symptoms Score (IPSS). Multivariate linear regression models were used to study the association between a dependent outcome variable (NBD, IPSS) and several independent variables. All the analyses were Bonferroni corrected.

Results: 14 per cent of MS patients showed bowel symptoms of moderate/severe entity (NBD>10), whereas 47 per cent of MS patients showed bladder symptoms of moderate/severe entity (IPSS>8). Bowel and Bladder dysfunctions are more frequent in progressive phenotypes of MS and in MS patients with: higher disability, older age, longer disease duration. NBD is associated to female sex, ambulation impairment and bladder symptoms. Bladder symptoms are associated to bowel symptoms and disability.

Conclusion: This study confirms the high prevalence of moderate/severe bladder and bowel dysfunction in a large, unselected, multicenter, MS population. Bowel and bladder symptoms are closely related each other and strictly associated with disability level in MS.

Disclosure: Nothing to disclose

EPO1244

The brief international cognitive assessment for multiple sclerosis (BICAMS) in georgian population

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Background and aims: Cognitive impairment is a common symptom of Multiple Sclerosis (MS). It has an unfavorable impact on a patient's quality of life and employment status. Early detection of cognitive impairment is important for adequate management. In 2011 the Brief International Cognitive Assessment for MS (BICAMS) was introduced by an international expert committee as a fast and effective tool for the assessment of cognitive status in patients with MS. We aimed to validate the Georgian version of BICAMS and to provide normative data for the battery.

Methods: 108 Healthy subjects were recruited from western and eastern regions of Georgia. Initially, the BICAMS was translated in accordance with ITC guidelines for translating and adapting tests. The battery was administered by a neurologist and a trained psychologist.

Results: The main characteristics of the study population are outlined in Table 1. The mean age of study population was 39±12.2. The mean SDMT score was 44±12.2, the mean CVLT II score was 56.4±9.0 and the mean BVM-T-R score was 24.5±7.5. Table 2 shows differences in mean scores between different age groups. Test scores tend to decline with increasing age.

Overall number	108
Age mean ± DS	39 ± 12.2 (20-65)
Gender	
Female	71 (66%)
male	37 (34%)
Employment status	
Employed	85 (79%)
Unemployed	23 (21%)
Education	
=11 years	24 (22%)
12-14 years	16 (15%)
=15 years	68 (63%)
Residence	
Urban	96 (90%)
Rural	12 (10%)
BICAMS mean raw scores ± SD	
SDMT	44 ± 12.2
CVLE II	56.4 ± 9.0
BVMT-R	24.5 ± 7.5

Table 1. Basic characteristics of study population

	N	Female/Male	Raw Scores \pm SD		
			SDMT	CVLT II	BVMT-R
20-29	33	16/7	51 \pm 13.8	60 \pm 14.0	27.5 \pm 7.0
39-40	25	16/9	46 \pm 10.2	59. \pm 29.0	25.2 \pm 7.9
41-49	24	18/6	40 \pm 9.6	54.2 \pm 10.0	24.7 \pm 8.0
50-59	21	17/4	38 \pm 8.5	50.7 \pm 7.6	19.6 \pm 6.2
>60	5	4/1	34 \pm 8.9	55.6 \pm 7.0	22.6 \pm 6.3

Table 2. Mean differences between age groups

Conclusion: In conclusion, our study provides normative means for the Georgian version of BICAMS. The mean SDMT score in the Georgian population is somewhat lower than demonstrated by other validation studies.

Disclosure: Nothing to disclose

EPO1245

Montreal Cognitive Assessment (MoCA) test in evaluating cognitive dysfunction in patients with Relapsing Remitting Multiple Sclerosis (RRMS) and Secondary Progressive Multiple Sclerosis (SPMS)

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Background and aims: MoCA is a scale that allows us to evaluate many cognitive functions such as, short-term memory, executive functions, viziyoşpasyal skills, language, attention, concentration, working memory and orientation. In this study, we have aimed to evaluate the availability of MoCA test to demonstrate cognitive dysfunction in RRMS and SPMS patients by comparing SDMT (Symbol-Digit-modality-Test) and 9-hole-PEG test results.

Methods: The study included 95 RRMS and 33 SPMS MS diagnosed patients with similar demographic features. Through the evaluation in which RRMS and SPMS patients were evaluated in terms of their age, gender, educational status and EDSS, SDMT positive and negative scores and SDMT duration and 9-hole-PEG test right and left hands duration were recorded with MoCA test results .

Results: As the level of education increased, MOCA total score increased ($p < 0.001$). EDSS was significantly higher in patients with MoCA test result < 21 compared with > 21 ($p = 0.01$) and the 9-hole-PEG test showed increased left hand duration ($p = 0.017$) and SDMT duration was found to be extended ($p < 0.02$). When the content of the MoCA test was evaluated, a greater impact on planning and organization, attention and phonemic fluency were observed on SPSM patients when compared to RRMS patients.

Conclusion: MoCA test can help us to plan more specific and comprehensive review of the affected area. MoCA, an internationally recognized and valid test that can be easily administered without any specialized equipment, can be used as an appropriate screening test to show cognitive effect on MS.

Disclosure: Nothing to disclose

EPO1246

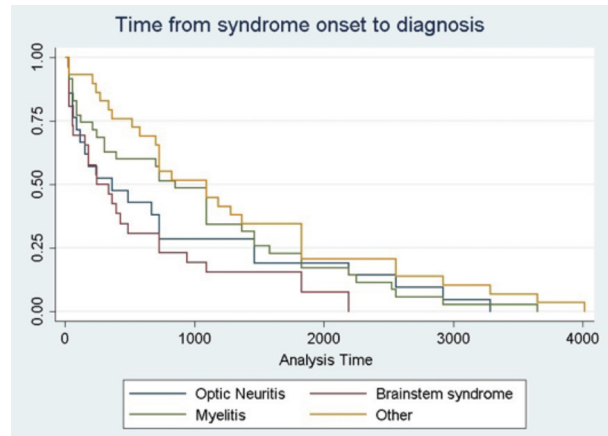
Brainstem syndrome can led to an early MS diagnosis in Peru: a national referral center cohort

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Background and aims: Multiple Sclerosis epidemiological data in Peru is scarce. In Lima, there is an estimated prevalence of 7.69 per 100000. We aim to describe the clinical and epidemiological characteristics of patients with MS in a national referral center in Lima-Peru.

Methods: We performed a retrospective study of MS patients diagnosed at the Instituto Nacional de Ciencias Neurológicas (INCN) between January 2010 and December 2018. A descriptive analysis was carried out. 4 different syndromes were selected for analysis as a 1st manifestation (Optic Neuritis, Brainstem syndrome, Myelitis and Other)

Results: We identified 268 medical records with the diagnosis of MS, 125 fulfilled the study criteria. We found misdiagnosis in 97 records (36.2%). The majority of patients belong to Lima (49.6%). As seen in Figure 1 distribution of patients in the study is related to population density of Peru. The main epidemiological and clinical characteristics are shown in table 1. The mean EDSS score was 2.85. Optic Neuritis is 2.87 (1.13-7.93) times the probability of being the initial symptom in SPMS compared to other syndromes (p=0.0145). Brainstem syndrome was associated with an early time to diagnosis compared to other syndromes (p=0.0261, Figure 2).



Conclusion: This study provides information about the main characteristics of MS patients at INCN. Optic neuritis was more frequent as the 1st presentation in SPMS compared with other syndromes. Brainstem syndrome at symptom onset was related to an early time to diagnosis. Our results will help us create a structure evaluation for our patients in order to make a better and faster diagnosis.

Disclosure: Nothing to disclose

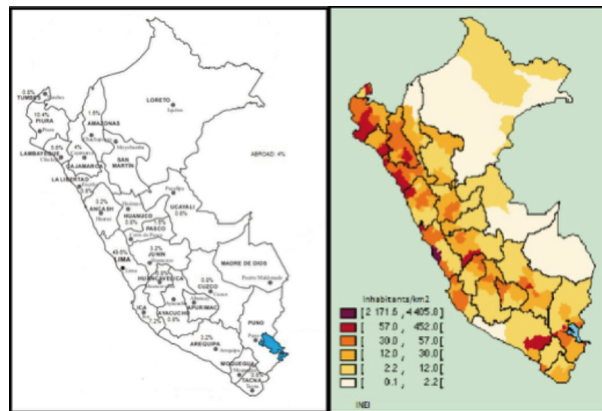


Table 1. Epidemiological and clinical characteristics

Characteristics	Phenotype	CIS		RRMS		SPMS		PPMS		TOTAL	
		n	%	n	%	n	%	n	%	n	%
Gender	Female	11	91.67%	37	50%	9	60%	15	62.50%	72	57.60%
	Male	1	8.33%	37	50%	6	40%	9	37.50%	53	42.40%
Age at diagnosis	mean (SD)	32.17	14.12	28.18	9.14	37.67	14.56	39.04	9.95	31.78	11.46
	mean (SD)	1	0	2.32	1.31	2.27	1.33	0.13	0.34	1.77	1.43
Time to diagnosis (months)	mean (SD)	19.19	35.20	33.89	70.74	82.79	76.20	41.43	46.80	39.80	66.36
	mean (SD)	1	0	3.04	1.68	2.53	1.68	0.13	0.34	2.22	1.85
Syndrome onset	Optic Neuritis	6	50%	16	21.62%	3	20%	2	8.33%	27	21.60%
	Brainstem Syndrome	4	33.33%	21	28.38%	2	13.33%	4	16.67%	31	24.80%
	Myelitis	0	0%	27	36.49%	4	26.67%	9	37.50%	40	32.00%
	Other	2	16.67%	15	20.27%	6	40%	11	45.83%	34	27.20%
Gad enhancement	Other	3	25.00%	48	64.86%	8	53.33%	16	66.67%	75	61.98%
	Treatment	0	0.00%	47	63.51%	5	33.33%	6	25.00%	58	46.40%

EPO1247

Antiaquaporin-4 retroconversion in NMO patients treated with Rituximab

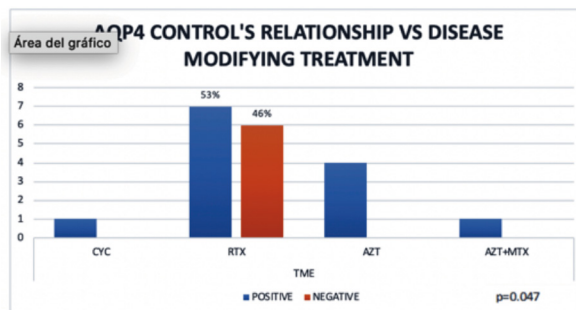
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 CDMX, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, CIUDAD DE MEXICO, Mexico

Background and aims: NMO is an autoimmune “aquaporinopathy” of the central nervous system that causes inflammatory demyelinating lesions predominantly in the spinal cord and optic nerve. Rituximab (RTX) is a chimeric monoclonal antibody directed against CD20 epitope expressed on pre-B and mature B cells, used to treat antibody-mediated autoimmune diseases.

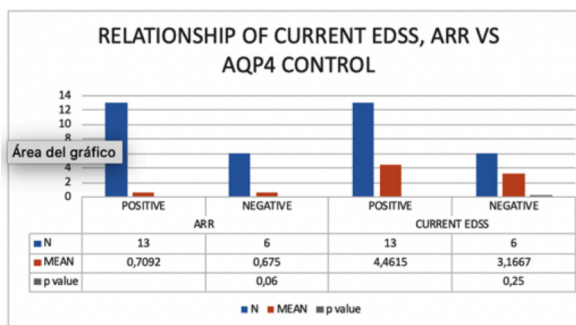
Objectives: To establish a relationship between seroconversion, different treatments and clinical outcomes in the follow-up of AQP4+ NMO patients.

Methods: A prospective and longitudinal descriptive study was carried out in patients of the National Institute of Neurology and Neurosurgery in Mexico City who met the inclusion criteria: diagnosed by Wingerchuk 2015 criteria, positive serostatus of AQP4-IgG and a subsequent AQP4-IgG serostatus at any given time.

Results: 17 (89.5%) were women and 2 (10.5%) men. The mean age was 47.84 years. Mean EDSS at clinical onset was 3.8 and ARR was 0.81. Disease modifying treatment included rituximab (RTX) (26.3%), cyclophosphamide (CYC) (5.3%), azathioprine (AZT) (21.1%), CYC+RTX (21.1%), CYC+AZT+RTX (21.1%), AZT+ MTX (methotrexate) (5.3%). Seronegative conversion was documented in 6 patients in the RTX group (p=0.047). A lower ARR and an improvement in the EDSS was observed in those patients with negative AQP4 after RTX treatment (mean ARR 0.6, mean EDSS 3.1), unlike those who remained positive had higher ARR and EDSS (mean ARR 0.7, mean EDSS 4.4).



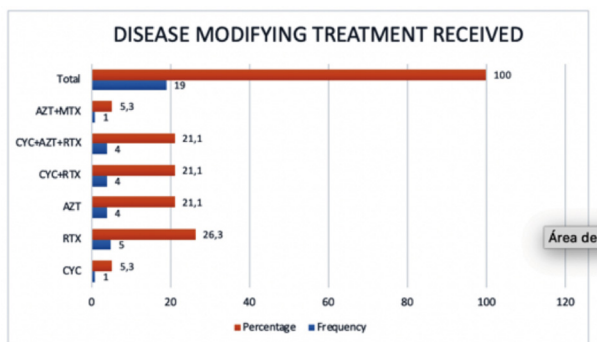
AZT (Azathioprine), MTX (methotrexate), CYC (Cyclophosphamide), RTX (Rituximab).



Comparison between AQP4 control (positive and negative) and the clinical evolution measured by the EDSS and ARR. There was a better clinical evolution in those who converted to negative AQP4, who presented a decrease in EDSS and ARR. *AQP4 (Aquaporine 4), EDSS (Expanded Disability Score Status), ARR (Annualized Relapse Rate).

Conclusion: Treatment with Rituximab in Mexican patients with NMO AQP4 seropositive can lead to retroconversion, and improvement ARR and EDSS.

Disclosure: Nothing to disclose



Number of patients treated with DMT (Disease Modifying treatment) is shown in orange and the percentage in blue. As can be evidenced, most patients were treated with Rituximab, either at baseline or as an escalation therapy. * AZT (Azathioprine), MTX (Methotrexate), CYC (Cyclophosphamide), RTX (Rituximab).

EPO1248

Rituximab is effective regardless of initial and maintenance doses in Neuromyelitis Optica Spectrum Disorders (NMOSDs). experience from a national health institute in Mexico.

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Background and aims: NMOsd is an inflammatory condition of the central nervous system which preferentially affects optic nerves and spinal cord. Classic neuromyelitis optica is characterized by concurrent episodes of optic neuritis (ON) and transverse myelitis (TM). Rituximab is a monoclonal antibody directed against CD20 epitope expressed on pre-B and mature B cells and is used to treat antibody-mediated autoimmune diseases.

Objectives: To demonstrate rituximab clinical efficacy regardless doses administered in NMOsd patients.

Methods: In a retrospective and longitudinal observational study starting from January 1, 2010 to August 1, 2019 66 NMOsd patients under different RTX doses were identified. Univariate, multivariate and post hoc analysis of variables was performed.

Results: 12 patients (18.2%) were male, 54 (81.1%) female. 66.7% were AQP4 antibody positive. The most frequent RTX induction regimen was 2000mg 15 day apart (51.5%), followed by 1000mg (40.9%) each 6 months. Single 500mg of RTX each 6 months in 5 patients (7.5%). ARR reduced from 1.15±1.18 to 0.46 with RTX ($p \leq 0.0001$). In patients with relapses, ARR dropped from 1.66 to 1.22 relapses per year, 73.49% relative risk relapse decrease. Previous to RTX ARR in 500mg subgroup was 1.36, with RTX 0.4. For 1000mg initial and maintenance doses ARR was 0.7 and follow-up 0.4

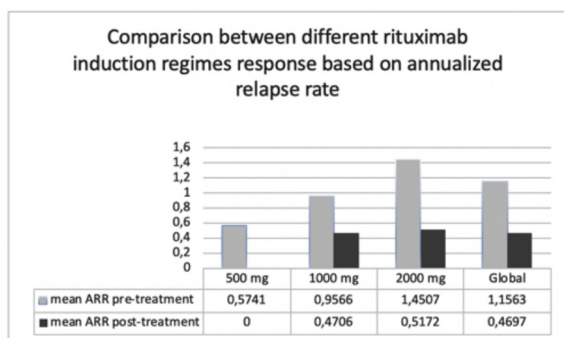


Figure 1. Comparison in response different rituximab induction regimes response based on annualized relapse rate

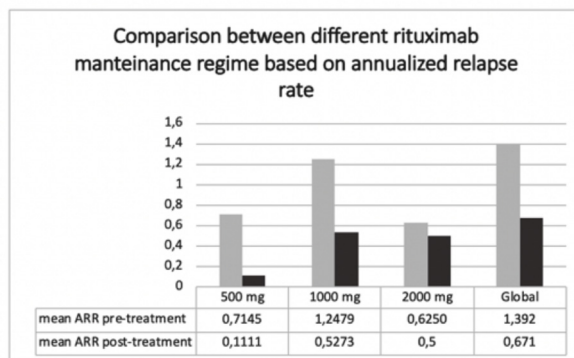


Figure 2. Comparison in response in different rituximab maintenance regime

Conclusion: The treatment of NMOSDs with rituximab in Mexican patients demonstrate marked and sustained ARR reduction regardless initial and maintenance regimen

Disclosure: Nothing to disclose

MS and related disorders 2

EPO1249

How understanding of MS patient experiences, with respect to conversations about disease progression, differs among healthcare professions

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Background and aims: The MS in the 21st Century initiative is led by a Steering Group of international multiple sclerosis (MS) healthcare professionals (HCPs) and people with MS (PwMS) committed to improving communication between HCPs and PwMS, currently focussing on understanding factors that influence outcomes of conversations about disease progression.

Methods: A 6 question electronic survey on the topic was conducted at international congress and online.

Results: Responses were received from 130 PwMS, 74 neurologists, 55 nurses and 43 other HCPs (GPs, physical therapists, psychologists). 13rd (32.7%) of PwMS reported that their HCP had never discussed disease progression with them; however, 98.0% of neurologists reported discussing the topic with their patients. Respondents from all groups reported the reason discussions take place is because it is important to be open about MS, with neurologists (52.0%) and PwMS (41.6%) stating this most consistently. Neurologists reported that discussions improve treatment adherence (54.0%) with nurses (23.8%) the next most likely group to state this. Both neurologists and PwMS reported patients' 1st reactions to discussions about progression as "worried", "overwhelmed" or "frightened". Nurses also included "upset" in their top 3, while other HCPs were the only group to report PwMS as "hopeful" in these conversations. None of the HCP groups included inevitability of decline as a major concern of PwMS despite 46.9% of PwMS reporting that this concerns them.

Conclusion: These data highlight the sometimes contradictory perspectives of HCPs and PwMS on disease progression. Greater collaboration between multidisciplinary teams could help HCPs to align perspectives and provide more effective care.

Disclosure: The MS in the 21st Century initiative is financially supported by Merck KGaA, Darmstadt, Germany with secretariat support, editorial input, and medical writing assistance provided by Cello Health Communications, Farnham, UK.

EPO1250

Association of sarcoidosis and multiple sclerosis: an important lesson in neuroimmunology

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Background and aims: Sarcoidosis is a rare association of multiple sclerosis (MS); in a large retrospective study, only 10 cases were identified in an MS population of over 15,000.

Methods: We reviewed our own database and literature regarding the association of sarcoidosis and MS.

Results: We identified 1 patient of sarcoidosis in our database of over 1000 patents with MS. This was a female patient in her 50s with a previously confirmed diagnosis of pulmonary sarcoidosis and presented with a subacute onset of progressive left leg weakness and foot drop. MRI of her brain and cervical spinal cord showed disseminated demyelinating lesions. CSF was positive for oligoclonal bands; serum was weakly positive with fewer and less intense bands. The course of her MS remained benign; over next 10 years, she experienced no new relapse or disability progression. Her pulmonary sarcoidosis was quiescent on Prednisolone 5mg once daily. She had a persistent mild lymphopenia and was not treated with disease modifying therapy.

Conclusion: We present an index case of sarcoidosis with MS followed up for over 10 years with a clinically benign course. We postulate that the state of mild immunosuppression, lymphopenia and normal or increased levels of 1,25 OH-vitamin D3 in sarcoidosis is protective against disease activity in MS. This is supported by the low incidence of MS in patients with sarcoidosis, and development of acute sarcoidosis reported in patients with MS following treatment with beta-interferon, alemtuzumab and daclizumab, probably from a shift of immune response and macrophage activity.

Disclosure: Nothing to disclose

EPO1251

Preliminary results of high-dose immunosuppressive therapy with autologous hematopoietic stem cell transplantation in progressive and relapsing-remitting multiple sclerosis

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Background and aims: To evaluate the efficacy of high-dose immunosuppressive therapy with autologous hematopoietic stem cell transplantation (HDIT + AHSCT) in patients with progressive (PMS) and relapsing-remitting (RRMS) multiple sclerosis (MS).

Methods: The study involved 5 patients with PMS and 1 patient with RRMS (mean age was 40.8 ± 9.9 years, disease duration - 6.0 ± 4.3 years) diagnosed according to McDonald criteria (2017). Inclusion criteria: an increase of the Expanded Disability Status Scale (EDSS) score during the last year; an increase of the lesion number and/or the Gd+ lesion number on magnetic resonance imaging (MRI) of the brain; the inefficacy of the I or II line of disease modified therapy. Monitoring was conducted by EDSS and MRI assessment before, just after (only for EDSS) and 6-8 months later the treatment.

Results: The average EDSS before treatment was 5.6 ± 0.7 , immediately after treatment -5.5 ± 0.8 , 6-8 months later -5.0 ± 1.0 . In all patients on the brain MRI before treatment there were revealed multiple Gd+ lesions. 6-8 months after HDIT + AHSCT no new lesions and no other signs of lesion activity were fixed on MRI.

Conclusion: The neuroimage and EDSS monitoring indicate the absence of exacerbations and disease progression because of continuous suppression of immune system 6 months after HDIT + AHSCT in all patients with RRMS and PMS.

Disclosure: Nothing to disclose

EPO1252

A heterogeneity of relationships between sleep/wake parameters and physical functioning, mental health and cognitions in multiple sclerosis

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Background and aims: Sleep/wake disorders are common for multiple sclerosis (MS). There is a certain association of them with fatigue, anxiety, depression, and cognitive impairments. The aim was to investigate connections of sleep/wake components with psychometric and neurocognitive parameters in patients with MS.

Methods: Sleep/wake assessments with the Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI) and psychometric and neurocognitive examinations were performed in 20 patients with MS (Figure 1).

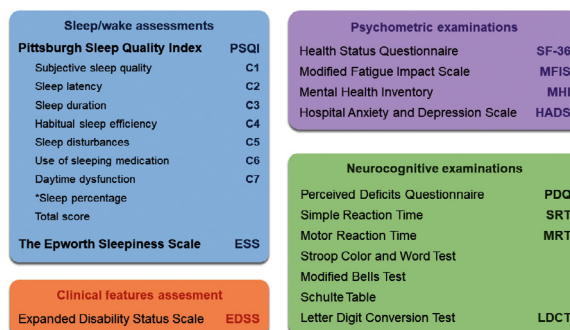


Figure 1. Methods of assessment

Results: The daytime sleepiness (ESS score) was significantly associated with fatigue ($k=0.75$), depression ($k=0.75$ for HADS and $k=-0.68$ for MHI), perceived cognition deficits ($k=0.82$), emotional conditions ($k=-0.55$) and mental health ($k=-0.75$) for SF-36. The daily sleepiness had no connections with physical functioning ($k=-0.02$ for SF-36) and a simple ($k=0.12$) and motor ($k=0.23$) reaction time. The PSQI total score less correlated with fatigue ($k=0.64$), scores of PDQ ($k=0.47$), HADS ($k=0.43$), emotional conditions ($k=-0.43$) and mental health ($k=-0.50$) for SF-36, than the ESS, but the PSQI was more connected with physical functioning ($k=-0.66$ for SF-36) and a motor reaction time ($k=0.48$). The PSQI components had relationships of different power with the parameters examined (Figure 2). Cognitive conditions, particularly speed of the test performing, were more connected with sleep efficiency, latency, and percentage; whereas psychometric parameters were connected stronger with sleep disturbances, duration, and efficiency.

	Scale or Test	Sleep latency	Sleep duration	Sleep percentage	Sleep disturbances	Sleep efficiency
Clinical features	EDSS	0,73	-0,09	-0,49	0,01	0,38
Fatigue	MFIS	-0,11	0,49	-0,29	0,61	0,45
Physical functioning	SF-36 (PCS)	-0,58	-0,28	0,63	-0,2	-0,69
	SF-36 (MCS)	0,34	-0,50	0,11	-0,58	-0,22
Mental health	MHI	0,21	-0,52	0,35	-0,59	-0,46
	MHI (MHD)	0,26	-0,44	0,38	-0,54	-0,49
Depression	HADS D	0,00	0,65	-0,41	0,45	0,39
	MHI (MHA)	0,17	-0,19	0,13	-0,44	-0,28
Anxiety	HADS A	-0,28	0,72	-0,29	0,52	0,34
Cognitions	PDQ	-0,18	0,19	-0,27	0,38	0,43
Simple reaction time	SRT	-0,03	0,02	-0,16	0,04	0,12
Motor reaction time	MRT	0,00	-0,38	-0,27	0,25	0,26
Cognitive tiredness	Schulte Tables, Stroop Test, Modified Bells Test, LDCT	0,45	-0,08	-0,48	-0,08	0,43
	Schulte Tables	0,53 to 0,68	-0,10	-0,48	0,05	0,45
	Stroop Test	0,58	-0,16	-0,36 to -0,42	0,16	0,42
Time of performing	Modified Bells Test	0,65	-0,23 to -0,33	-0,24 to -0,32	0,07	0,28
	LDCT	0,58 to 0,62	0,07	-0,56	-0,05	0,47 to 0,51

EDSS – Expanded Disability Status Scale; MFIS – Modified Fatigue Impact Scale; SF-36 – Health Status Questionnaire; SF-36 (PCS) – Physical Components Summary Scale; SF-36 (MCS) – Mental Component Summary Scale; MHI – Mental Health Inventory; MHI (MHD) – Mental Health Inventory Depression Subscale; MHI (MHA) – Mental Health Inventory Anxiety Subscale; HADS – Hospital Anxiety and Depression Scale; PDQ – Perceived Deficits Questionnaire; LDCT – Letter Digit Conversion Test

Figure 2. Heatmap of relationships between sleep/wake parameters and physical functioning, mental health and cognitions in multiple sclerosis

Conclusion: In MS, ESS total score was connected stronger with psychoemotional conditions, whereas PSQI total score had stronger connections with physical functioning and cognitions. Along with this, PSQI certain components also were connected significantly with psychoemotional conditions.

Disclosure: Nothing to disclose

EPO1253

Central nervous system inflammatory disease: between grey matter lesions and white matter vanishing hyperintensities

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Background and aims: Inflammatory diseases of the central nervous system (CNS) are heterogenous as we identify more antibodies and their targets in the pathological immune background. While the traditional theory of multiple sclerosis (MS) physiopathology refers to a white matter disease, the grey matter lesions are considered by some a signature of MS. White matter changes are common in a wide spectrum of inflammatory diseases of the CNS, nevertheless disappearing T2/FLAIR MRI white matter hyperintensities are uncommon.

Methods: We present the case of a 52-year-old woman with a long history of fluctuating neurological deficits. In 1997 she was diagnosed with left optic neuritis. In 2006 she underwent a brain MRI showing one T2/FLAIR white matter hyperintensity of her left parietal lobe. From 2010 she starts having recurrent paresthesias in her left leg, face, then both hands; a new brain MRI reveals multiple hyperintense T2/FLAIR lesions in both cerebral hemispheres and under the tentorium.

Results: Glucocorticoids are administered several times with good recovery. In 2016, the brain MRI performed shows no trace of white matter lesions but moderate atrophy and few grey matter T2/FLAIR hyperintensities. She was addressed to our department with progressive gait disturbance. Brain MRI proved to be unchanged, but a C2-C4 T2/FLAIR hyperintensity was identified on her spinal MRI.

Conclusion: The complete antibody workup we performed proved to be negative, but we initially considered a seronegative CNS inflammatory disease. However, the presence of oligoclonal bands, the radiological features and the evolution made the most likely diagnosis that of an atypical presentation of MS.

Disclosure: Nothing to disclose

EPO1254

Safety of Alemtuzumab Over 9 Years in Patients With Non-MS Autoimmunity

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Background and aims: In the CAMMS223 (NCT00050778) and CARE-MS trials (NCT00530348, NCT00548405), alemtuzumab significantly improved efficacy outcomes versus subcutaneous interferon beta-1a in RRMS patients. Efficacy was maintained in 2 consecutive extension studies (NCT00930553, NCT02255656). Here, we investigate the relationship of preexisting non-MS autoimmunity with subsequent onset of new autoimmune adverse events (AIAEs) after alemtuzumab.

Methods: In clinical trials, safety monitoring included monthly complete blood counts, serum creatinine, urinalysis with microscopy, and quarterly thyroid function tests. All patient- and investigator-reported AEs were recorded. AIAEs were counted at baseline if occurring before first alemtuzumab dose or if collected in the medical history database.

Results: A total of 1216 patients from the alemtuzumab clinical development program who received alemtuzumab 12 mg were included in the analysis. 96 had baseline non-MS autoimmunity. Up to 9 years after alemtuzumab initiation, AIAE incidences were similar in patients with baseline non-MS autoimmunity (≥ 1 postbaseline AIAE, 35.4%; ≥ 2 postbaseline AIAEs, 5.2%) or without baseline autoimmunity (35.3%, 8.2%). Most patients with thyroid disorders at baseline did not experience AIAEs after alemtuzumab initiation; postbaseline AIAE incidence in patients with baseline hypothyroidism, hyperthyroidism, and autoimmune thyroiditis was 13.5%, 14.3%, and 16.7%, respectively. Thyroid AE incidence after a 3rd alemtuzumab course remained consistent between patients who had thyroid AEs before Course 3 (1.7%) and those who did not

(2.0%). Postmarketing data indicate thyroid AEs that developed post alemtuzumab were not associated with other treatment-emergent AIAEs.

Conclusion: Preexisting non-MS autoimmunity was not associated with subsequent new AIAE occurrence up to 9 years after alemtuzumab initiation.

Disclosure: STUDY SUPPORT: Sanofi and Bayer HealthCare Pharmaceuticals.

EPO1255

Autoimmune neurological adverse events related to biological drugs: a case series

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Background and aims: Biologic drugs (biologics) are an established therapeutic option for autoimmune diseases and malignancies targeting specific pathways of the immune system or cellular processes. Despite their selective mechanisms of action, biologics may have a variety of adverse events, including neurological complications that should be promptly recognized and treated.

Methods: We describe a case series of patients who developed complications affecting the central nervous system (CNS) while on treatment with biologics for autoimmune diseases or malignancies.

Results: Anti-tumor necrosis factor alpha (anti-TNF α) (Infliximab, Etanercept, Adalimumab or Golimumab) were prescribed to 9 patients (6M, 3W) for psoriatic arthritis (n=4), ankylosing spondylitis (n=3), seronegative spondyloarthritis (n=1) and Crohn disease (n=1). During treatment, 4 patients developed an isolated CNS demyelinating syndrome; 1 was diagnosed with multiple sclerosis (MS); 1 experienced worsening of preexisting MS, 1 had isolated optic neuritis and 1 isolated pontine demyelination. All these 8 patients had MRI scans suggestive for MS-like demyelination. Complete or partial resolution of symptoms occurred after anti-TNF α therapy discontinuation and steroids. A 55-year-old patient developed opsoclonus myoclonus syndrome associated with anti-Glu3 antibodies, with no recovery after anti-TNF α therapy discontinuation, steroids, intravenous immunoglobulins and plasma exchange. The last patient was a 50-year old female who developed a fatal acute diffuse leukoencephalopathy while on an anti-cytotoxic T-lymphocyte associated antigen-4 monoclonal antibody (Ipilimumab) for advanced melanoma.

Conclusion: Our observation supports a possible association between biologics and unexpected neurological complications. Therefore, in clinical practice an active surveillance is mandatory for an early detection of neurological adverse events, which may require a prompt discontinuation of the drugs.

Disclosure: Nothing to disclose

Case	Gender, Age	Disease	Name of Biologics	Treatment duration	CNS complication	Outcome (follow-up)
1	M, 48 years	Psoriatic arthritis	Etanercept	2 months	Isolated optic neuritis	CIS (17 months)
2	M, 31 years	Psoriatic arthritis	Infliximab	3 months	CIS	CIS (20 months)
3	W, 37 years	Crohn disease	Infliximab	3 months	CIS	CIS (16 months)
4	W, 54 years	Psoriatic arthritis	Adalimumab	6 months	CIS	RRMS (13 months)
5	M, 50 years	Ankylosing spondylitis and RRMS (EDSS:2)	Adalimumab	11 months	Worsening of preexisting symptoms	SPMS (EDSS 7.5)
6	M, 27 years	Psoriatic arthritis	Etanercept	6 months	RRMS	RRMS stable (18 months)
7	M, 64 years	Ankylosing spondylitis	Etanercept	8 months	Autoimmune Encephalitis (Anti Glu3 antibodies positive)	Improved. Mild cognitive impairment (22 months)
8	F, 28 years	seronegative spondyloarthritis	Infliximab	3 months	CIS	RRMS (12 months)
9	M, 40 years	Ankylosing spondylitis	Golimumab	Unknown	Isolated pontine demyelination	Complete resolution (12 months)
10	F, 52 years	Metastatic melanoma	Ipilimumab	6 months after ipilimumab discontinuation	Acute diffuse leukoencephalopathy	Exitus

Footnotes: CIS = clinically isolated syndrome, RRMS= relapsing remitting multiple sclerosis, EDSS= expanded disability status scale

Table 1: Demographic and clinical characteristics of the cases.

EPO1256

Clinical features and treatment efficacy in Neuromyelitis Optica Spectrum Disorder

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Background and aims: Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune disease characterized by optic neuritis and longitudinally extensive transverse myelitis. The progression of disability is mostly related to the severity of the attacks. Therefore, appropriate therapy should be started immediately. The aim of this study is to evaluate the clinical features of NMOSD and the efficacy of treatments.

Methods: Patients were recruited to this study who were fulfilling the 2015 International Diagnostic Criteria for NMOSD. The study design was retrospective, cross-sectional, and observational. The inclusion criteria were being older than 18 years, receiving any treatment longer than 12 months, having a clinical follow-up for more than 1 year, and having annual magnetic resonance imaging (MRI). The exclusion criteria were the presence of a co-morbid disease, which may cause neurological disability.

Results: We included 20 patients (15 females - 75%) in the study. The mean age was 38.5±20.4 years, and the mean disease duration was 74.5±30.7 months. The first symptoms in the onset of the disease were motor weakness (50%), brainstem involvement (10%), visual loss (55%), sensory loss (55%), and bowel-bladder involvement (30%). All therapies used for the treatment were oral steroid (80%), azathioprine (40%), Rituximab (75%), and Cyclophosphamide (10%). The annual relapse rate was 0.54 and showed a marked decrease to 0.16 (p<0.001). MRI was stable in 90% of the patients after 12 months.

Conclusion: NMOSD may present with different clinical findings. The appropriate treatments may prevent the progression of disability, the presence of attacks, and new lesions in MRI.

Disclosure: Nothing to disclose

EPO1257

Immunoglobulin free light chains in Multiple Sclerosis: Is a parallel increase of kappa and lambda associated with higher neuronal damage?

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Background and aims: Increased levels of cerebrospinal fluid (CSF) immunoglobulin free light chains (FLC) are typical hallmark of multiple sclerosis (MS). Research has focused on the kappa FLC because most of the patients exhibits a CSF kappa to lambda ratio higher than that in serum. Moreover, kappa FLC (KFLC) index is currently employed in the diagnostic work-up of MS. Little is known, however, about role played by lambda FLC (LFLC).

Methods: Patients with MS with detectable intrathecal synthesis (kappa index >5) enrolled in the study were divided in 2 groups: KFLC index >10 and LFLC index <10 (group 1; n=20) and KFLC index >10 and LFLC index >10 (group 2; n=25). Kappa and lambda FLC and IgG were measured in serum and CSF by nephelometry. Oligoclonal bands (OCB) were detected by isoelectrofocusing (IEF). Tau, p-tau, b-amyloid and neurofilament light chain (NF-lc) were measured by ELISA.

Results: Comparison of the biochemical features of the two groups is detailed in the following Table

	Group 1	Group 2	p
CSF IgG mg/dL	5,79±2,63	5,04±3,89	0,218
CSF LFLC/IgG ratio	6,11±3,65	47,18±29,79	<0,0001
LFLC quotient (*1000)	18,72±10,60	136,32 ± 106,15	<0,0001
LFLC index	4,10±1,99	29,74±16,84	<0,0001
KFLC index/LFLC index	49,94±63,88	1,74±1,15	<0,0001
Tau (pg/ml)	119,79±89,61	126,47 ± 51,28	0,397
β-amyloid (pg/ml)	514,65±152,99	570,94 ± 210,60	0,184
p-Tau(pg/ml)	31,48±15,47	29,56±9,35	0,349
NF-lc (pg/ml)	831±558	1638±1161	0,002

Comparison of the biochemical features of the two groups

Conclusion: These results suggest that, in MS, a contemporary increase of KFLC and LFLC absolute concentrations and indexes is associated with increased neuronal damage, as revealed by increased levels of NF-lc.

Disclosure: Nothing to disclose

EPO1258

Cortical thickness and serum neurofilament light chain levels predict subtle neuropsychological impairment at early stages of Multiple Sclerosis

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Background and aims: The aim of this research was to examine the biomarkers related to ongoing neuroaxonal degeneration, radiological measures of cortical and subcortical gray matter damage, and clinical parameters to explore its association with subtle neuropsychological impairment in early-diagnosed multiple sclerosis (MS) patients.

Methods: 35 Relapsing-Remitting MS patients and 21 Healthy Controls (HC) matched in gender and age were enrolled in our study. All participants underwent magnetic resonance imaging (MRI) examination and neuropsychological and clinical assessments. In addition, regional brain GM volumes and Cortical Thickness (CT) were calculated and neurofilament light chain (NfL) blood levels were obtained from all participants.

Results: Compared to HC, MS patients showed statically poorer performance in information speed processing and verbal memory subtests as well as bilateral thalamic atrophy and cortical thinning in temporal-parietal areas. Moreover, stepwise multiple regression analyses revealed that state-anxiety scores, NfL levels, and global CT explained and predicted neuropsychological impairment (NI) in MS patients. Specifically, CT of right supramarginal gyrus (rSMG) accounted for the greater NI variance.

Conclusion: State anxiety, serum NfL levels as the biomarker of axonal injury, and global CT were the most significant variables explaining neuropsychological performance in patients recently diagnosed with MS. Precisely, CT of rSMG was the strongest regional measure predicting neuropsychological status in our MS sample. rSMG is a key brain area within fronto-parietal network involved in cognitive and attentional control, thus, rSMG thinning could represent an early radiological surrogate of MS-related cognitive decline at disease onset stage.

Disclosure: Nothing to disclose

EPO1259

Withdrawn

EPO1260

The incidence of infusion associated reactions in Ocrelizumab-treated Relapsing-Remitting Multiple Sclerosis patients.

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Background and aims: Ocrelizumab is a disease modifying therapy (DMT) licensed for treatment of active relapsing-remitting Multiple Sclerosis (RRMS). Infusion-associated-reactions (IARs) are a common side effect (SE) of Ocrelizumab especially during the initial infusions. Tolerability is an important factor patients take into account when selecting a DMT; the local MS centre experience with a DMT could also influence such decision. We sought to assess the frequency of such IARs in our cohort of Ocrelizumab-treated RRMS-patients at Brighton & Sussex University Hospitals MS Centre.

Methods: All Ocrelizumab-treated RRMS-patients data from February 2019 to January 2020 was reviewed. IARs classified as mild, moderate, severe and life-threatening based on the Ocrelizumab-proforma, during and 1 hour post infusion were recorded. Patients were advised to contact the infusion nurses if they experienced further symptoms in the next 24 hours post infusion.

Results: 28 patients received Ocrelizumab: 20 (71%) females; mean age 41.7 years old (range 25-58); median EDSS 2 (range 0-6). 12 (42.8%) patients had received no prior DMTs. 23 (82.1) patients reported either nil or mild IARs; 7 (25%) patients had mild IAR. 2 (7.1%) patients had moderate IAR; 2 (7.1%) patients had severe IAR, 1 (3.6%) patient experiencing throat pain, swelling, rhinorrhoea and dyspnoea. 1 (3.6%) patient experienced significant raised liver enzymes; 1 (3.6%) patient had acute respiratory distress syndrome requiring treatment discontinuation.

Conclusion: Our data suggest that Ocrelizumab is generally well tolerated, however caution should be exercised and patient should be monitored closely especially in the initial infusion. Real world data provides useful information to share with patients when they are consented.

Disclosure: Nothing to disclose

EPO1261

Spectrum of Neuromyelitis optica spectrum disorders

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Background and aims: Neuromyelitis optica spectrum disorders (NMOSD, previously known as Devic disease or neuromyelitis optica [NMO]) are inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and spinal cord. The aim was to study the clinical, radiological, immunological profile and treatment outcomes of neuromyelitis optica spectrum disorder (NMOSD).

Methods: The study was carried out at a tertiary care multi-specialty hospital in Western Maharashtra. The study protocol was approved by the institutional ethics committee. The study design was a prospective, observational study with patients recruited over a period of 1 year from December 2018 to November 2019. The 2015 International consensus diagnostic criteria were used for the diagnosis of NMOSD. 30 patients of NMOSD were studied with detailed history, clinical evaluation, radiology, and serological workup.

Results: Female preponderance with 60% was seen. Aquaporin 4 antibody was positive in 60% of patients, the remaining 40% had positive myelin oligodendrocyte glycoprotein antibody. The mean age of presentation was 28 years. Isolated optic neuritis was the most common presentation. Recovery was directly related to the time of onset of therapy in the acute stage. Plasma exchange showed clinically significant only if it started up to 2 weeks of the acute event. Rituximab was most effective in the prevention of relapse as compared to other options.

Conclusion: NMOSD is the most common cause of vision loss in young patients. The spectrum of NMOSD is expanding. MOG antibody should be tested in all Aquaporin 4 antibody-negative NMOSD

Disclosure: Nothing to disclose

EPO1262

A 2-year Study to Evaluate the Onset of Action of Cladribine Tablets in Subjects with Highly Active Relapsing Multiple Sclerosis: Results from MAGNIFY-MS Baseline Analysis

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Background and aims: Better characterisation of how the effects of cladribine tablets on lymphocytes translate into clinical benefits, and the time-course of clinical benefits, is the subject of the ongoing MAGNIFY-MS study. The baseline characteristics of eligible patients in MAGNIFY-MS are reported.

Methods: MAGNIFY-MS is a prospective phase IV, open-label, single-arm, multi-centre, multi-country, 2-year study to determine the onset of magnetic resonance imaging (MRI)-detectable disease control following treatment with cladribine tablets 1 mg (3.5mg/kg cumulative dose over 2 years). Eligible patients are ≥ 18 -years-old, with highly active RMS and Expanded Disability Status Scale score ≤ 5.0 . The primary endpoint is change in the number of combined unique active MRI lesions during the first 6 months versus baseline. Secondary endpoint is characterisation of immune cell subsets at pre-defined intervals versus baseline.

Results: A total of 313 patients have been enrolled. In total, 260 patients have been assigned to active treatment (cut-off for baseline analysis, June 2019). Baseline demographics and clinical characteristics are shown in Table 1.

Table 1. Baseline demographics and clinical characteristics of patients enrolled in MAGNIFY-MS (ITT population, June 2019 cut-off)	
Parameter	Cladribine tablets 3.5 mg/kg (n=260)
Female, n (%)	172 (66.2%)
Race, n (%)	
White	217 (83.5)
Black/African-American	1 (0.4)
Asian	2 (0.8)
Other	11 (4.2)
Not collected	29 (11.2)
Age, years, mean±SD	37.7±9.7
Age categories, n (%)	
≤40 years	146 (56.2)
>40-65 years	114 (43.8)
EDSS at baseline, median (range)	2.5 (0-5)
Time since MS onset, months, mean±SD	83.4±83.9
Time since first relapse, months, mean±SD	53.0±71.2
Relapses within 12 months of baseline, n (%)	
0	8 (3.1)
1	112 (43.1)
2	114 (43.8)
>2	26 (10.0)
≥1 T1 Gd+ lesion, n (%)	97 (37.3)
≥1 new or enlarging T2 lesion, n (%)	30 (11.5)
≥1 T1 Gd+ or new or enlarging T2 lesion, n (%)	127 (48.8)
EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; ITT, intent-to-treat; MS, multiple sclerosis; SD, standard deviation.	

Table 1

Conclusion: Baseline characteristics of those recruited reflect the anticipated patient population as specified in the protocol. MAGNIFY-MS will provide key information on changes in early immune phenotype and the onset of treatment effect, marked by MRI-detectable disease activity following treatment with cladribine tablets.

Disclosure: This study was sponsored by Merck KGaA, Darmstadt, Germany.

EPO1263

Key Factors for Patient Persistence in Dimethyl Fumarate Patient Support Programs

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Background and aims: Patient Support Programs (PSP) for patients with multiple sclerosis (MS) provide critical support services and address patient needs through personalization. The impact of PSP participation was examined using persistence on delayed-release dimethyl fumarate (DMF), an oral MS therapy.

Methods: De-identified data from Australia, Canada, Germany, and the UK for all PSP participants starting DMF before October 2017 (≥12 months [M] of data) were analyzed. Persistence rate survival curves evaluated support call type, frequency, and financial assistance. Hazard ratio analyses assessed association of patient characteristics with persistence.

Results: Persistence in Australia was influenced by total number of support calls; moderate (10-20) call volume was most consistently correlated with short- and long-term sustained persistence. In Australia, calls during weeks 2–3 post-initiation positively influenced persistence up to 12M, with similar persistence at 12M regardless of early outbound check-up calls (Fig1). Similarly in Canada, check-up calls during 0–6M resulted in higher short-term persistence (up to 12M) for moderate (5-15) and high (15+) call groups (Fig2); however after 6M, persistence for the high (15+) call group fell below the low (0-5) call group at 12M. Financial assistance increased persistence for up to 3 years post-initiation in Canada. In Germany, temporal associations with persistence remained after stratification of PSP participants by adherence risk.

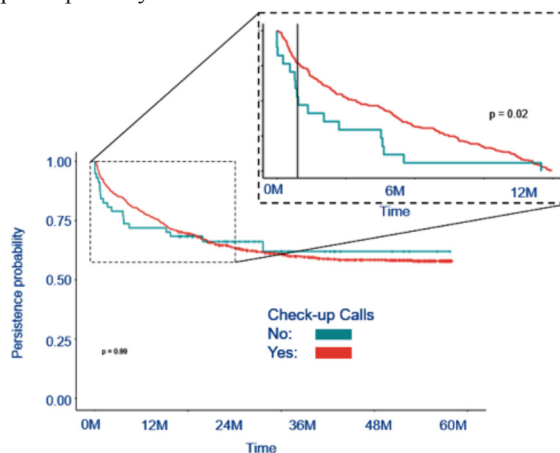


Figure 1. Persistence probability based on frequency of Australian outbound calls during weeks 2-3

Figure 1. Persistence probability based on frequency of Australian outbound calls during weeks 2-3

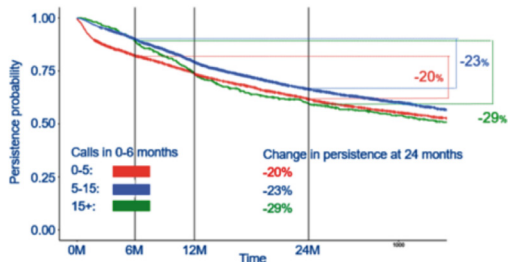


Figure 2. Persistence probability according to frequency of Canadian PSP check-up calls

Conclusion: Support calls in DMF PSPs are positively associated with persistence, demonstrating the value of PSPs. Additional analyses segmenting by patient phenotype and risk factors are required to provide definitive PSP design recommendations to further improve persistence. Support: Biogen

Disclosure: Supported by Biogen; the authors are full-time employees of and hold stock/stock options in Biogen.

EPO1264

Retinal nerve fiber layer and disease course. Is this a relationship despite disability?

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Background and aims: Optical coherence tomography (OCT) measures thickness of the retinal nerve fiber layer (RNFL), commonly associated with disability. We studied the relationship of previous disease course with RNFL thickness despite disability.

Methods: We retrospectively analyzed RNFL thickness and demographic features, optic neuritis and annualize relapse rate (ARR) at year 1, 2 and 5 from diagnosis, of remitting-relapsing MS(RRMS) patients.

Results: We analyzed 24 patients with a mean age of onset of 31y (15-48y), 75% women and a medium follow-up of 10y from diagnosis to OCT. Eleven patients had at least 1 optic neuritis (ON).

RNFL thickness was $\leq 90\mu\text{m}$ in both eyes in 71% (17/24), 10 of them with previous ON.

RNFL thickness was normal in 7 patients, only 1 with previous ON.

Differences in RNFL thickness in patient with or without previous ON are shown in table 1. Presence or absence of ON is the event most related to RNFL thickness.

In our cohort time from onset to OCT independently influence RNFL thickness, showing that patients with longer course presented more decrease(table 2).

No differences were found in RNFL thickness respecting ARR at year 1, 2 and 5, age at onset (table 3) or sex.

Table 1. RNFL thickness and optic neuritis, age of onset and disease course.

	RNFL AO	RNFL OD	RNFL OS	Age at onset	Time at OCT	TAB 1	TAB 2	TAB 5
All patients (n=24)	85,0 ± 9,6	86,5 ± 10,2	83,5 ± 11,6	31y	10y	1,57	1,91	2,96
With ON (n=11)	81,0 ± 11,1	82,6 ± 12,7	79,4 ± 11,1	31y	10y	1,82	2,18	3,55
With 1 ON (n=4)	83,3 ± 18,4	79,3 ± 20,0	87,3 ± 18,0	30y	12y	2,75	2,75	3,75
With 2 ON (n=6)	78,8 ± 5,5	84,5 ± 8,2	73 ± 8,8	35y	7,6y	1,5	1,67	2,83
Without ON (n=13)	88,4 ± 6,9	89,7 ± 6,5	87,1 ± 8,4	30y	10,6y	1,33	1,67	2,42

AO: Both eyes; OD: Right eye; OS: Left eye

Table 3. RNFL related to age at diagnosis

Age at diagnosis	RNFL AO	RNFL patients with ON	RNFL patients without ON
Less 18y (n=1)	76	76	
18-28y (n=5+5)	83,95 ± 8,7	77,4 ± 7,3	90,5 ± 4,0
28-38y (n=2+6)	87,68 ± 11,7	94,3 ± 20,9	85,5 ± 9,1
38-48y (n=3+2)	84,6 ± 8,8	79,3 ± 8,3	91,8 ± 1,8

Conclusion: RNFL thickness in patients with MS seem to be decrease, despite ON. In our cohort, 71% of patients present RNFL thickness $\leq 90\mu\text{m}$ in both eyes, 41% without ON. Progressive degeneration of RNFL in RRMS is not only associated with disability but also with disease duration. ARR, age at onset or sex do not seem to influence RNFL.

Disclosure: Nothing to disclose

EPO1265

Cognitive-motor interaction: Its role in Multiple Sclerosis patient's quality of life.

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Background and aims: Recent evidence suggests that patients with Multiple Sclerosis (PwMS) present deficits when performed simultaneously cognitive and motor tasks (Cognitive-Motor Interaction, CMI). The impact of this deficits in patient's quality of life has been sparsely studied.

Objectives: 1) To compare performance in CMI between PwMS and healthy controls. 2) To examine the impact of CMI in health-related quality of life (HRQoL).

Methods: 91 patients with relapsing remitting MS and 20 healthy controls were included. Age: 38.58±11.37, 34.00±14.25; Education: 13.26±3.82, 14.50±2.65 respectively; EDSS: 2.20±1.30; Evolution: 9.70±9.01. Outcome measures: Clinical variables: EDSS; Fatigue Severity Scale; Beck's Depression Inventory II. HRQoL: MS International QoL Questionnaire (MusiQoL); Cognitive variables: BICAMS Battery; Dual tasks: Two CMI tasks (walking while performing verbal fluency/counting). Difference between subject performance in simple and dual task was obtained. It was quantified: time, steps and cognitive performance. Parametric and nonparametric statistics were performed, p value <0.05 was accepted.

Results: patients and controls were similar in age and education (p=0.124, p=0.104). Significant differences were found between groups in CMI, in time and steps of counting task (p=0.015, p<0.05), and in the performance of both cognitive tasks (fluency p=0.028, counting p<0.01). Significant associations were found between CMI and disease evolution (p=0.027), EDSS (p=0.031), SDMT (p=0.018). Significant negative correlations were found between CMI and HRQoL dimensions (rS=0.297 to 0.564). Adjusting by clinical variables, CMI was established as a predictor of HRQoL (R²=0.36, p<0.05).

Conclusion: PwMS show alterations in CMI. This performance has a significant impact in HRQoL that should be considered in patient's treatment.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 1

EPO1266

Vestibular impairment in Guillain-Barré syndrome

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Background and aims: The Guillain-Barré syndrome (GBS) is a common, treatable, acute peripheral neuropathy that can produce imbalance. We evaluated the vestibular function in GBS patients order to find out if vestibular impairment could contribute to the imbalance.

Methods: We measured postural stability with a battery comprising the modified Clinical Test of Sensory Integration and Balance, the Berg Balance Scale, the Dynamic Gait Index, the Fall Efficiency Scale, and the International Cooperative Ataxia Rating Scale and semicircular canal (SCC) vestibular function in 11 GBS patients (7M/4F) by the video Head Impulse.

Results: Of the 11 patients, 8 had vestibular impairment, ranging from mild-affecting just a single SCC to severe - affecting all 6 canals. Although the severity of the vestibular impairment did not correlate either with the severity of the postural imbalance or of the peripheral neuropathy, our data show that vestibular impairment be an additional challenge to balance it some GBS patients.

Conclusion: Measuring SCC in GBS patients is easy with the video Head Impulse Test and can yield useful information for patient management.

Disclosure: Nothing to disclose

EPO1267

Multifocal Motor Neuropathy secondary to infection by *Rickettsia conorii*.

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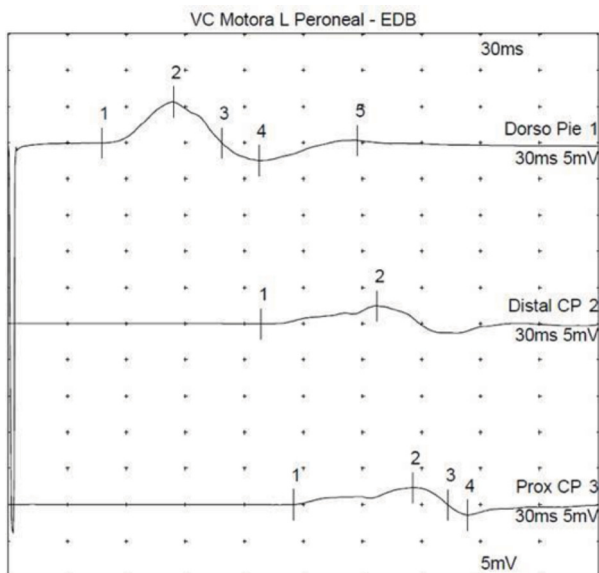
Background and aims: Mediterranean spotted fever caused by *Rickettsia conorii* (RC) is endemic in the Mediterranean countries. Typical clinical features include fever, myalgia, cervical lymphadenopathy, headache, generalized maculopapular rash and an inoculation eschar at the site of the tick bite. RC diagnosis is supported by positive IgM and fourfold increase of IgG. Neurological manifestations, mostly manifested as meningoencephalitis, have been reported in up to 28% of patients. Involvement of peripheral nervous system is considered extremely rare.

We are reporting a patient who developed tetraparesis secondary to a multifocal motor neuropathy secondary to infection by RC.

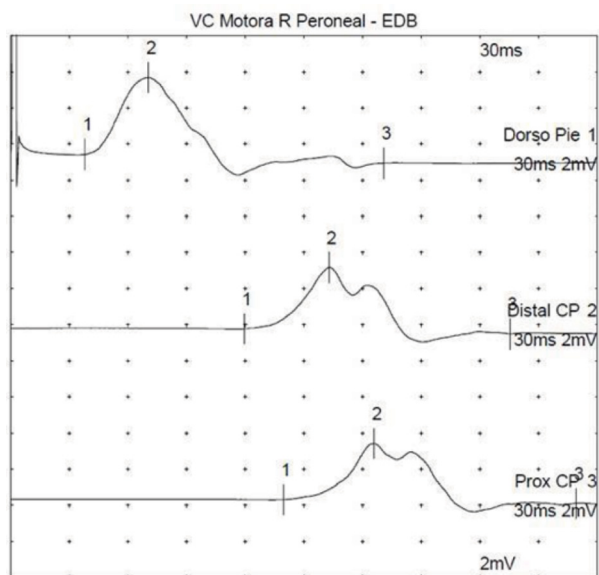
Methods: A 46-year-old man who came at our outpatient clinic due to generalized weakness accompanied by dysesthesias and progressive deterioration in walking in the last 5 days. 3 weeks earlier, the patient was bitten by a tick. The neurological examination showed asymmetrical distal quadriparesis with motor weakness of the feet and to a lesser degree in hands, arreflexia in lower limbs and hyporreflexia in upper limbs without sensory involvement. A eschar at the site of the bite was also observed.

Investigations included routine serological testing which was normal. Nerve conduction studies showed Multifocal Motor Neuropathy (MMN) with conduction blocks and IgM positive for RC was also obtained.

Results: Thanks to these findings, MMN secondary to infection by RC was diagnosed and doxycycline 200mg daily for 10 days was started. Over the next few weeks, the patient had a marked improvement in clinical and neurophysiological parameters.



Conduction blocks on peroneal nerve.



Improvement of motor nerve conduction on peroneal nerve after antibiotic treatment.

VC Sensitiva

Nervio / Lugares	Reg.	Latencia ms	Ampl. µV	Distancia mm	VC m/s
L Mediano - vs Ulnar					
Dedo II	Med	3.20	16.5	170	53.1
Dedo V	Cub	2.90	8.1	140	48.3
R Radial					
Ant	Tab ana	2.20	26.1	110	50.0
L Sural - Mal Exter	Mal Lat	3.00	16.0	150	50.8
Sura	Mal Lat	2.15	14.3	130	60.5
R Superficial peroneal	Dorso pie	2.85	7.1	120	42.1
L Superficial peroneal	Dorso pie	2.50	10.9	125	49.0

VC Motora

Nervio / Lugares	Latencia ms	Ampl. mV	Dur. ms	Dist. cm	VC m/s	Reg
R Mediano - Apb	4.45	6.7	7.70			APB
Muñeca	9.75	2.1	6.80	290	54.7	
Codo	13.10	2.1		240	71.6	
Ep	14.90	1.9	7.20			
L Mediano - Apb	4.00	7.3	8.65			APB
Muñeca	8.90	3.7	6.95	270	55.1	
Codo	12.50	3.5	6.50	240	69.7	
Ep	14.35	3.1				
R Ulnar - Adm	4.25	4.9	10.50			ADM
Muñeca	8.95	1.0	9.00	210	44.7	
Codo	10.80	0.8	8.30	180	72.7	
Ep	16.10	0.3	10.35			
L Ulnar - Adm	4.90	3.8	8.65			ADM
Muñeca	7.80	0.5	11.55			
Codo	8.80	0.4	12.75			
Ep	13.05	0.3	15.95			
Ep	16.55	0.2	17.85			
L Peroneal - EDB						EDB
Dorso Pie	4.75	6.7	6.10			
Distal CP	12.85	2.5		380	46.9	
Prox CP	14.50	2.4	7.85	190	40.5	
L Tibial						AH
Mal Int	8.20	1.2	10.65			
Hueso Popl	20.10	0.4	4.70	430	36.1	
R Tibial						AH
Mal Int	9.00	2.9	11.70			
Hueso Popl	20.85	0.3	11.65	430	38.3	

PRE TREATMENT

VC Sensitiva

Nervio / Lugares	Reg.	Latencia ms	Ampl. µV	Distancia cm	VC m/s
R Mediano - y Ulnar Dedos					
Dedo I	Mal	3.20	12.9	180	55.4
Dedo V	Mal	2.70	6.4	130	50.0
L Mediano - y Ulnar Dedos					
Dedo I	Mal	3.10	14.3	180	51.4
Dedo V	Mal	2.65	5.4	140	52.8
R Radial					
Ant	Tab ana	2.30	36.7	120	52.2
L Radial					
Ant	Tab ana	2.30	33.9	120	52.2
L Sural - Mal Exter	Mal Lat	2.85	17.0	130	47.4
R Sural - Mal Exter	Mal Lat	2.35	16.5	120	53.3
Sura	Mal Lat	2.35	16.5	120	53.3
R Superficial peroneal	Dorso pie	2.70	8.5	120	45.5
L Superficial peroneal	Dorso pie	2.70	7.9	130	48.1

VC Motora

Nervio / Lugares	Latencia ms	Ampl. mV	Dur. ms	Dist. cm	VC m/s	Reg
R Mediano - Apb	3.45	8.3	6.45			APB
Muñeca	8.00	3.8	11.80	280	50.6	
Codo	13.15	1.9	14.85	250	80.2	
Ep	15.65	2.0	15.85			
L Mediano - Apb	3.65	11.4	10.45			APB
Muñeca	8.50	5.3	20.40	380	61.8	
Codo	13.05	4.4	20.85	250	54.0	
Ep	15.25	4.3	21.00			
R Ulnar - Adm	3.20	5.6	11.35			ADM
Muñeca	7.80	2.5	15.80	230	51.1	
Codo	10.35	2.5	14.20	120	47.1	
Ep	15.10	2.2	16.20	240	50.9	
Ep	17.65	2.0	14.30			
L Ulnar - Adm	3.15	6.0	20.90			ADM
Muñeca	7.40	2.3	24.10	320	51.8	
Codo	9.70	2.5	23.05	130	56.5	
Ep	13.90	2.1	28.05	220	52.4	
Ep	16.25	1.9	28.85			
R Peroneal - EDB						EDB
Dorso Pie	3.80	4.3	15.30			
Distal CP	11.95	3.4	13.80	360	47.9	
Prox CP	13.95	3.1	15.00	190	50.2	
L Peroneal - EDB						EDB
Dorso Pie	4.25	4.8	8.45			
Distal CP	11.75	3.8	9.80	370	49.3	

POST TREATMENT

Comparison table of motor conduction velocities.

Conclusion: MMN peripheral involvement, although rare, can occur as a complication of infection by *R. conorii*.

Disclosure: Nothing to disclose

EPO1268

Camptocormia as a presenting symptom of Myotonic Dystrophy Type 2: an overlooked cause of axial myopathy

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Background and aims: Myotonic dystrophy type 2 (DM2) is an autosomal dominant multisystemic disorder most commonly presenting with proximal leg muscle weakness and myotonia between the 4-6th decade of life. Axial involvement and camptocormia are rare and misdiagnosis often occurs especially in the elderly.

Methods: Case-report

Results: A 83-year old man was admitted to the neurology department due to predominant progressive camptocormia, difficulty climbing stairs and arising from a chair over the last 10 years. His past medical history involved early-onset cataract, Wolff-Parkinson-White syndrome with atrial fibrillation, and arterial hypertension. His family history was negative regarding any neurological disorder. Physical and neurological examination revealed frontal balding, mild atrophy of temporalis muscles, camptocormia exacerbated upon walking, muscle weakness of neck flexors (4+/5 MRC), neck extensors (4/5 MRC) and hip flexors (4/5 MRC). Myotonic phenomenon was also elicited on the calf muscles. Biochemical analysis revealed mildly elevated creatine kinase levels without any other significant abnormalities. Nerve conduction studies showed mild sensorimotor axonal polyneuropathy, whereas electromyography demonstrated small amplitude, brief, polyphasic action potentials in biceps brachialis, deltoid, quadriceps, paraspinal and rectus abdomini muscles, with rare mild myotonic discharges in biceps brachialis and trapezius muscle. Clinical suspicion of DM2 was set based on clinical and electrophysiological findings. Genetic testing revealed a CCTG repeat expansion of the CNBP gene, confirming the clinical diagnosis.

Conclusion: We present an unusual elderly-onset DM2 case with prominent camptocormia, expanding the clinical spectrum and differential diagnosis of axial myopathies. Detailed electrophysiological testing is essential for the detection of myotonic disorders, while the appropriate genetic testing confirms the diagnosis.

Disclosure: Nothing to disclose

Table 2. RNFL and time from onset of MS

Years of disease	RNFL patients with ON	RNFL patients without ON	RNFL AO
<5 years (n=2+3)	91,83 ± 15,9	82,5 ± 14,8	88,1 ± 14,4
5-10 years (n=3+4)	77,5 ± 1,5	91,5 ± 3,9	85,5 ± 8,0
>10 years (n=7+5)	76,6 ± 7,6	88,3 ± 5,8	83,4 ± 8,7

EPO1269

Expanding the phenotype of p.R1460W mutation in SCN4A gene: a family report

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Background and aims: SCN4A gene encodes the α subunit of the voltage-gated sodium channel. The homozygote LOF p.R1460W mutation has been described in a patient affected with myasthenic congenital myopathy at birth. Both heterozygote parents were asymptomatic, suggesting a recessive transmission.

Methods: We report a family complaining about muscle cramps and stiffness after physical activity. The brothers experienced episodes of periodic paralysis improved after potassium administration. Genetic analysis showed the heterozygote p.R1460W SCN4A mutation in all the siblings. Their asymptomatic mother showed no mutation, while the father was not tested because he died early. EMG study showed in the younger brother myopathic abnormalities and was normal in the other subjects. Muscle biopsy performed on the younger brother showed only mild non specific findings (fiber diameter variability and scattered atrophic fibers). The role of others genes involved in muscle channelopathies, such as CLCN1 and CACN, was excluded by performing NGS study.

Results: To our knowledge, this is the second family harbouring the p.R1460W variant in SCN4A reported in literature. However in our family this mutation appears to be inheritend in an autosomal dominant manner and associated with a new “hypoPP, muscle pain and cramps” phenotype. No signs of myasthenia were detected.

Conclusion: Our findings expand the phenotypical spectrum associated with the p.R1460W mutation in SCN4A, by reporting a novel phenotype and a novel inheritance pattern. Further investigation on related genes and epigenetic factors are mandatory in order to better define and understand the mechanisms underlying the variable clinical expression.

Disclosure: Nothing to disclose

EPO1270

Inclusion body myositis: presentation with asymptomatic hyperCKemia

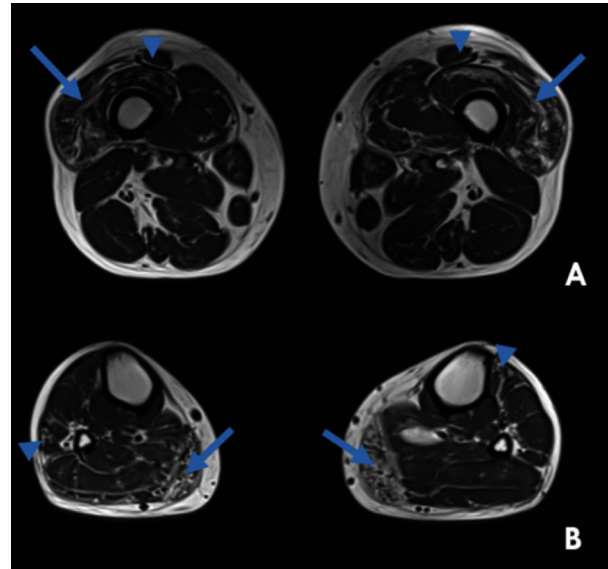
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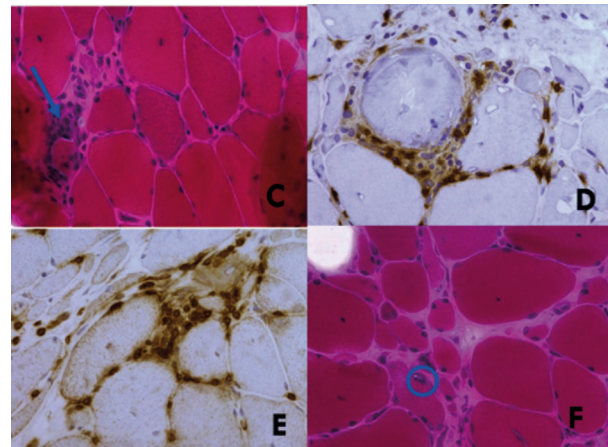
Background and aims: Sporadic Inclusion body myositis (sIBM) is a myopathy that usually presents with progressive muscle weakness in a characteristic anatomical distribution and is typically accompanied by normal or only slightly increased serum creatine kinase (CK).

Methods: Case report.

Results: Male of African descent with persistent asymptomatic CK elevation (maximum 1300IU/L) incidentally detected after an Acute Myocardial Infarction by the age of 63. At the time, neurological examination was unremarkable, and both EMG and deltoid biopsy were normal. Two years later he began experiencing mild muscle discomfort and, by the age of 71, weakness finally became apparent, with selective involvement of long finger flexors. Over the next 2 years, hand weakness progressed and leg weakness (plantar flexion and especially foot dorsiflexion) emerged. A 2nd EMG was performed, then showing myopathic changes in finger flexors and leg muscles, with abundant fibrillations. Lower limb MRI showed moderate fatty infiltration in vastus lateralis and medial gastrocnemius, and mild infiltration in tibialis anterior and peroneal muscles, with relative sparing of rectus femoris and posterior thigh. Accordingly, vastus lateralis was selected for a 2nd muscle biopsy and endomysial inflammatory infiltrates (predominantly CD8⁺) coexisting with rimmed vacuoles were found. Serum anti-cN1A antibody was positive, further supporting the diagnosis of sIBM.



Lower limb MRI: moderate fatty infiltration in vastus lateralis (A, arrow), and relative sparing of rectus femoris (A, arrowhead) and posterior thigh; moderate fatty infiltration of the medial gastrocnemius (B, arrow) and mild infiltration in tibialis anterior and peroneal muscles (B, arrowhead).



Vastus lateralis biopsy: endomysial inflammatory infiltrates (C, arrow), predominantly CD8⁺ (D) T lymphocytes (E) and presence of rimmed vacuoles (F, circle).

Conclusion: We herein describe a case of sIBM presenting with asymptomatic hyperCKemia preceding in 8 years the onset of muscle weakness. This feature is probably very unusual but suggests that sIBM should be included among the differential diagnoses of asymptomatic hyperCKemia above the age of 50 years.

Disclosure: Nothing to disclose

EPO1271

Anti-NXP2-Antibody Positive Late Onset Pompe Disease Misdiagnosed as Polymyositis

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Background and aims: Pompe Disease (PD) is caused by lysosomal acid-alfa glucosidase (AAG) deficiency. A partial reduction of enzyme activity results in a late-onset form of the disease mainly consisting of proximal myopathy and elevated creatine kinase (CK) levels, which it may be confused with inflammatory myopathies.

Methods: Male, 54-year-old, with a previous diagnosis of polymyositis supported by progressive proximal limb weakness, elevated CK and serum anti-nuclear matrix protein 2 (antiNXP2) antibodies. Despite of treatments with steroids, azathioprine, intravenous immunoglobulin and rituximab, he had continued to suffer from muscle pain and limb weakness.

Results: From the clinical history some red flags for a diagnosis of polymyositis emerged: asymptomatic hyper-CK-emia since the age of 30, the absence of spontaneous activity or insertion irritability at electromyography, atrophy and fatty infiltration without no major inflammatory changes of bilateral glutei, adductors and biceps femoris at muscle MRI (fig. 1). Neurological examination showed bilateral weakness of biceps femoris (MRC 4/5) and iliopsoas (MRC 4+/5) without atrophy, fasciculations or myotonia. Laboratory test confirmed elevated serum CK levels (650Iu/L) and high titer of antiNXP2 antibodies. Diagnosis was reconsidered and additional tests were planned. EMG showed myopathic abnormalities, particularly in biceps femoris and paraspinal muscles. Enzymatic tests showed reduction of AAG activity and the diagnosis was confirmed by genetic test. The patient started AAG replacement therapy with reduction of muscle pain and CK levels normalization.

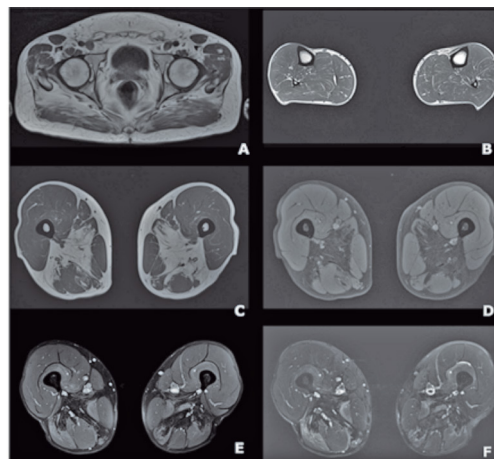


Fig. 1. Muscle MRI: Spin Echo T1 (A, B, C); T1 with fat sat after contrast enhancement (D); T1 with fat sat after contrast enhancement (E); STIR (F). Fatty infiltration can be seen in glutei (A), adductor muscles and biceps femoris (C,D). Mild-moderate STIR hyperintensity (F) without contrast enhancement (E) can be seen in both biceps femoris (right>left) and right adductors. Muscles of legs (B) appeared to be spared.

Conclusion: PD screening for AAG deficiency should be recommended in cases of inflammatory myopathies refractory to immune therapies, particularly when some red flags of better explanation are present.

Disclosure: Nothing to disclose

EPO1272

How do patients with cervical dystonia (CD) experience their Botulinum Neurotoxin Type A (BoNT-A) treatment cycle: results from an international online survey

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Background and aims: BoNT-A is established as CD gold standard treatment. However, BoNT-A injection effects last around 3-4 months and CD symptoms usually recur at the end of a treatment cycle. The aim of this study is to better understand patients' experience of the waning of BoNT-A effects.

Methods: An Internet-based survey was conducted through Carenity, an online patient community, from May to September 2019 in France, Germany, Italy, UK and USA. Adult patients with CD who had received ≥ 2 previous BoNT-A injections and were currently treated with BoNT-A or had stopped in the last 12 months were eligible.

Results: 209 respondents (80.9% women, mean age 49.7 years) answered the questionnaire. Motor/non-motor symptoms and conditions related to CD experienced by those patients in the past 12 months are listed in Table 1. 87.6% experienced the reappearance of CD-related symptoms between 2 BoNT-A injections. Pain (84.2%) was the most reported recurring symptom. Waning of BoNT-A effect started on average 73.6 days after BoNT-A injection. The intensity of CD-related symptoms was rated between 2.6-3.1/10 at maximum BoNT-A effect (0=no symptom; 10=very strong symptom), 5.4-5.8/10 when effects started to wear off, and 7.1-8.0/10 at 1 day before next injection (Table 2). The impact of CD on patients' Quality of Life (QoL) evolved similarly (Table 3). Many patients reported that recurring symptoms affected their comfort (66.4%) and efficiency (65.6%) at work.

Motor/non-motor symptoms and CD-related conditions most experienced*	Overall (N=209)
Motor symptoms; n (%)	
Neck pain or other related pain	179 (85.7)
Muscle spasms	149 (71.3)
Abnormal positioning of the head/neck	145 (69.4)
Involuntary movement of head or shoulder	133 (63.6)
Loss of head range of motion	120 (57.4)
Non-motor symptoms and CD-related conditions; n (%)	
Difficulty at work	113 (54.1)
Fatigue	111 (53.1)
Mood disorders	108 (51.7)
Sleep disorders	106 (50.7)

*symptoms and conditions with frequencies >50%.

Table 1: Motor/non-motor symptoms and conditions most experienced by patients in the past 12 months*

	Intensity of the symptoms reappearing between two sessions of BoNT-A injections (N=183)		
	At peak treatment effect	When pre-existing symptoms start reappearing	1 day before next BoNT-A injection
Neck pain or other related pain (n=154)	2.6	5.4	7.8
Involuntary movement of head or shoulder (n=126)	2.8	5.6	7.9
Muscle spasms (n=120)	2.8	5.6	8.0
Abnormal positioning of the head/neck (n=118)	2.9	5.6	7.8
Loss of head range of motion (n=108)	3.1	5.8	7.9
Tremors (n=84)	2.9	5.6	7.5
Shoulder elevation (n=80)	2.9	5.4	7.1

*mean scores out of 10: 0=no symptom, 10=very strong symptom.

Table 2: Patients' perception of the intensity of the symptoms reappearing between two sessions of BoNT-A injections*

	Impact of the symptoms reappearing between two sessions of BoNT-A injections (N=183)		
	At peak treatment effect	When pre-existing symptoms start reappearing	1 day before next BoNT-A injection
Ability to work	2.7	5.1	7.0
Ability to have social interactions	2.5	5.0	6.8
Ability to drive	2.5	4.6	6.3
Sleep disturbance	2.2	4.4	6.3
Ability to perform daily tasks	2.1	4.4	6.3

*mean scores out of 10: 0=no symptom, 10=very strong symptom.

Table 3: Patients' perception of the impact of the symptoms reappearing between two sessions of BoNT-A injections on QoL*

Conclusion: The waning of BoNT-A effects between treatment cycles has a negative impact on patients' CD related symptoms and on overall QoL and professional life.
Disclosure: Ipsen Pharma funded the study

EPO1273

Exome sequencing: mutilating sensory neuropathy with spastic paraplegia due a mutation in the FAM134B geneS. Wakil¹, J. Finsterer²¹ Department of Genetics, King Faisal Specialist Hospital and Research Centre, Riyadh, Riadh, Saudi Arabia, ²Vienna, Austria

Background and aims: Hereditary sensory and autonomic neuropathies (HSANs) are a clinically and genetically heterogeneous group of disorders involving various sensory and autonomic dysfunctions. The most common symptoms of HSANs include loss of sensations of pain and temperature that frequently lead to chronic ulcerations in the feet and hands of the patient.

Methods: Case report

Results: In this case study, we present the clinical features and genetic characteristics of 2 affected individuals from 2 unrelated Saudi families presenting mutilating sensory loss and spastic paraplegia. We employed homozygosity mapping and exome sequencing which is an efficient strategy to characterize the recessive genes, thus obtaining a rapid molecular diagnosis for genetically heterogeneous disorders like HSAN. Subsequently, a nonsense mutation (c.926 C>G; p.S309*) in FAM134B was identified. In addition, we confirmed that the mutant FAM134B transcripts were reduced in these patients presumably disrupting the receptors of the degradative endoplasmic reticulum pathways that facilitate the autophagy processes

Conclusion: We describe the second family with HSAN-II associated with HSP due to the mutation p.S309X in the FAM134A gene. However the pathogenetic role of FAM134A in sensory neuropathy with spastic paraplegia remains largely unknown and this study expands the phenotypic heterogeneity caused due to variants in FAM134A.

Disclosure: Nothing to disclose

EPO1274

Suboptimal Control of Generalized Myasthenia revealed by implementation of systematic follow-up in a French-Canadian Community neurology practice

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Background and aims: Little is published on actual management of generalized myasthenia in community practice. According to a recently published American registry, 7% of myasthenic patients are refractory and experiencing worse scores on MG-15-item Quality of Life (MG-QOL-15).

Methods: From 19-10-24 to 19-12-20, 16 consecutive patients from Western Quebec coming for regular follow-up with the author, were asked to complete both a MG-Activities of Daily Living (MG-ADL) and MG-QOL-15 instrument. The author, his nurse, and his EMG technician completed Quantitative Myasthenia Gravis score (QMG), Myasthenia Gravis Foundation of America Clinical Classification (MGFA), spirometry and dynamometry.

Results: Almost all scales were successively completed. Eleven patients were AARA positive on a standard essay (69%). 14 were using 2nd line treatment of therapy and 12 (75%) were on continuous IVIg, plasmapheresis or rituximab. 2 are MGFA=4. The mean MG-ADL is 5.5 (7 equal or more than 6), MG-QOL-15 is 11.1 (6 equal or more than 15), QMG is 7.3 (7 equal or more than 10). 5 (31.3%) correspond to the definition of refractory generalized myasthenia and would be eligible for the phase-3 REGAIN study on eculizumab. Another is currently seronegative and less than 12 months of duration. Qol-15 and QMG are worse in refractory patients.

Conclusion: Implementation of a systematic follow-up is feasible in an out-of-hospital community neurology practice. Many of the author's patients remain negatively impacted despite following current clinical care guidelines. According to American Registry definition, about one third of patients are refractory, and would fulfill criteria for the REGAIN Study.

Disclosure: Nothing to disclose

EPO1275

A benchmarking audit of the pre-diagnosis pathway in patients with Duchenne muscular dystrophy

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Background and aims: Duchenne muscular dystrophy (DMD) is a genetic disorder causing progressive muscle weakness, cardio-respiratory impairment and early death. Early diagnosis is key to proactive treatment. This audit aimed to understand the patient pathway to diagnosis and identify opportunities for timeline improvement.

Methods: A multi-centre audit of 9 centres in the United Kingdom & Ireland. Eligible patients were those with a definitive diagnosis of DMD (based on molecular genetics /muscle biopsy) ≤3 years prior to December 2018. Retrospective data were collected from patients’ medical records.

Results: A total of 122 eligible patients were included (1 antenatal diagnosis). A family history of DMD was recorded in 21% (26/122) of patients. The mean age (months) at; a) symptom onset (observed by parents) was 36.4 (n=66, standard deviation [SD] 26.8); b) 1st healthcare professional (HCP) engagement for DMD symptoms was 49.9 (SD=28.9, n=106); c) 1st serum creatine kinase test was 53.8 (SD=30.1, n=97); and d) definitive diagnosis was 53.9 (SD=29.7, n=120). The mean time (months) from 1st symptom onset to first HCP engagement was 19.0 (SD=22.7, n=62); and 4.4 (SD=8.1, n=106) from 1st HCP engagement to definitive diagnosis.

Table 1 shows the distribution of documented motor (n=106) and non-motor (n=57) symptoms.

Table 1. Distribution of symptoms recorded in patient notes¹

Motor Symptoms	n	% (n=106) ²
Gross motor delay	58	55%
Gowers’ sign on rising from floor	54	51%
Calf pseudohypertrophy	52	49%
Difficulty climbing stairs	50	47%
Difficulty running or climbing	44	42%
Abnormal gait	40	38%
Frequent falling or clumsiness	38	36%
Inability to keep up with peers	36	34%
Decreased endurance	26	25%
Inability to jump	22	21%
Muscle pain or cramping	22	21%
Toe walking	19	18%
Hypotonia	14	13%
Flat feet	6	6%
Decreased head control when pulled to sit	3	3%
Loss of motor skills	3	3%
Other	17	16%
Non-Motor Symptoms	n	% (n=57) ³
Speech delay or articulation difficulties	42	74%
Learning and attentional issues	27	47%
Cognitive Delay	19	33%
Behavioural issues	14	25%
Failure to thrive/Poor weight gain	3	5%
Other	8	14%

¹ Not mutually exclusive as may have presented with more than one symptom

² Percentages have been derived from number of patients who had at least one motor symptom recorded

³ Percentages have been derived from number of patients who had at least one non-motor symptom recorded

Table 1- Distribution of symptoms recorded in patient notes

Conclusion: Whilst the time from first HCP engagement to definitive diagnosis appeared shorter compared to a previously published audit, there may still be delays from onset of symptoms to 1st engagement with HCP and subsequent diagnosis, which need to be further explored.

Disclosure: Financial support for the series of service evaluations reported in this project was provided by PTC Therapeutics.

EPO1276

Diagnostic yield of muscle biopsies in pediatric population

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Background and aims: Despite the advances in neuromuscular pathologies diagnosis, muscle biopsy remains a valuable tool for the evaluation of these patients. Nevertheless, data regarding diagnostic yield can be disappointing, with a minority of procedures providing a definite diagnosis. We aimed to analyze the diagnostic yield in a tertiary center in Lisbon, in the pediatric population.

Methods: We performed a retrospective analysis from the muscle biopsy database of a neuropathology laboratory to identify patients (<18 years old), submitted to muscle biopsy between January 2015 and August 2019. Demographics, clinical suspicion, biopsy reports, and follow-up were evaluated.

Results: We included 106 patients, 52.8% (n=56) were male. Median age at biopsy was 8 years (IQI 3, 14). The clinical suspicions were mitochondrial (n=31), congenital (n=9), inflammatory (n=8) and metabolic myopathies (n=4), muscular dystrophies (n=6), hyperCKemia (n=7), weakness/other neuromuscular symptoms (n=29) and multiple suspicions (n=12). Muscle biopsies showed alterations in 52.9% patients (n=56), 48.2% (n=27) of which providing specific diagnostic features, and the remaining showing unspecific myopathic alterations. In 47.2% (n=50), biopsies were normal. Concerning the cases with specific diagnostic features, 88.9% (n=24) provided a definite diagnosis, 18.5% (n=5) patients had a change in diagnosis and 4 patients had a change on treatment. Median follow-up was 1 year (IQI 0.3).

Conclusion: In this cohort, muscle biopsy provided a definite diagnosis in 22.6%. Although this number is low, biopsies presented alterations in 52.9% and still helped narrowing differential diagnosis, confirming myopathic alterations or lead to a therapeutic change.

Disclosure: Nothing to disclose

EPO1277

The safety of enzyme replacement therapy during pregnancy and lactation in Pompe disease- a longitudinal follow up

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Background and aims: It is a generally accepted practice in the medical society throughout the world to avoid any medication during pregnancy unless it is necessary for the protection of fetus. Although, when it comes to the headline what impact different kind of medication may have on the development of fetus or child post partum, we face a little amount of knowledge. In these cases most of the time only animal and in vitro studies are available we can rely on. Pompe disease is a rare genetically determined lysosomal storage disease treatable with enzyme replacement therapy (ERT) since 2006. Though, until recent time only one case report is known on the safety of ERT in Pompe disease during pregnancy. Our aim was to contribute additional information on the safety of ERT during pregnancy.

Methods: We have performed a longitudinal follow up of 2 pregnancies where mothers have received ERT to Pompe disease. Regular check-ups including effect and safety of ERT treatment was evaluated before, during and afterward of pregnancies both for mothers and children.

Results: Both ERT treated mothers featured a stable disease course throughout the pregnancy. The development of fetus and children after delivery was normal during the follow up. 2 children received breastfeeding for 22 months combined while receiving ERT.

Conclusion: The continuation of alglucosidase alfa for the treatment of Pompe disease was safe during pregnancy and lactation. Neither mother nor fetus have shown any side effects. The limited data available suggest that treatment of alglucosidase alfa can be continued during pregnancy and lactation.

Disclosure: Nothing to disclose

EPO1278

Diaphragm ultrasound in neuromuscular disease (NMD) patients

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Background and aims: Respiratory failure is 1 of the main causes of death in NMD. Detection of the diaphragm dysfunction using ultrasound may be a diagnostic possibility of reveal respiratory failure at the early stages. To examine the diaphragm function in NMD patients using ultrasound

Methods: Ultrasound was performed on 34 subjects (16 patients with NMD—the main group, 18 healthy volunteers – the control); 13(38%) men, 21(62%) women; age Me49[34;60]years. NMD-9 myasthenia gravis patients and 7 motor neuron disease patients without signs respiratory failure. Research was carried on the HD11XE(Philips) device using sensors of linear and convexy formats with a frequency 5-12 and 2-5MHz along the midclavicular line symmetrically from 2sides in the patient's supine position.

Results: In NMD the diaphragm dysfunction was detected. Decrease of the diaphragm movement amplitude during quiet breathing in NMD was revealed: on the right NMD/control Me0.86 [0.75;1.14]cm/1.24 [1.03;1.58]cm (U, p=0.011), on the left Me0.985 [0.685;1.26]cm/1.225 [1.08;1.82]cm (U, p=0.017). The decrease of the diaphragm movement amplitude during deep breathing in NMD: on the right Me3.305 [1.91;5.04]cm/4.885 [3.98;6.37]cm (U, p=0.015), on the left Me3.82 [2.995;4.635]cm/4.69 [4.11;5.81]cm (U, p=0.011). When studying the thickness of the diaphragm during quiet breathing and the thickening ratio difference was not found: U, p=0.772 and U, p=0.088 accordingly.

Conclusion: Statistically significant decrease in the diaphragm movement amplitude during quiet and deep breathing was revealed in the main group while ultrasound, that indicates significant diaphragm dysfunction in NMD

Disclosure: Nothing to disclose

EPO1279

Nocturnal sleep in myasthenia gravis (MG) patients

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Background and aims: Sleep related disorders are more common among MG patients than in general population that leads not only to a decrease in the quality of sleep and life, but also worsen the course of the disease. Identification of these violations allows planning the care for MG patients. Aim. To examine the features of nocturnal sleep in MG patients using polysomnography (PSG).

Methods: PSG was performed on 56 subjects (35 MG patients - the main group, 21 healthy volunteers - the control group). MG: 8 patients with ocular form, 27 with generalized (12 with bulbar dysfunction, 15 without it). The groups corresponded by gender (χ^2 , p=0.120), age—Me57[44;66] years/43 [41;57] years (U, p=0.051), BMI—Me26.2 [23;29.7]/24.2 [22.9;27.1] (U, p=0.156). Research was carried on the SOMNOlabV2.19 system (Weinmann, Germany).

Results: We revealed specific features of nocturnal sleep in MG. Reducing the total cycle time at MG: MG/control Me0.18[0.15;0.21]h/ 0.22[0.18;0.24]h (U, p=0.035). Reduced sleep efficiency at MG: Me83.1 [73.8; 88.3]%/89.4 [81.7;91.5]% (U, p=0.009). Increased arousals at MG: Me16.9 [11.7;25.7]%/ 10.2 [8.5;18.2]% (U, p=0.009). Reduced REM stage at MG: Me14.5 [9.8;20.8]%/ 19.5 [17.5;24.3]% (U, p=0.011). When studying S1-S4 stages difference was not found (U, p>0.05).

Conclusion: Statistically significant decrease in the total cycle time and sleep efficiency, reduction of the REM, increase of arousals was revealed in the main group. The results indicate fragmentation of sleep, violation of its structure, decrease in the quality of sleep in MG.

Disclosure: Nothing to disclose

Neuroimaging 1

EPO1280

Superficial siderosis of central nervous system associated with parkinsonism: a case report

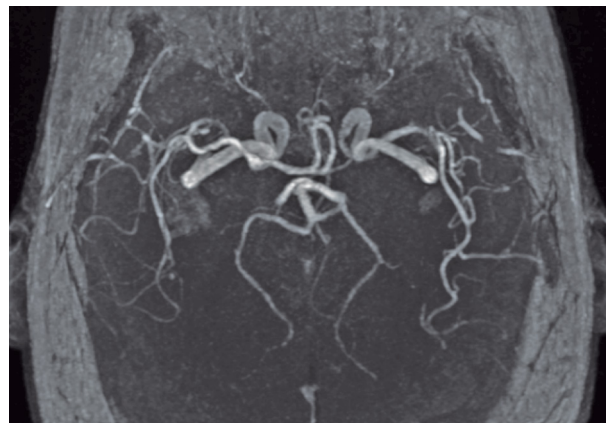
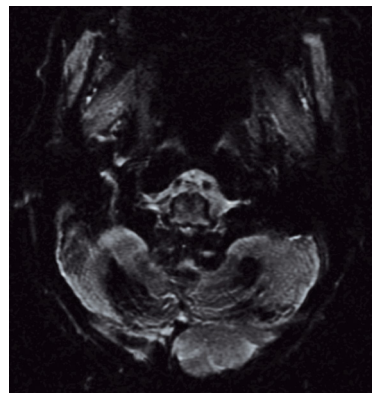
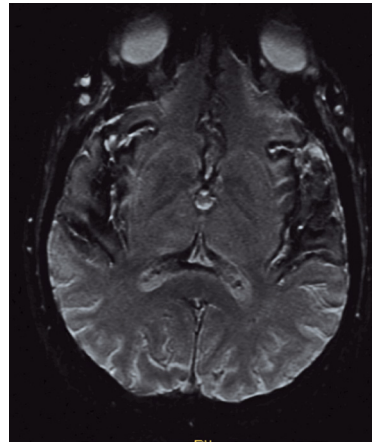
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Background and aims: Superficial siderosis of central nervous system (SS-CNS) is a rare disease that results from toxic accumulation of hemosiderin on the surface of the brain and spinal cord. The most common causes of SS-CNS are aneurysm, trauma, tumor, and arteriovenous malformation. Although in most cases, there is no obvious source of bleeding. We present an atypical case of SS-CNS associated to parkinsonism.

Methods: A 79-year-old woman with a 5-year history of hypothyroidism, cognitive impairment and progressive hypoacusia. On the physical examination she presented a cephalic horizontal tremor, oromandibular dyskinesia, rigidity and bradykinesia in both upper and lower limbs, mild axial rigidity. She began treatment with levodopa/carbidopa with partial response. The patient died 3 months later due to sepsis.

Results: Brain MRI showed hypointense images in gradient-echo sequence in subarachnoid spaces, predominantly localized on both temporal lobes, affecting the emergency of both VIII cranial nerves, cerebellar vermis and cerebellar folia. The appearance of the substantia nigra was normal. Intracranial MRI angiography showed no significant findings. Spinal cord MRI showed hemosiderin deposits, predominantly on cervical segments. There were no signs of hepatic or cardiac iron deposits.



Conclusion: SS-CNS is an infrequent entity. Cognitive deterioration must be suspected in patients with neurosensorial hypoacusia and cerebellar ataxia. We suggest that in our case that SS-CNS with generalized injuries of the central nervous system might be associated with parkinsonism. The patient presented some improvement after dopaminergic therapy. This association has only been shown once in the literature.

Disclosure: Nothing to disclose

EPO1281

The role of magnetic resonance imaging in positive and etiological diagnosis in laminar cortical necrosis

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Background and aims: Laminar cortical necrosis is neuronal ischemia associated with glial reaction. It occurs following cerebral hypoxia. Cerebral magnetic resonance imaging (MRI) is the key examination: establishes the diagnosis, focuses on the etiology and assesses the evolution of the lesions thereafter. The objective of our study is to analyze the clinical profile of our patients, to clarify the role of cerebral MRI in the positive diagnosis and lesional assessment of laminar cortical necrosis and to describe the main etiological forms.

Methods: This is a retrospective study on the medical file of 18 patients, collected in the neurology department of the Mohammed VI CHU of Oujda, during a period from January 2015 to december 2019.

Results: The average age of our patients was 29 years old with a sex ratio (M/F) of 2. The reasons for admission were various, dominated by disorders of consciousness (44%), status epilepticus 33% and neurological deficit 16%. Encephalic MRI allowed positive diagnosis of all patients. Etiological reasoning was based on a bundle of clinical, radiological, biological and evolutionary arguments. MRI data were highly suggestive of etiological diagnosis in 66% of patients. The etiologies were polymorphic, with the predominance of herpetic meningo-encephalitis which accounted for 27% followed by status epilepticus in 22%. Other causes were: hypoglycemia, Gayet Wernicke encephalopathy, toxic origin, hypoxic encephalopathy and ischemic strokes.

Conclusion: Laminar cortical necrosis can complicate any situation of cerebral hypoxia. Their etiological diagnosis remains difficult. The clinical context and the brain MRI are the 2 keys in the diagnostic approach of this pathology.

Disclosure: Nothing to disclose

EPO1282

Cerebral hemosiderosis is a rare cause of cerebellar ataxiaM. Ben Hmidene¹, I. Bedoui¹, M. Messelmani², M. Mansour¹, A. Riahi³, H. Derbali¹, B. Ines¹, J. Zaouali¹, R. Mrissa⁴*¹Neurology department, Military Hospital of Tunis, Tunis, Tunisia, ²Department of neurology, Military Hospital, Tunis, Tunisia, ³Tunis, Tunisia, ⁴Neurology, Military Hospital, Tunis, Tunisia*

Background and aims: Cerebral hemosiderosis is a rare cause of cerebellar ataxia. We report a case of CH presenting with instability.

Methods: cas report of cerebellar ataxia secondary to Cerebral hemosiderosis i

Results: A 53-year-old male, with a past history of subarachnoid hemorrhage presented rapidly progressive hearing and vision loss for 2 years, who was admitted with gait disturbances progressing over the previous 15 months. Neurological examination showed cerebellar and ataxia associated with deafness and reduced visual acuity. Cerebral MRI revealed T2* hyposignal edging extending to the surface of the brain stem, cerebellar and cerebral parenchyma in relation to hemosiderin deposits. The patient was undergone fer chelator and intravenous corticosteroids, stability was obtained.

Conclusion: Cerebral hemosiderosis should be considered in patient with Cerebellar ataxia specially if there is a past history of subarachnoid hemorrhage

Disclosure: Nothing to disclose

EPO1283

3-D High Resolutional MR-Protocol in pharmacoresistant epilepsy patients.

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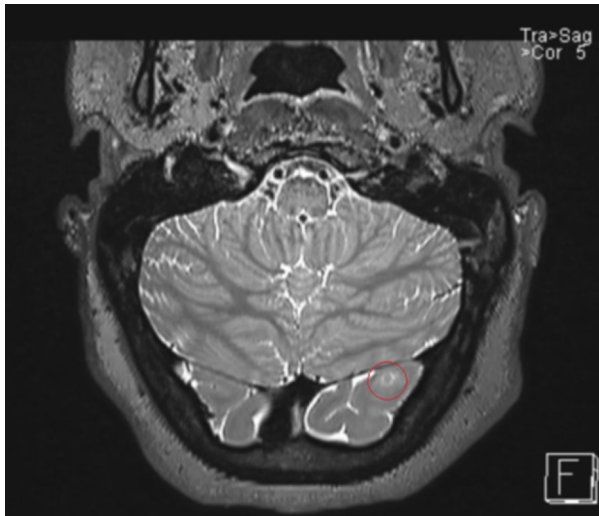
Background and aims: According to the recommendations of ILAE, MRI is obligate in most of epilepsy patients. For more detailed imaging, high-resolution MR sequences have been developed, but even using the recommended dedicated protocols (ex. HARNESS-MRI) comprehensive assessment of brain changes can be challenging due to the loss of the quality when multiplanar reconstructions used. Loss of the quality of examination during movement of the patient is another reason.

Aim: To show the advantages of high-resolution 3D MR-protocol in patients with pharmacoresistant epilepsy using general anesthesia.

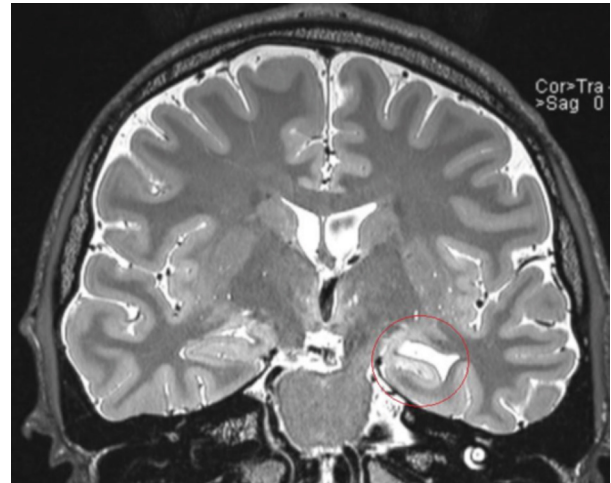
Methods: All patients have been examined using 3T MR scanner (Siemens Magnetom Skyra) with T2 3D sequence (isotropic voxel 0.6x0.6x0.6mm), T1 3D sequence (0.8x0.8x0.8mm), T2 Flair (1.0x1.0x1.0mm). Additional 2D/3D sequences (PD, SWI, T1-IR, ASL) were made.

All examinations were performed using general anesthesia.

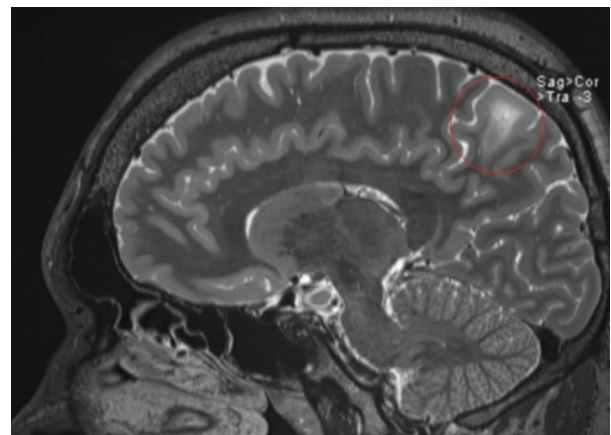
Results: Total number of 235 patients were included in the study. FCDs were detected in 28% (66 patients), heterotopy of the grey matter in 6% (14), mesial temporal sclerosis in 29% (68). DNET and other tumors 8% (19). Posttraumatic or postischemic changes - 25% (59), encephalocele - 4% (9).



T2 WI. Ganglioglioma (axial plane reconstruction)



T2-WI. Mesial Temporal Sclerosis (coronal plane reconstruction)



T2-WI. DNET (sagittal plane reconstruction)

Conclusion: Detection rate of epileptogenic foci using high-resolution 3D sequences increased in comparison with 2D MR-protocol. Analysis of highly detailed images and possibility of multiplanar reconstructions allows to determine the possible cause of epilepsy in a more precise way. Use of general anesthesia almost completely excludes motion artifacts, as well as virtually eliminates the development of an epileptic seizure during the examination.

Disclosure: Nothing to disclose

EPO1284

Idiopathic ventral spinal cord herniation: a cause of invisible myelopathy on magnetic resonance

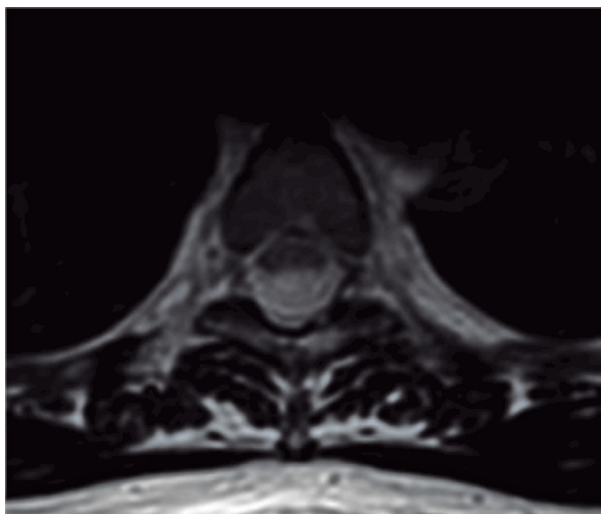
A. Celdrán de Castro García¹, F. Rodríguez Jorge¹, J. Gómez Corral¹, R. Sainz Amo¹, B. Baena Álvarez¹, N. García Barragán², F.J. Buisan Catevilla¹

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Background and aims: Idiopathic spinal cord herniation (ISCH) is an exceptional entity, possibly related with embryonic development and potential cause of myelopathy. In the literature there are barely 200 cases described. Brown-Sequard Syndrome or progressive paraparesis with or without sphincter dysfunction, are the main presentations. It seems to constantly affect thoracic segments between D4 and D8. There is a preponderance of female sex, with an average duration of symptoms up to diagnosis from 2 months to years.

Methods: Case study

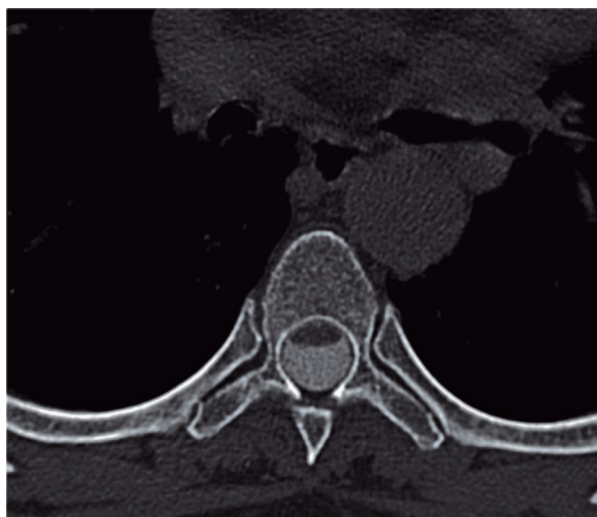
Results: 67-year-old woman with a history of goiter and urinary incontinence, goes to neurology consultation due 6 month duration left submammary pain, without other symptoms (including zoster clinic). The examination highlighted a left hemihypoesthesia with a D4-D5 sensory level and generalized hyperreflexia. A thoracic MRI showed an anterior displacement of the spinal cord at the level of D4-D5. To perform the differential diagnosis between posterior arachnoid cyst or an anterior dural defect, a myeloTC was performed, confirming the 2nd option and establishing the diagnosis of ISCH. Conservative management was decided in consensus with Neurosurgery.



Initial magnetic resonance



ISCH in sagittal section



ISCH in axial section

Conclusion: Although uncommon, ISCH is an entity to consider in the differential diagnosis of myelopathy. Its diagnostic difficulty by MRI makes necessary to perform myeloTC when the index of suspicion is high. Our case was atypical because of the indolent clinical presentation. Concerning treatment, it is not established, there is a potential risk of spinal injury despite the apparent benignity.
Disclosure: Nothing to disclose

EPO1285

High value (2000s/mm²) DWI MRI findings in TGA: a prospective study

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Background and aims: Transient global amnesia (TGA) is a clinical syndrome characterized by the sudden onset of anterograde amnesia, lasting up to 24 hours, without compromise of other neurologic functions. Vascular, epileptic and migrainous events have been proposed as responsible pathophysiologic mechanisms. Early brain MRI (48-72h from onset) may reveal focal diffusion-weighted imaging (DWI) hippocampal hyperintensities, which may be reversible.

Methods: To assess the efficacy of high value DWI MRI in the early phase of TGA, and compare these findings with follow-up brain imaging.

Results: 15 patients were included (male/females:4/11). The mean age was 65 years [SD±4.4]. Diagnostic work-up included brain MRI, EEG, clinical and neurocognitive examination. Mean time from TGA onset to MRI was 3 days [SD±2.5]. A follow-up MRI was conducted 34 days after baseline MRI[IQR:28,55]. High value DWI MRI was normal in 2 patients, and in 2 revealed hippocampal sulcus remnant cysts. Bilateral high 2000-DWI hyperintense hippocampal lesions were noted in 2 patients. A unilateral left hippocampal lesion was depicted in 5, and a right in 4. 1000-DWI MRI revealed hyperintense hippocampal lesions only in 4/13 patients, while in 1/4 additional lesions were revealed in the 2000-DWI MRI. In all cases, the follow-up 2000-DWI MRI revealed no findings. No follow-up brain imaging was conducted in the patients where hippocampal remnant cysts were found.

Conclusion: The majority of our patients revealed high signal lesions in high value DWI MRI conducted in the early phase of TGA, which disappeared in the follow-up neuroimaging. Our study further supports the theory of transient vascular disturbance.

Disclosure: Nothing to disclose

EPO1286

Imaging the human brain at the nanoscale level with STochastic Optical Reconstruction Microscopy (STORM)

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Background and aims: For many years, the diffraction barrier (~250nm) remained a resolution limit for conventional light microscopes, hindering the precise characterization of subcellular brain structures. Recently, a microscopy technique named STochastic Optical Reconstruction Microscopy (STORM) overcame this limit, increasing resolution towards the nanometre scale (~20-50nm). However, to date, STORM has mainly been used to image cultured cells, while no experiment on human cortex has been performed so far. In this work, we combined super resolution microscopy and neuropathological techniques to perform STORM on human brain samples from control subjects and patients with neurodegenerative disorders.

Methods: Cryopreserved post-mortem brain samples were immunostained and placed on the stage of an inverted microscope Eclipse Ti-E (Nikon Instruments) equipped with a CFI SR APO TIRF 100X ON1.49 objective, a total internal reflection fluorescence ILas2 module (Roper Scientific) and a single-photon sensitive Evolve 128TM EMCCD camera (Photometrics). Acquisition of images were proceeded using Metamorph 7.7 software (Molecular Devices). More than 300 STORM images have been acquired and analysed.

Results: Physiological brain structures such as axons, myelin sheaths and synapses were imaged in control samples with a nanometre-scale precision. Aβ, Tau, α-synuclein and TDP-43 pathological aggregates were also imaged with unprecedented details in brain sections from patients affected with neurodegenerative disorders.

Conclusion: These very 1st super-resolution STORM images of physiological and pathological brain structures open further gates to a more comprehensive understanding of the human brain organization and revelations about the underlying mechanisms responsible for common neurological diseases.

Disclosure: This work was supported by the University Hospital of Angers (Grant N° 2019-264 900_036), the French National Institute for Health and Medical Research (INSERM Research Fellow 2017–2019), and the European Regional Development Fund (ERDF).

EPO1287

Dopamine transporter imaging in corticobasal syndrome patients with or without underlying Alzheimer's disease pathology.

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Background and aims: Corticobasal syndrome (CBS) is characterized by primarily asymmetrical parkinsonism, myoclonus, dystonia, apraxia and alien limb phenomena. Alzheimer's disease (AD) can underlie CBS. The aim of this study was to investigate dopamine transporter imaging status in CBS patients with or without AD underlying pathology (CBS-AD vs. CBS-non-AD).

Methods: All patients included were examined at our Clinic from 2011 to 2019. All patients fulfilled clinical diagnostic criteria for possible or probable CBS. Dopamine transporter imaging (DaT-scan) and classical CSF biomarker data were available in all patients. CSF beta-amyloid (A β 42), total tau (τ T) and phosphorylated tau at threonine 181 (τ P-181) were used to establish an in vivo AD diagnosis. All CSF analyses were performed by commercially available enzyme-linked immunosorbent assay kits (ELISAs). Patients were characterized as CBS-AD according to the AT(N) classification system. DaT-scans were characterized as normal or abnormal according to qualitative image analysis and semi-quantitative binding specific indices (BSIs) of basal ganglia.

Results: A total of 18 CBS patients had CSF-biomarker and DaT-scan data available. 7 patients (39%) had a CSF-AD profile and 11 patients (61%) had a CSF-non-AD profile. 5 of the 11 CBS-non-AD patients (45.5%) had a normal DaT-scan. 1 of the 7 CBS-AD patients (14.3%) had an abnormal DaT-scan.

Conclusion: Pathological dopamine transporter imaging is indicative of non-AD pathology in CBS patients. A pathological DaT-scan was highly specific (86%) but lacked sensitivity (55%) for a non-AD diagnosis in CBS.

Disclosure: Nothing to disclose

EPO1288

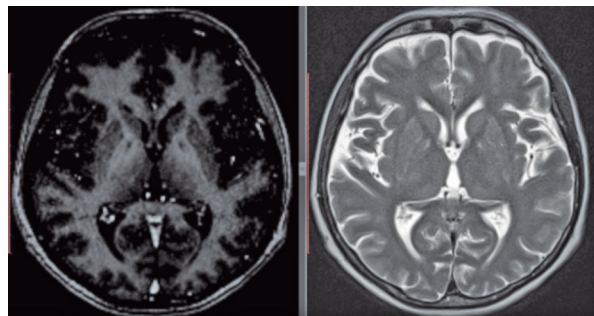
T1 reverse eye-of-the-tiger in chronic acquired hepatocerebral degeneration

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Background and aims: Chronic acquired hepatocerebral degeneration (CHAD) is a rare complication of liver cirrhosis responsible for a complex movement disorder with particular MRI lesions.

Methods: A 59-year-old female with a history of cirrhosis secondary to chronic hepatitis B and C and multiple episodes of hepatic encephalopathy presented to our clinic for upper limb tremor, imbalance and slowness of movements gradually developed in the last year. Clinical examination revealed bilateral symmetrical parkinsonian syndrome, trunk and limb ataxia, action tremor, slight chorea and dystonic posturing of the hands with isolated myoclonic jerks. She also presented striking synkinesis of the contralateral hand and jaw, brisk tendon reflexes and cognitive impairment. Brain MRI revealed increased T1 signal bilaterally in the globus pallidus with central T1-hypointense/T2-hyperintense lesions suggesting central gliosis. There was also marked increase in T2/FLAIR signal of the pyramidal tract in the internal capsule. Workup for Wilson's disease was negative whereas serum manganese levels were highly increased.



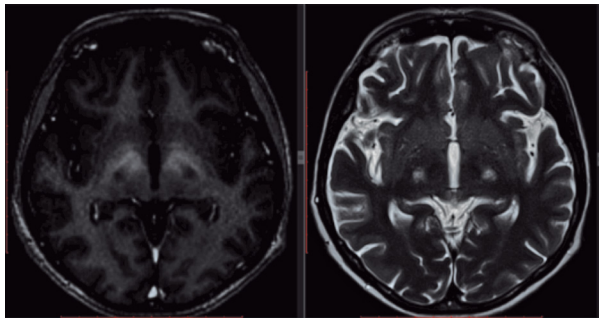
Brain MRI. Left - axial T1W-imaging showing increased signal bilaterally in the globus pallidus with central hypointensity. Right - axial T2W-imaging showing small T2 hyperintensity in the globus pallidus bilaterally.

Brain MRI. Left - axial T1W-imaging showing increased signal in the cerebral peduncles with hypointensity of the pyramidal tracts. Right - axial T2W-imaging showing increased signal of the pyramidal tracts.

Results: The complex clinical picture in the presence of cirrhosis with T1-hyperintensity of the globus pallidus and high serum manganese indicate CHAD. T1-hyperintensity of the globus pallidus is highly characteristic for CHAD, but MRI lesions suggestive of central gliosis have not been reported. This particular feature is similar to the eye-of-the-tiger sign commonly described on T2W-imaging in neurodegeneration with brain iron accumulation, but in this case the sign is seen on T1W-imaging with a reversed signal intensity.

Conclusion: We describe lesions of the basal ganglia in a patient with CHAD with a particular MRI pattern of a T1 reverse eye-of-the-tiger.

Disclosure: Nothing to disclose



EPO1289

Carotid Distensibility evaluation on a cohort of hypertensive patients.

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Background and aims: Cerebrovascular risk factors are associated with progressive stiffness and reduction of arterial wall distensibility in the pre-symptomatic phase. These can be noninvasively assessed through carotid ultrasound. We evaluated the intima-media thickness (IMT) and distensibility indexes, namely Carotid Arterial Strain (CAS), Arterial Compliance (AC), arterial distensibility (AD), Stiffness Index (SI), Pressure-strain modulus (PSM) and Young Elastic Modulus (YEM), in a cohort of chronic hypertensive patients.

Methods: Supine B-mode carotid ultrasound IMT was recorded in the right common carotid artery, according to Mannheim criteria. Videos of the same arterial section were obtained for at least 5 complete cardiac cycles. Supine blood pressure was measured. We analysed the correlation between distensibility, IMT and clinical-demographic variables.

Results: We evaluated 46 patients, aged 63±11 years old. IMT did not significantly correlate with distensibility indexes except the SI (Rho Spearman (rs)=0.341, p=0.020), but showed a positive correlation with age (rs=0.425, p=0.003). On the other hand, most distensibility parameters (AC, YEM and PSM) did not correlate with age but rather with systolic blood pressure (AC: rs=-0.435, p=0.003; YEM: rs=0.373, p=0.011; PSM: rs=0.412, p=0.004). AD, in turn, correlated with both systolic blood pressure (rs=-0.338, p=0.021) and age (rs=-0.453, p=0.002).

Conclusion: IMT is significantly influenced by age. However, distensibility indexes appear to correlate with systolic blood pressure, regardless of normal vascular aging. Distensibility parameters obtained by carotid ultrasound seem promising for studying different pathophysiological aspects of early vascular disease.

Disclosure: Nothing to disclose

EPO1290

Peak width of skeletonized mean diffusivity (PSMD) is linked to cognition in relapsing-remitting MS

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Background and aims: Peak width of skeletonized mean diffusivity (PSMD) is a novel MRI biomarker of altered white matter (WM) microstructure, which has showed in cerebral small vessels diseases a significant association with reduced information processing speed.

We aimed here to investigate, in a group of relapsing-remitting multiple sclerosis (RR MS) patients, the relationship between PSMD and cognitive performances, in comparison with other MRI measures

Methods: RR MS patients (n=60, age: 42.5±10 years, 76.7% female, median EDSS: 1 [range 1-3], cognitive impairment in 36.7%) and age-matched normal controls (NC, n=15, age: 42±10 years, 46.7% female) underwent a 3T MRI examination. WM lesion volume and brain volumes (brain, grey matter [GM] and WM) were computed. PSMD was obtained through "skeletonization" of WM tracts and diffusion histograms. Cognition was assessed in MS with Rao's Brief Repeatable Battery (BRB).

Results: As expected, all MRI measures of MS were different from NC (p<0.001), including PSMD (4.2±1.3 in MS vs 2.9±0.6 x 10⁻⁴ mm²/s in NC, p<0.001). In RRMS, in general MRI measures variably correlated with BRB cognitive tests, with the closest correlation found between higher PSMD and lower symbol digit modalities test (SDMT, r=-0.70, p<0.001). On multiple regression analysis, PSMD contributed to the SDMT variance more than other MRI measures (R²= 0.54, p<0.001).

Conclusion: In RR MS, PSMD explained the SDMT performance better than other MRI measures, confirming the great relevance of this novel MRI biomarker in predicting information processing speed dysfunction in MS.

Disclosure: Nothing to disclose

EPO1291

Patients' understanding of incidental findings and brain magnetic resonance imaging: a mixed-methods study involving people with cognitive symptoms

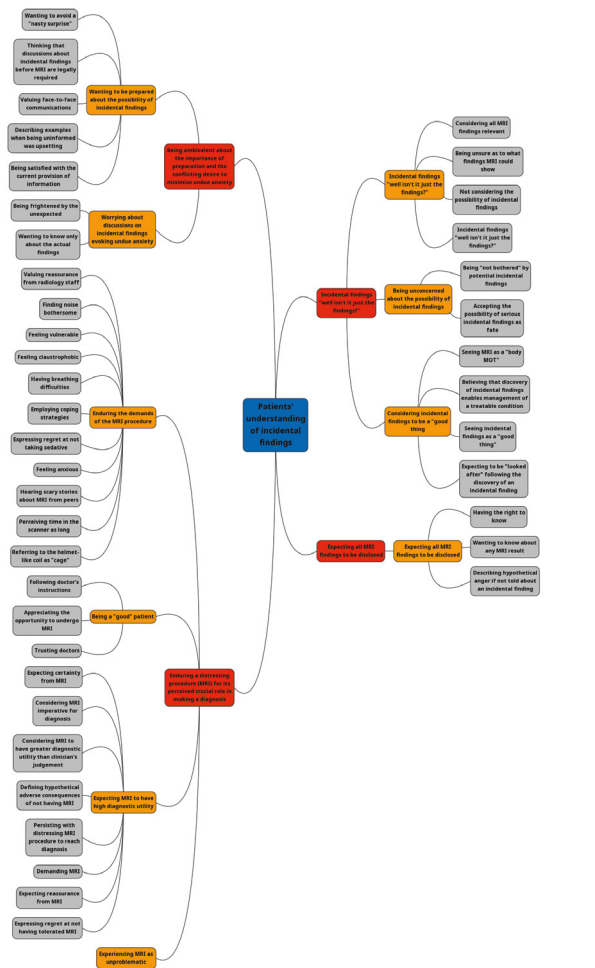
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Background and aims: Incidental findings are common in neuroimaging for investigation of cognitive symptoms, particularly brain magnetic resonance imaging (MRI). Understanding of incidental findings among people with cognitive symptoms has not been explored in the literature. Our objective was to examine patients' understanding of incidental findings and the role of brain MRI in diagnosing a cognitive disorder, their preferences regarding the disclosure of incidental findings and their views regarding discussions on the risk of incidental findings prior to imaging.

Methods: We conducted in-depth semi-structured interviews with purposefully selected patients attending a cognitive disorders clinic. Questionnaires comprising Likert-style and multiple-choice questions were also administered. Patients with a significant incidental finding were excluded. Analysis was based on constructivist grounded theory.

Results: 15 patients were interviewed of whom 7 had a diagnosis of dementia. 7 participants were awaiting brain MRI and 8 had undergone brain MRI prior to interview. 4 theoretical codes emerged from the analysis: incidental findings "well isn't it just the findings", being ambivalent about the importance of preparation and the conflicting desire to minimise undue anxiety, expecting all MRI findings to be disclosed, and enduring a distressing procedure (MRI) for its perceived crucial role in making a diagnosis.



Mindmap of coding structures. Theoretical codes are coloured in red, focussed codes in yellow and initial codes in grey.

Question	Question type and scoring	Result
How well informed did you feel about the process of undergoing a brain scan before your scan?	Like7: 1-10 where 10 indicates "very well informed"	Median: 9 (IQR 7-9)
How important do you feel a brain scan is in securing a diagnosis?	Like7: 1-10 where 10 indicates "very important"	Median: 10 (IQR 9-10)
How should future patients attending the clinic be informed about brain scans and incidental findings?	Multiple choice: (Participants can choose more than one option) Discussion with healthcare staff Information leaflet Information video Interactive website Smartphone app Other (please state)	Discussion (n=12) Information leaflet (n=8) Information video (n=3) Interactive website (n=1) Smartphone app (n=1)
How would you rate the amount of detail you received about incidental findings during the consultation? ¹⁾	Multiple choice: Just right Not enough detail Too much detail	Just right (n=7) Not enough detail (n=0) Too much detail (n=0)
Your brain scan did not identify an incidental finding - this is a hypothetical question: If your brain scan had identified an incidental finding, would you have wanted this information disclosed to you? A) A harmless incidental finding that does not require follow-up or treatment B) An incidental finding that is unlikely to cause problems but for which regular clinic appointments for observation are recommended C) An incidental finding that could have an impact on life expectancy and/or quality of life but is treatable D) An incidental finding that has an impact on life expectancy and/or quality of life but that is NOT treatable.	Multiple choice: I would want to know I am not sure if I would want to know I would NOT want to know	A-D: I would want to know (n=6) I am not sure if I would want to know (n=0) I would NOT want to know (n=0)

Table 2. IQR: interquartile range. 1) Only participants with whom the risk of incidental findings was discussed during the consultation were asked this question (n=7). 2) Only participants who had successfully undergone brain MRI were asked this question (n=7), one participant did not complete the questionnaire but participated in the interview.

Table 1. Participants' answers to quantitative questions.

Conclusion: It is helpful to define the term incidental finding and to outline the role of brain MRI alongside clinical history and cognitive testing. Our findings could facilitate discussions between clinicians and patients with cognitive symptoms regarding the risk of incidental findings and the role of brain MRI in diagnosing a cognitive disorder.

Disclosure: Nothing to disclose

EPO1292

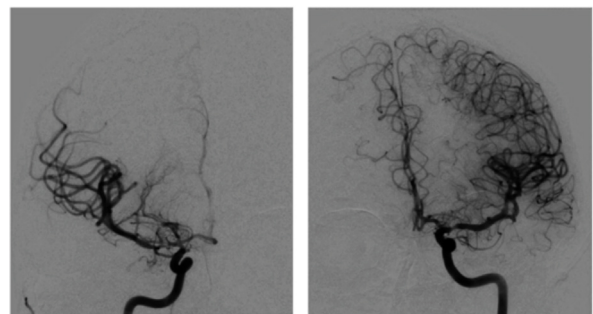
Transient ischemic attack in a 29-year-old male might be a smoke ball

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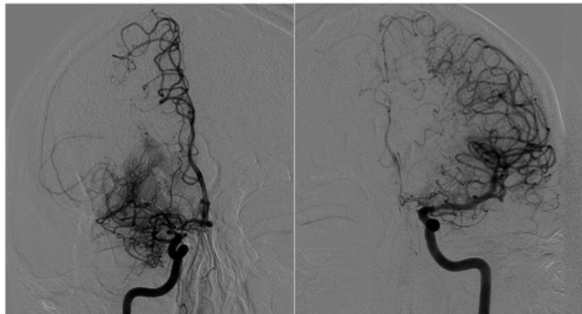
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Background and aims: Moyamoya disease (MMD) is a chronic progressive cerebrovascular disease characterized by bilateral stenosis with prominent arterial collateral circulation. It can cause ischemic and hemorrhagic strokes. **Methods:** 29-year-old male patient with DM and consumer of THC. This patient had an abrupt and self-limited episode of loss of strength in the upper right limb with further disorientation and confusion. A CT scan was performed in which multiple lesions were observed in the right MCA territory.

Results: MRI multiple hyperintense lesions in cortical and subcortical T2 made us think as differential diagnosis ischemic vs demyelinating. Cerebrospinal fluid analysis: growth of Streptococcus alactolyticus in bacterial culture. In CT brain angiography, a decretase in size of the M1 segment of right MCA and ACA was observed. We performed an arteriography that informed us of stenotic-occlusive non-atheromatous vasculopathy in intracranial segments of both ICA compatible with MMD. After a year of this dx we made a new arteriography and see a progression in intracranial stenosis and now we are arguing different options with neurosurgery for this young man.



Significant stenosis of both intracranial ICA: segment M1 and A1 of the right side and a very significant slowdown of hemispheric filling. Moderate stenosis of the origin of the M1 segment of the left MCA. Significant stenosis of the origin of segment A1 of the left ACA on which the filling of both ACAs depends.



Progression of the terminal RICA stenosis, showing occlusion of the M1 with the formation of a Moya-Moya arteriolar-arteriolar type. Progression of the stenosis at the origin of the left A1 that presents a filiform flow and compensation from a Moya-Moya arteriolar-arteriolar network from lenticulostriates arteries of the left MCA.

Conclusion: This case leads us to make a broad differential diagnosis of TIA. We must take into account diseases such as vasculitis and MMD of the CNS when we see ischemic lesions in a young patient. In a review of the literature, articles with MMD secondary to pneumococcal meningitis have been found, so we cannot be sure if the *Streptococcus* found in the CSF culture has a triggering role in our case. However, MMD treatment is unfortunate in most cases.

Disclosure: Nothing to disclose

EPO1293

Volumetric study of subcortical structures in motor neuron disease and dystonia

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Background and aims: Recent studies indicate a widespread involvement of different CNS structures in MND and dystonia. In our previous works on volumetric studies, we have found that in dystonia the volumes of right thalamus and right cerebellar cortex were significantly lower compared to controls; in MND we demonstrated decrease in the volume of thalami.

Aim: to study volumes of subcortical structures in patients with MND and dystonia.

Methods: We studied volume of subcortical structures in a group of 29 MND patients, 55[51;64] years old (Me [25%; 75%]), 2 with PLS, 8 with bulbar onset ALS, 19 with spinal onset ALS; in 32 dystonia patients, 54[46;60.25] years old; and in 76 control subjects without focal MRI lesions or neurological signs, 44[32;57.25] years old. Structural MRI was acquired using isotropic T1 sequence, and segmented using FreeSurfer software. We measured and analyzed volumes of cerebellar white matter and cortex, thalami, caudate nuclei, putamina, globi pallidi, brain stem.

Results: We revealed significant difference between the groups for volumes of thalami (U, $p < 0.001$), volumes being less in the MND and dystonia groups, and for the brain stem in dystonia (U, $p = 0.004$), volume being less in dystonia.

Structure	Control, mm ³	MND, mm ³	p-value	Dystonia, mm ³	p-value
Left thalamus	7632.9[6992.2; 8326.5]	6994.6[6571.3; 7356.0]	0.00014	6754.0[6380.5; 7391.0]	0.00009
Right thalamus	7332.7[6729.6; 8079.7]	6746.0[6380.1; 7048.6]	0.00011	6542.7[6064.0; 7089.0]	0.00006
Brainstem	21296.1[19591.8; 22446.8]	20812.1[17850.4; 22805.5]	0.13879	19286.4[18118.0; 21104.6]	0.00448

Volumes of thalamus and brainstem in MND, dystonia, and control group; respective Mann-Whitney (1-tailed) p-values when comparing MND and dystonia groups to control.

Conclusion: Results of this research confirm our previous results on the involvement of the thalamus in MND. In dystonia, we confirm decrease in thalamic volume, but with more subjects we can not confirm decrease in cerebellar cortex volume. Volume of brain stem in dystonia is, probably, decreased, but this result needs further investigation.

Disclosure: Nothing to disclose

EPO1294

The importance of MRI tractography in the examination of adult patients with cerebral palsy

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Background and aims: The aim of the study is to determine the peculiarities of microstructural changes in the white matter pathways of the brain in adult patients with cerebral palsy using diffusion tensor magnetic resonance imaging (DT-MRI) and tractography and to make a comparison between the clinical picture and the MRI examination data.

Methods: 50 adult patients with cerebral palsy were examined. All the patients underwent magnetic resonance imaging of the brain (structural, diffuse tensor with tractography). Functional anisotropy and average diffusion coefficient (FA and ADC) were obtained in the symmetric regions of the cerebral hemispheres.

Results: There was a slight decrease in functional anisotropy and an increase in the average diffusion coefficient along the corticospinal tract on the side opposite to the paresis in patients with spastic hemiparesis. FA was found to reduce in the cerebral cortex along the corticospinal tract and in thalamus along the spinothalamic tract. ADC was the highest in thalamus throughout the sensory tracts. FA and ADC of the spinothalamic pathways had a correlation with the level of GMFCS. Throughout the sensory pathways ADC and FA were higher in cerebral palsy patients with pain syndrome compared to cerebral palsy patients without pain syndrome.

Conclusion: These microstructural changes determined clinical manifestations in cerebral palsy and could be used in the dynamic observation of patients and determining the level of functioning. The level of functioning will allow to classify cerebral palsy patients, prescribe a rehabilitation complex according to their condition, which is important for both clinical practice and science.

Disclosure: Nothing to disclose

EPO1295

Clinical and radiological characteristics of reversible splenial lesion syndromeS. Lee¹, S.-Y. Bae²*¹Daegu, Korea, Republic of, ²Neurology, Daegu Fatima Hospital, Daegu, Korea, Republic of*

Background and aims: Reversible splenial lesion syndrome (RELES) is a reversible syndrome involving the splenium of the corpus callosum (SCC) and subcortical white matter. Etiology of RELES is diverse, including infectious disease, seizures, antiepileptic drug (AED) withdrawal, high altitude cerebral edema (HACE), or metabolic disturbances. We describe etiology, clinical and radiological characteristics of RELES.

Methods: We retrospectively analyzed brain MRI and medical records of patients diagnosed as RELES from February, 2010, through December, 2018.

Results: 10 patients were consisted of 7 male and 3 female, and their age ranged from 10 to 82 years (mean age, 37.5 years). 4 patients presented with fever and headache (2) or mental change (2), 2 patients with seizure, and cheek pain (1), headache (1), dizziness (1) and leg weakness (1). RELES was caused by various etiologies, such as viral encephalitis (3), AED (2), HACE (1), sepsis (1) and unknown (3). MRI showed small, round or ovoid cytotoxic edema at central area of SCC with bilateral symmetric shape without gadolinium enhancement in all patients. All 5 follow-up MRI showed complete resolution of the splenial lesions. 8 patients had good clinical outcome and fair in 1 case. 1 patient died of underlying sepsis.

Conclusion: Infectious disease such as viral encephalitis and sepsis and AED were common cause of RESLES. Characteristic MRI finding is diffusion restriction without abnormal enhancement at the central area of SCC, which were completely reversible. Most patients had good clinical outcome. Therefore, RESLES is a benign condition clinically and radiologically.

Disclosure: Nothing to disclose

EPO1296

Spinal haemangiomas imaging

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Background and aims: Vertebral haemangiomas (VH) are often found on imaging in patients with back pain or neurological symptoms. VHs impair vertebra strength and in 8% of cases lead to pathologic fractures worsening the severity of clinical presentations. Surgical indications are disputable, particularly those for asymptomatic VHs with radiologic aggressive signs.

Methods: Software Spine-1 for calculation of support ability in VH affected vertebrae has been developed. It uses CT-obtained geometric parameters of both the affected vertebra and VH to calculate its cavity space ratio to vertebra dimensions. Support ability disorder index results from multiplying the patient's height, age and vertebra number by previously calculated cavity space to vertebra ratio as well as the coefficient defined by the patient's sex. The examination results of 86 patients have been analyzed.

Results: The results show that in 31 patients (36.1%) VHs do not impair their vertebra strength. In 28 patients (32.5%) the support ability decreased by 30% and in 27 patients (31.4%) by 50% or more. It has been established that in patients with strength properties decreased for 30% or more, and in more than 58% of cases they suffered from persistent moderate pain syndrome (VAS 6±2), and in 5 patients (6%) with strength decreased by 30% no pain syndrome was reported (VAS 0).

Conclusion: VHs reduce vertebra support ability and are unfavorable predictive factors of clinical presentations development including neurological symptoms. The decrease in vertebrae strength for 30% and more may be an indication for vertebroplasty even with asymptomatic aggressive VHs.

Disclosure: Nothing to disclose

Neuroimmunology 1

EPO1297

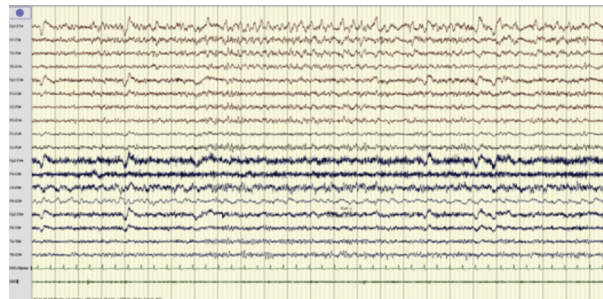
Refractory Morvan Syndrome Responding Dramatically to Rituximab

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Background and aims: Morvan syndrome is a rare autoimmune disorder characterized by peripheral nerve hyperexcitability, dysautonomia and encephalopathy. No clear treatment guidelines are available.

Methods: N/A

Results: The patient is a 44-year-old man with a history of seropositive myasthenia gravis and recurrent thymoma, status-post thymectomy and chemotherapy, who presented with acute-onset amnesia that followed a progressive course of fatigue associated with diffuse muscle cramps and twitching that limited his ability to ambulate. He also complained of profuse sweating and severe insomnia. His physical examination revealed tachycardia and diffuse fasciculations. Brain MRI was unremarkable. Cerebrospinal fluid analysis showed an elevated protein level. Electromyography revealed evidence of spontaneous activity in the form of neuromyotonic discharges and complex repetitive discharges. During a long-term video/EEG study, nine subclinical seizures of left temporal origin were recorded. Antibody screening revealed high serum and CSF titers of Caspr2 and LGI1 antibodies. The electrographic seizures were controlled with lacosamide. The diffuse fasciculations associated with severe pain required treatment with morphine, gabapentin and duloxetine and failed to respond to intravenous pulse steroid and to 2 courses of IVIG. Following administration of the 1st dose of rituximab, there was a dramatic improvement in the painful fasciculations with near complete resolution of signs and symptoms 2 weeks later, following administration of the 2nd dose. He remained in remission at his last follow-up 4 months later with a gradual taper of the analgesic and antineuralgic medications.



EEG showing ictal activity

Conclusion: Rituximab appears to be a very promising therapy for patients with anti-Caspr2 syndrome who failed to respond to steroids or IVIG.

Disclosure: Nothing to disclose

EPO1298

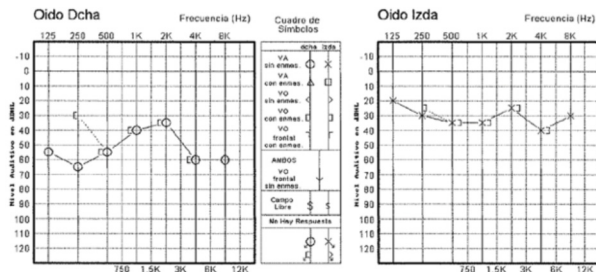
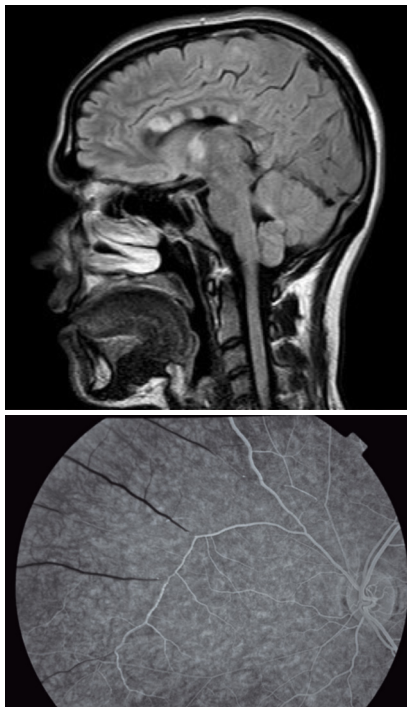
Sex hormones secondary players in Susac's Syndrome

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Background and aims: Susac's Syndrome (SS) is a rare immune-mediated endotheliopathy defined by the clinical triad of encephalopathy, branch retinal artery occlusion and hearing loss. As autoimmunity is generally more common in females, female predominance in SS is in line with the putative autoimmune aetiology. This report presents clinical and paraclinical findings in a female-male transgender contributory to SS diagnosis and offers different perspective on sex hormones contribution to the disease.

Methods: The most important diagnostic procedures involved in diagnosis were brain MRI, audiometric testing and retinal fluorescein angiography.

Results: A previously healthy 22-year-old female-male transgender under treatment with testosterone for 3 years, presented with psychomotor slowing and behavioral changes. He had also been experiencing recurrent episodes of vertigo in the last 2 weeks. On admission, neurological examination showed severe inattention, short-term memory impairment, frontal release signs, gait instability and pyramidal signs. Brain MRI revealed a spectrum of findings previously described in SS: "snowball"-shaped lesions in corpus callosum and the characteristic "string of pearls" lesions in internal capsule. Audiometry showed sensorineural hearing loss in low frequency range. The fluorescein angiography disclosed branch retinal artery occlusion. Based on the association of subacute encephalopathy, branch retinal artery occlusion, hearing loss and typical MRI findings, we diagnosed that the patient had SS and started immunosuppressive therapy.



Conclusion: To the best of our knowledge, this is the first case of SS described in a female-male transgender and it may illustrate that sex hormones could be only secondary players in a process triggered by genetic predisposition, stochastic immune responses and environment.

Disclosure: Nothing to disclose

EPO1299

Treatment Patterns of a Large US Sample of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Patients

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare, immune-mediated neuropathy, and intravenous immunoglobulin (IVIG) is a 1st-line therapy option. We examined real-world practices with IVIG, including ramp-up, dosing patterns, switching, discontinuation, and add-on therapy. We describe treatment patterns among patients with CIDP initiating IVIG treatment.

Methods: Adults with CIDP without prior immunoglobulin treatment were identified in MarketScan[®] insurance database between 2008-2018. Patients subsequently initiating IVIG were identified. Data on timing and frequency of dosing, switching to other immunoglobulin treatments, discontinuation of the index IVIG and initiation of other CIDP treatments were described.

Results: A total of 32,090 immunoglobulin-naïve patients with CIDP were identified; 3,975 initiated IVIG. Few patients had previous non-immunoglobulin CIDP therapy, except for high-dose corticosteroids (34%). Median number of doses during 14-day ramp-up was 1 (interquartile range [IQR] 1-3). After ramp-up, the median interim between doses was 21 days (IQR 7-28) and median treatment duration 129 days (IQR 85-271). At year 1 of follow up a higher proportion (27%) of patients discontinued the index IVIG compared with those who switched immunoglobulin treatment (6%). Most patients who discontinued did so by the 4th treatment month; 45% of patients initiated another non-IG CIDP treatment after IVIG initiation.

Conclusion: Most patients that initiated IVIG treatment did not have prior CIDP treatment. IVIG is typically administered at an interval of 1 to 4 weeks. Many patients discontinued treatment by the 8th dose; after which less discontinuation happens, which is consistent with rates in the literature.

Disclosure: This work was supported by Takeda Pharmaceuticals.

EPO1300

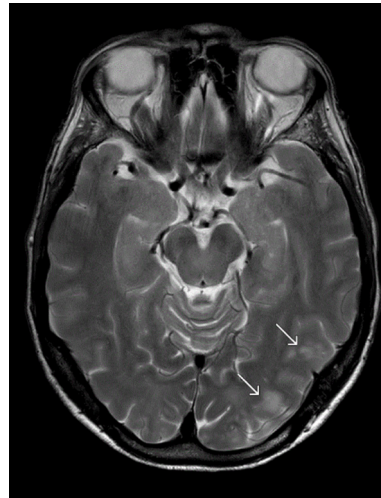
Guillain-Barré syndrome with posterior reversible white matter lesions

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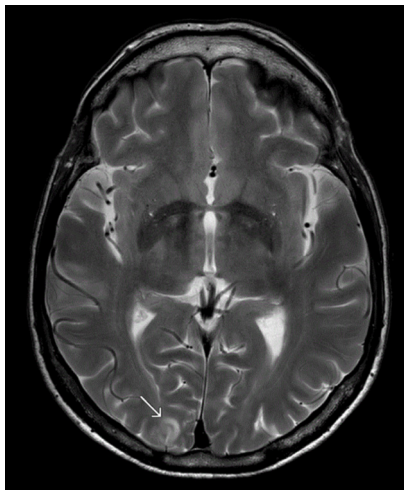
Background and aims: Guillain-Barré syndrome (GBS) is an immunologically mediated acute demyelinating polyneuropathy, usually selectively affecting the peripheral nervous system. Here, we report the case of a 72-year-old woman presenting with a typical Guillain-Barré syndrome, whose brain MRI showed bilateral posterior lesions in cerebral white matter.

Methods: On examination, all deep tendon reflexes were absent, kinesthetic sensitivity was reduced and waking was unsteady. 2 brief nocturnal episodes of confusion and visual alteration were reported to the medical staff. The anti-ganglioside antibody panel was negative. The CSF showed albumin-cytologic dissociation; oligoclonal bands were absent. The neurophysiological studies revealed reduction of motor conduction velocity and prolonged distal latency in both tibial nerves and absent F waves. T2-FLAIR weighted brain MRI demonstrated hyperintense areas involving the juxtacortical white matter in the bilateral parieto-occipital lobes, without diffusion restriction nor contrast enhancement.

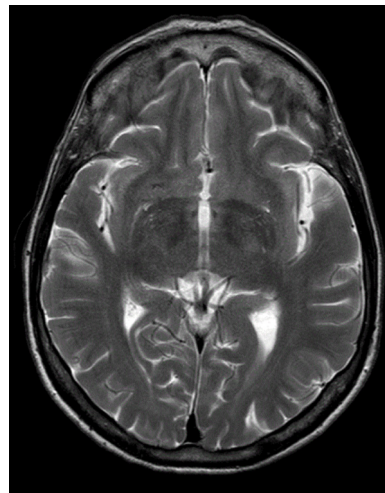


Brain MRI at onset. Axial T2-weighted imaging showing juxtacortical white matter lesions involving the occipito-parietal lobe

Results: The patient was diagnosed as GBS and intravenous immunoglobulin therapy was started. Her symptoms gradually resolved in two weeks. The multiple CNS lesions showed on MRI may be mainly suggestive of demyelination or posterior reversible encephalopathy syndrome (PRES). The juxtacortical localization and the U-shaped morphology of some lesions makes them compatible with an inflammatory-demyelinating origin, despite the lack of contrast enhancement. However, the episodes of confusion and visual alteration together with the radiological characteristics of the lesions and their total disappearance in the follow-up examination would direct towards a diagnosis of PRES.



Brain MRI at onset. Axial T2-weighted imaging showing U-shaped white matter lesions involving the occipito-parietal lobe



Axial T2-weighted imaging of the head demonstrating the complete resolution of the white matter abnormalities three months after symptom onset and IVIg treatment

Conclusion: GBS can be considered as an independent risk factor of PRES, due to dysautonomia as well as to increased capillary permeability caused by cytokine production.

Disclosure: Nothing to disclose

EPO1301

Aquaporin-4-antibody neuromyelitis optica spectrum disorders: three cases of late-onset longitudinally extensive transverse myelitis

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Background and aims: Neuromyelitis optica spectrum disorders (NMOSD) mediated by aquaporin-4-antibody (AQP4-Ab) affect predominantly optic nerve and spinal cord. Only 1/3rd presents after 50 years old, mostly with longitudinally extensive transverse myelitis (LETM): these late-onset NMOSD are frequently underestimated despite severe outcomes.

Methods: Case1: 54-year-old woman with acute weakness and paresthesia at lower limbs. MRI: C1-T12 LETM. Comorbidities: arthritis with serum anti-dsDNA.

Case2: 62-year-old woman with subacute asymmetric tetraparesis, vomiting and urinary retention. MRI: T2-hyperintensity midbrain-T4. Comorbidities: monoclonal gammopathy of undetermined significance.

Case3: 75-year-old woman with progressively worsening weakness at lower limbs. MRI: C6-T6 LETM. Spinal relapse 4 months later. Comorbidities: venous thrombosis with serum anti-dsDNA and antiphospholipid antibodies suggestive for Lupus erythematosus with Antiphospholipid syndrome.

Results: A 5-day course of methylprednisolone with marginal benefit was administered in all cases. Cyclophosphamide was started in case 1 with radiological improvement after 2 months. Plasmapheresis was performed for case 2 with no changes in 1 month (infections delayed other treatments). The case 3 commenced azathioprine after the relapse with radiological stability. All cases had severe motor and sphincteric outcomes.

Conclusion: A late-onset NMOSD with AQP4-Ab should be considered in isolated LETM with onset after 50 years. Autoimmune comorbidities could cause misdiagnosis but a prompt identification of NMOSD is necessary to start early immunosuppressive therapies, sometimes difficult in older cases. Our 3 patients represent typical cases of AQP4-Ab mediated LETM with severe outcome that represented a diagnostic and therapeutic challenge.

In conclusion AQP4-Ab NMOSD must be suspected in isolated LETM over 50 years old.

Disclosure: Nothing to disclose

EPO1302

A challenging case of loss of vision: Susac's Syndrome

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Background and aims: Susac's syndrome is a rare immune-mediated endotheliopathy that is characterised by the triad of encephalopathy, branch retinal artery occlusion, and sensori-neural hearing loss.

Methods: A 35-year-old Caucasian woman presented an abrupt onset of right impaired vision, and arrived to our attention 2 weeks later. She had a miscarriage (and 2 normal pregnancies) several years before. Recently she had mild dizziness. The patient had no known family history of neurological disease. She underwent a fluorescein angiography showing branch retinal artery occlusions and a brain MRI revealing several supra- and infratentorial FLAIR-hyperintense white matter lesions, some with contrast enhancement. Thrombophilic, autoimmune and infective (including HIV, Borrelia burgdorferi, HBV, HCV) screening was negative. CSF analysis showed intrathecal IgG synthesis. We suspected a Primary Central Nervous System Vasculitis, and iv steroids were started. 2 months later a 2nd brain MRI showed new lesions. Moreover she developed some cognitive deficit and bilateral hearing loss confirmed at audiometry. Reviewing the clinical history and MRI, she fulfilled diagnostic criteria for Susac's syndrome. Cyclophosphamide was started and continued for 6 months with clinical improvement.



Corpus callosum 1



Corpus callosum 2

Results: Susac's syndrome is often misdiagnosed. Brain MRI (with multiple hyper-intense small lesions through infratentorial structures), fluorescein angiography (retinopathy with multiple retinal artery occlusions) and audiometry (hearing loss may be asymptomatic) are essential for correct diagnosis.

Conclusion: Only 13% of patients has the characteristic clinical triad at disease onset, and Susac's syndrome must be suspected also in presence of 2 of the pathognomonic features and a targeted search for absent components of the triad is essential.

Disclosure: Nothing to disclose

EPO1303

Anti-glutamic acid decarboxylase antibody associated epilepsy spectrum

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Background and aims: Anti-glutamic acid decarboxylase antibodies (GAD), initially described in type 1 diabetics, have been recently identified in some patients with epilepsy. The purpose of our work was to characterize the anti-GAD antibodies associated epilepsy.

Methods: Case-study of 5 patients who had pharmaco-resistant epilepsy with positive Anti GAD antibodies

Results: We included in our study 5 patients, 3 women and 2 men. The mean age of the beginning of the epilepsy was 45.3 ± 3 years old. All of them had pharmaco-resistant epilepsy. Neuro-cognitive disorders were found in 3 cases and movement disorders in 2. A moderated lymphocytic pleocytosis was found in CSF examination in 3 patients. Anti GAD antibodies were positive in the blood in all patients, and in CSF in 3 cases. All patients received intravenous Immunoglobulin therapy with positive outcome in 4 patients.

Conclusion: Anti GAD antibodies are responsible of a neuronal hyperexcitability by inhibating the GABAergic neurotransmission. A better knowledge of the GAD antibodies associated neurological disorders seems to be necessary for a faster diagnosis and a better treatment.

Disclosure: Nothing to disclose

EPO1304

Cerebrospinal fluid oligoclonal bands in Neuroborreliosis are specific for *Borrelia burgdorferi*

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Background and aims: Cerebrospinal fluid (CSF) oligoclonal bands (OCB) occur in chronic or post-acute phase of inflammatory diseases of the central nervous system. Within this trial we aimed to determine whether CSF OCB in patients with neuroborreliosis (NB) are specific for *borrelia burgdorferi* sensu lato.

Methods: We performed isoelectric focusing (IEF) followed by immunoblotting in CSF of 10 NB patients and 11 controls (multiple sclerosis: 7, neuromyelitis optica spectrum disease: 2, dementia: 1, monoclonal gammopathy: 1). Immunoblotting was performed using an uncoated as well as a borrelia antigen pre-coated nitrocellulose membrane (NCM). The number of OCB was determined by visual inspection and photometric analysis using ImageJ. OCB were compared between uncoated and pre-coated NCM both in NB and controls. Replication experiments were performed for validation purposes to determine inter-assay precision by the coefficient of variation (CV).

Results: *Borrelia*-specific OCB were found in the CSF of 9 NB patients and in none of the control subjects (sensitivity: 90%, specificity: 100%). The number of OCB in NB patients did not statistically significantly differ between immunoblots using uncoated and pre-coated NCM (visual inspection: 12±5 vs. 9±5 bands, $p=0.190$, photometric analysis: 12±4 vs. 11±7; $p=0.579$). Determining OCB number by visual inspection in NB and controls revealed a CV of 27% and 15% when an uncoated NCM was used, while 31% and 0% in case of pre-coated NCM.

Conclusion: Immunoblotting on precoated membranes is a simple method to demonstrate antigen specificity of clonally selected IgG.

Disclosure: *Borrelia* antigens were provided free of charge by Euroimmun.

EPO1305

Epidemiology of paraneoplastic cerebellar degeneration: a 9-year retrospective study

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Background and aims: Paraneoplastic cerebellar degeneration (PCD) is a neurological syndrome characterised by cerebellar ataxia due to tumour-induced autoimmunity against cerebellar antigens. Epidemiological data are mainly based on selected cohorts from third-level neuroimmunology centres.

Methods: We performed a 9-year (2009–2017) population-based epidemiological study in Friuli-Venezia Giulia, Italy (983,190 people). A diagnosis of PCD was made following the 2004 diagnostic criteria. Age- and sex-adjusted incidence rates were calculated.

Results: We observed 24 cases of definite PCD. The age-standardised incidence rate was 0.22/100,000 person-years (95% confidence interval 0.13–0.31). Median age at onset was 69 (range 40–80); female patients were 75%. Onconeural antibodies were present in 37% (anti-Yo in 25%, anti-Hu in 8%, anti-Ma2 in 4%). A tumour was found in 92%. Brain magnetic resonance imaging showed normal findings in 46%, cerebellar atrophy in 25% and vascular encephalopathy in 4%. Onset was acute in 8%, subacute in 58%, chronic in 13% and unspecified in 21%. Immunological treatment was performed in 29%, oncological treatment was administered in 17% and both in 4%. Improvement was seen in 17%, stability in 38%, worsening in 33%, insufficient outcome data in 12%; no statistically significant effect of immunological ($p=0.288$) or oncological ($p=0.567$) treatments was observed.

Conclusion: The incidence of PCD in our population was 0.22/100,000 person-years. Female sex is predominant; most patients are seronegative. A significant benefit with treatments was not seen, possibly due to small sample size; nevertheless, since a subset of patients showed a clear improvement, an immunological and/or oncological treatment trial should be warranted whenever feasible.

Disclosure: Nothing to disclose

EPO1306

Pattern of onconeural antibodies in sera from patients with renal cell carcinoma

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Background and aims: Onconeural antigens expressed by tumor cells may trigger the expression of onconeural antibodies, which results in paraneoplastic neurological syndromes (PNS). We investigated the presence of 8 onconeural antibodies (amphiphysin, CRMP5, Nova/Ri, Cdr2/Yo, Elav/Hu, Zic4, Ma2, recoverin) and neurologic complaints and symptoms in 33 metastatic renal cell carcinoma patients. Overall survival (OS) and progression free survival (PFS) were also determined.

Methods: Sera were tested on dot blot of purified, recombinant, human onconeural antigens. Neurologic complaints were reviewed by a questionnaire and symptoms were determined by a neurologist. OS and PFS of patients were determined by Kaplan-Meier analysis.

Results: 57% of patients harbored at least 1 antibody, 39% of patients had multiple antibodies. 2 patients with cerebellar signs and 3 patients with polyneuropathy had onconeural antibodies, suggesting a definite PNS. 6 additional patients with polyneuropathy and without onconeural antibodies might have possible PNS. OS was significantly longer in patients harboring the anti-Hu antibody compared to those without it (median survival was 745 and 135 weeks, respectively).

Conclusion: Onconeural antibodies have surprisingly high occurrence in RCC patients potentially (like in the case of anti-Hu antibody) affecting their survival. Moreover, definite and possible PNS may have a negative impact on the quality of life of RCC patients.

Disclosure: Nothing to disclose

EPO1307

Severe dysautonomia as a remarkable manifestation of CLIPPERS

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Background and aims: CLIPPERS ('chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids') is a rare inflammatory disease of the central nervous system with predilection of the pons, brachium pontis and cerebellum. Histopathology shows perivascular and diffuse parenchymal (CD3+/CD4+) T-cell infiltration. CLIPPERS manifests in a subacute manner with symptoms essentially related to brainstem and/or cerebellum. MRI characteristically shows pontine and cerebellar punctate perivascular gadolinium enhancement. Responsiveness to glucocorticosteroid treatment is another core feature.

Methods: In 2017 a 65-year old female patient presented with subacute, progressive symptoms of bilateral pyramidal syndrome, asymmetrical sensory loss, diplopia and ataxia. MRI demonstrated patchy spot like hyperintense T2-/FLAIR lesions and gadolinium enhancement in pons, mesencephalon and middle cerebellar peduncles. The cervicothoracic spinal cord showed comparable lesions. Patient was initially treated successfully with glucocorticosteroid therapy. Mid 2018 patient developed a dilated pupil on the right with absent light reflex but intact ocular movements despite of immunosuppressive treatment. Furthermore, she developed severe dysautonomia consisting of recurrent syncope, orthostatic hypotension, hyperthermia and tachycardia. Patient was admitted to the intensive care unit and eventually passed away. Autopsy was performed.

Results: Brain pathological tissue from autopsy was examined and demonstrated severe encephalitis with CD3+ T-cell infiltration with perivascular predominance as well as parenchymatous involvement, mainly in the brainstem. Extension to the cerebral hemispheres with extensive parenchymatous T-cell aggregation in the hypothalamus was observed, as an explanation for severe dysautonomia.

Conclusion: This case report is the 1st to report severe dysautonomia as a clinical manifestation of CLIPPERS as a result of T-cell infiltration in the hypothalamus.

Disclosure: Nothing to disclose

EPO1308

Autoimmune vermian hypermetabolism: regarding three cases

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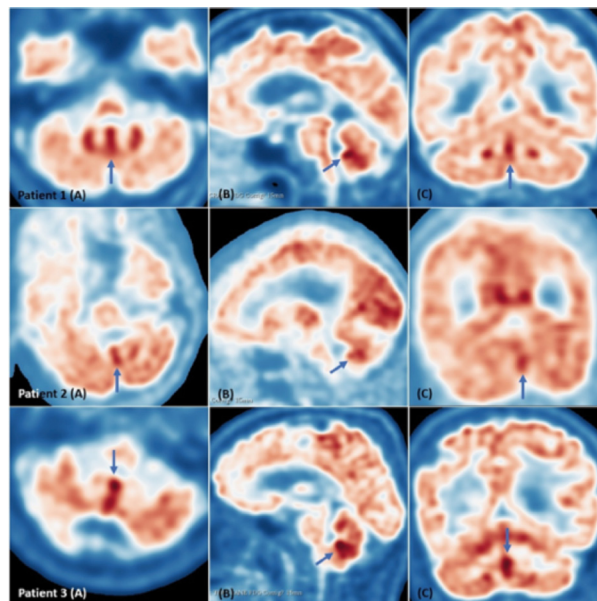
Background and aims: Cerebellar hypermetabolism is less commonly described than hypometabolism.

Methods: We report three cases of auto-immune cerebellar vermian hypermetabolism.

Results: Patient 1 is a 68-year-old man with excessive daytime sleepiness and progressive cerebellar syndrome. On 18F-FDG brain positron emission tomography (PET)-scanner, vermian maximum standard uptake value (SUV) normalized to lean body mass was 7.3 compared to 5.3 and 5 on right and left cerebellar hemispheres, respectively. Definite diagnosis was type 1 narcolepsy secondary to an anti-Ma2 encephalitis.

Patient 2 is a 63-year-old woman with new-onset seizures, progressive walk impairment, limb myoclonus and dysexecutive syndrome. On PET-scanner, vermian maximum SUV was 4.4 compared to 3.7 and 3.8 on right and left cerebellar hemispheres, respectively. Anti-Zic4 antibodies were eventually found in the serum.

Patient 3 is a 72-year-old man treated for a pulmonary adenocarcinoma. He presented with limbs myoclonus. Symptoms worsened with the appearance of a cerebellar syndrome after the 1st perfusion of an immune check-point inhibitor for tumour treatment. On PET-scanner, vermian maximum SUV was 7.3 compared to 5.2 and 5.6 on right and left cerebellar hemispheres, respectively. Symptoms subsided with immunosuppressive drugs although anti-neurons antibodies were absent.



18F-FDG brain positron emission tomography of the three patients. (A) Axial, (B) sagittal and (C) coronal view. Note the vermian hypermetabolism (arrows).

Conclusion: We reported 3 cases of auto-immune cerebellar hypermetabolism. There are only 12 previously published cases of auto-immune cerebellar hypermetabolism, some with known anti-neuron antibodies (anti-Ri and anti-Yo). Cancer was frequent but lacked in 2 cases. Other causes include Gayet-Wernicke encephalopathy, severe brain aggression, Huntington disease, dementia with Lewy bodies, Creutzfeldt-Jakob disease, essential tremor, Parkinson's disease and dystonia.

Disclosure: Nothing to disclose

EPO1309

CXCL13 marker levels for various forms of multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) is a chronic autoimmune inflammatory disease with an unclear prognosis. Cerebrospinal fluid (CSF) is an important component of MS diagnosis. Promising markers include the chemokine CXCL13. CXCL 13 regulates lymphocyte migration and reflects the inflammatory activity in MS.

This study aimed to investigate the differences in the concentrations of CXCL13 marker in CSF in patients with various forms of MS (primary progressive MS - PPMS, relapsing-remitting MS - RRMS) and clinically isolated syndrome (CIS).

Methods: Patients with CIS, different forms of MS and controls were included in the study. The control group consisted of patients with the non-inflammatory disease. Overall, 170 patients (46 CIS, 9 PPMS, 15 RRMS, 100 controls) CSF were examined.

Results: After the data processing, significantly higher values of CXCL13 were demonstrated in the patients with CIS and RRMS compared to the control group ($p=0.007$; $p<0.0001$). Based on the results of this study, we can observe different values of the CXCL 13 marker. In MS patients we can see a difference in the course of the inflammatory process, wherein patients with RRMS the inflammation activity is higher compared to PPMS. Furthermore, this work could be expanded to include a larger number of patients in the population, thereby supporting the robustness of existing results.

Conclusion: CSF examination has an irreplaceable role in the differential diagnosis of MS. The discovery of new markers could help to better determine prognosis and subsequent therapeutic intervention. In the future, we plan to expand the patient population.

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EPO1310

Light near dissociation in Anti-GQ1b Negative Miller Fisher syndrome.

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Background and aims: Miller Fisher syndrome (MFS) is a variant of Guillain Barre Syndrome characterised by ataxia, ophthalmoplegia and areflexia. As MFS is rare, signs and symptoms of the syndrome are not fully understood. We describe a case of anti GQ1b negative MFS associated with light-near dissociation.



Methods: Case report

Results: A 34-year-old woman presented to the emergency department with diplopia and ataxia following an upper respiratory tract infection 2 weeks prior. Past medical history included submandibular gland removal and a previous spontaneous abortion at 6 weeks gestation, both of which occurred a number of years previous.

Examination revealed complete ophthalmoplegia, bilateral ptosis, bilateral facial paraesthesia, areflexia and ataxia. Upper limb power was 3/5 throughout and lower limb power was 5/5. Pupils were mydriatic and unreactive to light but responsive to accommodation. Magnetic resonance imaging of the brain was normal and Anti-GQ1b and Anti-GM1 antibodies were negative. Routine laboratory studies, including full blood count, renal and liver profile, were normal. Cerebrospinal fluid analysis demonstrated a normal protein and cell count. The patient remained hemodynamically stable and was transferred to the intensive care unit for 1 to 1 nursing and supportive therapy. Intravenous immunoglobulin (IVIg) was given for a diagnosis of MFS.

Conclusion: The patient's upper limb power, ataxia, ophthalmoplegia and ptosis resolved with IVIg and rehabilitation, however the dissociated pupillary response and areflexia have persisted 2 years since presentation. Light-near dissociation with Anti-GQ1b negative MFS has not been previously described in the literature to our knowledge.

Disclosure: Nothing to disclose

EPO1311

Utility of SUV values on 18-FDG PET- CT in anti- NMDAr encephalitis.

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Background and aims: Anti-NMDAr is 1 of the most common causes of encephalitis. 18-FDG PET- CT has been used mainly to detect brain metabolic patterns. The determination of SUV allows the evaluation of regional metabolic changes in this disease.

Objective: To establish the relationship between clinical manifestations of anti-NMDAr encephalitis and SUV values on 18-FDG PET- CT.

Methods: We performed a retrospective, transversal study. Patients with diagnosis of anti-NMDAr encephalitis and 18-FDG PET-CT with regional quantification of SUV were included. The association of regional SUV and the presence of symptoms was evaluated through T test, considering significant values of <0.05. On those comparisons with statistical significance, ROC curves were performed to determine a cut-off point for a major risk of developing the clinical manifestation.

Results: There was a relationship between the presence of epileptic status and regional uptake in both right and left superior temporal gyrus ($p=0.05/0.02$). Dysautonomia was associated with 18-FDG uptake in the left insula ($p=0.05$).

Conclusion: Quantification of SUV in 18-FDG PET-CT allows to expand the utility of this study in the patients with immune-mediated encephalitis. This study shows that there is an association of regional uptake and the presence of certain clinical manifestations, although we couldn't establish a significant cut-off in SUV values for these regions. More studies with a greater number of patients are necessary to reproduce these findings.

Disclosure: Nothing to disclose

EPO1312

Clinical experience in LGI-1 encephalitis: time may be brain not only in stroke

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Background and aims: Antibodies against LGI-1 are a frequent cause of autoimmune encephalitis (AE). However, uncertainty about its clinical course and treatment may be related to the low prevalence of this entity. We aim to show our clinical experience.

Methods: Retrospective multicentric analysis of patients with positive antiLGI-1 antibodies testing by indirect immunofluorescence and transfected cells confirmation in our Immunology laboratory.

Results: A total of 10 patients were included (6 males, median age 74 years, range 56-83). 9 patients fulfilled diagnostic criteria for AE. Cognitive disturbances were present in all patients. Different types of seizures were present in 8 patients. 6 patients displayed typical faciobraquial dystonic seizures (median frequency 45/day, range 30-60). 6 patients had hyponatremia, and 2 had abnormalities in CSF. 6 patients showed altered EEG registers and 5 showed temporal hyperintensities on MRI. 1 of them was found to have a bladder cancer. 2 patients were tested for HLA DRB1*07:01, being positive. Median time to diagnosis was 90 days (range 1-1350). 8 patients received a 1st-line immunotherapy (4 high dose steroids pulses, 1 immunoglobulins and 3 both), and 3 a 2nd-line immunotherapy (mofetil mycophenolate). 7 patients received combined antiepileptic therapy without sustained response, presenting 2 patients adverse reactions. At 3 months after initiating therapy, 7 patients were independent, 2 patients remained with altered functional capacity and 1 patient had died. Poor prognosis was related to delayed both diagnosis and treatment.

Conclusion: Prompt recognition antiLGI-1 encephalitis is critical, as early treatment may improve prognosis. Immunotherapy is the cornerstone treatment for both seizures and cognitive alterations.

Disclosure: Nothing to disclose

EPO1313

Ocular flutter as the cardinal feature of anti-GM2 brainstem encephalitis

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Background and aims: Ocular flutter is a rare sign of abnormal ocular motility, consisting of back-to-back irregular horizontal saccadic intrusions without intersaccadic interval. It is usually encountered along with cerebellar and/or brainstem signs and is most frequently associated with infectious, paraneoplastic or autoimmune disorders.

Methods: A 26-year-old female with a history of Hashimoto's thyroiditis, presented with acute vertigo over a 3 week-period, followed by slowly progressive oscillopsia, mixed upper limb tremor, gait ataxia and behavioral changes over the next 1 year. The neurological examination revealed truncal and appendicular ataxia, action and postural upper limb tremor, pyramidal signs as well as ocular flutter, square wave jerks and blink nystagmus.

Results: Brain MRI and CSF examination were unremarkable. A thorough work-up for an underlying neoplasm, including whole body PET-CT and paraneoplastic antibodies as well as antibodies for autoimmune encephalitis, were normal. An ECG revealed slow-wave activity and an electrooculogram (EOG) verified the presence of ocular flutter. The patient tested positive for anti-GM2 IgM antibodies. She was administered a 5-day regimen of IV methylprednisolone 1gr/d, followed by methylprednisolone orally, with complete remission of her symptoms. At 6 months after treatment completion, the patient remained asymptomatic, with significant improvement of the EOG findings. Repeat testing of anti-GM2 antibodies at 6 months was still positive.

Conclusion: Ocular flutter has rarely been associated with anti-gaglioside antibodies (GQ1a, GD1a, GD1b, GM1). This is the first reported case of anti-GM2 brainstem encephalitis manifesting with ocular flutter.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EPO1314

Noninfectious Central Nervous System involvement in Late-Onset Combined Immune Deficiency mimicking Multiple Sclerosis

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Background and aims: Common Variable Immunodeficiency (CVID) is defined by defective antibody productions; Late-Onset Combined Immune Deficiency (LOCID) is a subset characterized by added severe T-cell defect, usually expressed with opportunistic infections. Central Nervous System (CNS) involvement in CVID is rare. We present a case of noninfectious CNS involvement, mimicking Multiple Sclerosis, as diagnostic debut of LOCID.

Methods: A 56-year-old man with hypertension and dyslipidemia developed acute episodes of burning pain along left mandibular division of trigeminal nerve territory, suggesting trigeminal neuralgia; no previous dental manipulation. Brain magnetic resonance (MR) showed multiple T2/Flair hyperintense lesions (suggestive of demyelinating disease), periventricular and infratentorial location, 1 of them closely to left trigeminal nerve in pons; no contrast-enhancement of any lesions. A lumbar puncture was performed, normal glucose, protein and cell count in cerebrospinal fluid; mirrored oligoclonal bands were detected. With suspicion of a systemic process, laboratory tests showed serum lymphopenia with panhypogammaglobulinemia; search for infectious agents, vasculitic or lymphoproliferative processes was negative. Carbamazepine treatment obtained pain control.

Results: The immunologic study confirmed total lymphopenia mainly B-cells, but significant T-cell defect (CD4+ T-cell count 280x10⁶ cells/L), diagnosis of probably LOCID. He's been treated with monthly intravenous immunoglobuline replacement. Evolutionary brain MR without changes, neurologically asymptomatic.

Conclusion: CNS involvement in immune deficiencies is rare, usually of infectious, granulomatous cause, or vitamin E deficiency. There are very few cases reported suggestive of autoimmune etiology, mainly spinal cord disease, T-cell defect probably implied. This case mimicks Multiple Sclerosis, with immune involvement supported by mirrored oligoclonal bands.

Disclosure: Nothing to disclose

EPO1315

Neurosarcoidosis: Clinical manifestations, diagnosis and treatment

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Background and aims: Sarcoidosis is a multisystemic granulomatosis of unknown etiology. Central nervous system involvement may reveal the disease or occur in a patient with known sarcoidosis. The intracranial lesions preferentially affect the meninges, the cranial nerves and the hypothalamo-pituitary axis. The objective of our study is to analyze the clinical and radiological aspects of our patients, to emphasize the role of MRI in the diagnostic approach, and to describe the different therapeutic arsenals.

Methods: This is a retrospective study on the medical file of 7 patients, collected at the neurology and radiology departments of the Mohammed VI University Hospital of Oujda, during a period from February 2015 to January 2020.

Results: The average age of our patients was 39.1 years. The sex ratio was 0.6. The etiological reasoning was based on the clinical context, MRI, the biological assessment, the anatomopathological study and the evolution under treatment. The clinical signs are multiple, made of the association with varying degrees of: multiple involvement of cranial nerves, dysfunction of the hypothalamic-pituitary axis, psychiatric manifestations, sensitivomotor deficiency, comitial crises and cephalgias. Encephalic MRI was suggestive of diagnosis in 5 patients, but the use of biology and pathological study proved necessary for diagnostic confirmation. All of our patients benefited from corticosteroid treatment and/or immunosuppressants with good clinical progress.

Conclusion: MRI is an essential examination in neurosarcoidosis. It provides evidence for diagnosis in cases of clinical suspicion, research subclinical impairment in patients with known sarcoidosis and can sometimes predict and especially appreciate the effectiveness of treatment.

Disclosure: Nothing to disclose

EPO1316

The multiple faces of Neurolupus

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Background and aims: The term Neurolupus is a generic definition that includes a wide variety of neuropsychiatric manifestations associated with systemic lupus erythematosus (SLE). Its prevalence is variable (15-95%).

Methods: We present a series of patients with Neurolupus, admitted between September 2017 and September 2019 in the Rheumatology and/or Neurology departments. Demographic, clinical, imaging and therapeutic data were retrospectively collected.

Results: We included 7 patients, 6 women and 1 man, with ages between 23 and 75 years. The neuropsychiatric diagnoses were: central nervous system vasculitis (2), recurrent ischemic stroke (2) recurrent reversible posterior encephalopathy syndrome (1), longitudinally extensive transverse myelitis (1), acute psychosis (1), multiple mononeuropathy (1), cranial mononeuropathy (1). The neuropsychiatric manifestation was the inaugural presentation of SLE in 2 patients. Associated multiorgan manifestations included immune (6), hematologic (5), mucocutaneous (6), musculoskeletal (5), renal (5), pulmonary (2), cardiac (1) and serositis (2) involvement. 3 patients had secondary antiphospholipid antibody syndrome (APS). All patients received hydroxychloroquine in combination with immunosuppressants/ immunomodulators, which included high dose glucocorticoids (7), cyclophosphamide (4), rituximab (4) and intravenous human immunoglobulin (3). Anticoagulation was also started in patients with secondary APS.

Conclusion: The diagnosis of Neurolupus can be extremely complex and requires extensive investigation for differential diagnosis. The treatment choice is based on the type and severity of the clinical manifestations and should take into account the infectious risk associated with immunosuppression. We intend to alert to the multiple faces of Neurolupus and to the importance of early recognition of this entity, due to its therapeutic and prognostic implications.

EPO1317

Different neurological affectation of granulomatosis with polyangiitis

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Background and aims: Vasculitis are systemic or localized syndromes in which blood vessels are damaged by inflammatory cells, causing a secondary ischemic injury. Granulomatosis with polyangiitis is a systemic vasculitis which affects both upper and lower airways, kidneys and, occasionally, the nervous system.

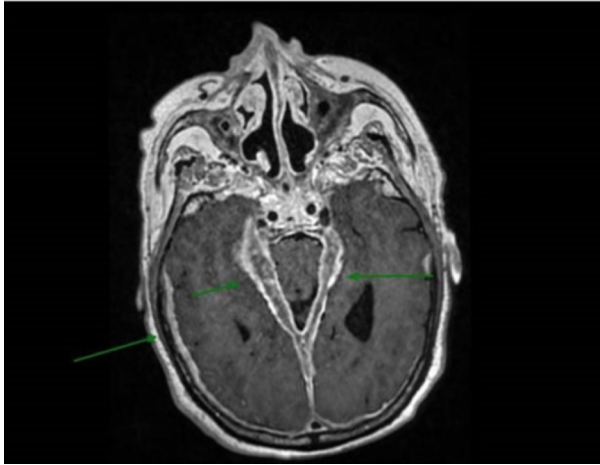
Methods: We expose 4 cases with a different affectation of the nervous system caused by this disease:

Results: The 1st is a 51 years old male patient with upper airways affectation who has also upper and lower limbs asymmetric hypoalgesia. Electroneurogram (ENG) was performed with a result of motor, asymmetric, demyelinating polyneuropathy (PNP) with conduction block, which evolved to axonal polyneuropathy in the end. Nasal mucosal biopsy was performed due to a non-responding sinusitis with the result of necrotizing granulomatosis. The 2nd is a 74-year-old male patient with sinusitis and non-responding cephalalgia. Blood tests were performed with MPO ANCA and MRI with pachymeningitis. 3rd patient: 76 years old male patient with cephalalgia and loss of vision. It was performed cerebrospinal fluid study with lymphocytic meningitis (pachymeningitis) and 61cmH₂O opening pressure. Meningeal biopsy was performed in which it was observed necrotizing granulomatosis.

4th patient: 78-year-old female patient with asymmetric progressive paraparesis, hematuria and proteinuria. ENG was performed with severe axonal PNP.



CT-Scan patient 1: sinusitis



MRI patient 3: pachymeningitis.

Conclusion: Granulomatosis with polyangiitis is a rare pathology that must be considered as it could lead to a severe, possibly incapacitating, and even mortal affectation, but it usually has a favorable evolution with proper treatment in the majority of cases.

Disclosure: Nothing to disclose

EPO1320

HSV-brainstem encephalitis revealing systemic lupus erythematosus

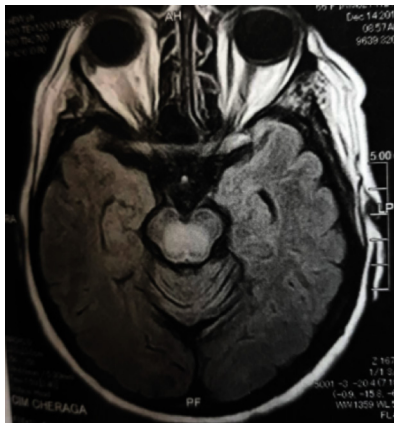
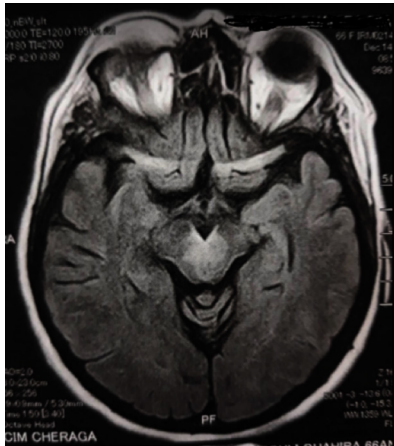
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Background and aims: Neuropsychiatric (NP) symptoms of systemic lupus erythematosus (SLE) can be related to disease activity or to its complications, distinction between this 2 conditions is a priority. Herpes simplex virus type 1 (HSV-1) encephalitis (including brainstem encephalitis) is a very rare condition in patients with SLE.

Methods: A 66-year-old woman presented with 6-day history of dysarthria and gait ataxia. Her medical history includes thrombocytopenia, pleurisy, and photosensitive rash 1 year prior. Neurological examination showed 3rd and 6th cranial nerve palsies, and hyperreflexia. Her brain MRI demonstrated T2-hyperintense, T1-hypointense lesions in midbrain. The patient was started on empiric acyclovir and ceftriaxone, leading to significant improvement of gait ataxia and dysarthria. Cerebrospinal fluid (CSF) cytology was normal, serum ganglioside antibodies, paraneoplastic panel, serology tests were negative. CSF viral PCR was positive for HSV-1. She presented simultaneously anemia, proteinuria, pericardial effusion, positive antinuclear antibodies, which along with her medical history raises the suspicion for SLE.





Results: Our patient presented acute neurological disorders and T2W MRI abnormalities consistent with the diagnosis of BE. BE has a broad causes, priority should be given to infectious etiologies, our patient was treated empirically while etiologic testing was performed. Her history was suggestive of SLE, which was confirmed with the positivity of autoantibodies. The positivity of HSV1 PCR and the good response to antiviral treatment is indicative of HSV1-BE complicating SLE.

Conclusion: HSV-BE is rare complication of SLE, it is associated with high risk of mortality and morbidity. An empirical treatment should be started once the diagnostic is suspected.

Disclosure: Nothing to disclose

EPO1321

A chiasmal visual defect in adult patient with phenylketonuria: a rare association

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Background and aims: Phenylketonuria (PKU) is a disease caused by deficiency in the phenylalanine hydroxylase enzyme, which leads to phenylalanine accumulation in the blood and in the brain. The most common neurological manifestations of PKU are progressive intellectual disability, microcephaly and epilepsy; particularly when there is a delay in the diagnosis.

Methods: The authors present a case report of a chiasmal visual defect in adult patient with phenylketonuria, from Santa Casa de Misericórdia de São Paulo.

Results: A 21-year-old man, with PKU diagnosed since birth and irregular treatment, was admitted to emergency department complaining of blurred vision on both eyes and eye pain, that started one day before admission. His neurological exam had no abnormalities besides a low visual acuity on his left eye (Snellen test 20/50). Initial investigation with ophthalmoscopic exam, computed tomography of the brain and cerebrospinal fluid analysis was not elucidatory. The brain magnetic resonance imaging (MRI) showed extensive white matter involvement, also affecting optic chiasma, without contrast enhancement. The lesions were compatible with previous descriptions of the disease involvement, but the extension to optic nerve and chiasma is rarely reported. The patient followed a strict phenylalanine-free dietary plan and had improvement of symptoms in a few days

Conclusion: Although PKU is a well-known cause of neurologic disorders, visual symptoms due to the disease are rarely described, especially with an acute onset and in a young adult with no other neurologic symptoms. The knowledge of this presentation is important for differential diagnosis in this specific population

Disclosure: Nothing to disclose

EPO1322

Posterior Encephalopathy Reversible Syndrome secondary to hypercalcemia due to hypervitaminosis D

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is a clinical and neuroradiological condition characterized by headache, visual disturbances, seizures or altered consciousness. Although the exact pathophysiology is not known, PRES is associated with arterial autoregulatory dysfunction and vascular injury. The syndrome affects patients in all age groups, with female predominance.

Methods: Data obtained from the patient's medical record.

Results: A 29-year-old woman with dermatomyositis on oral corticosteroid therapy and vitamin D supplementation (dose of 150,000 IU per day, external therapy to this service). From the entrance the patient had reduced proximal muscle strength and 3 episodes of generalized tonicoclonic seizures. Evolved at hospitalization in need of orotracheal intubation due to lowered level of consciousness. The neurological examination revealed proximal musculature weakness, without further findings. Magnetic resonance imaging showed a diffusely white T2/FLAIR hypersignal with predominance of posterior regions of both cerebral hemispheres. Laboratory tests revealed 15.22mg/dl seric calcium. Symptoms improved with complete resolution after serum calcium normalization, with a strong response to hydration and forced diuresis. Hypercalcemia was considered the only identifiable cause of PRES.

Conclusion: The number of conditions associated to PRES has increased, although hypertension, kidney disease, sepsis and immunosuppressive therapy remains the most common causes. This report is important as a warning to physicians and patients about the side effects of high dose vitamin D therapies. As shown in the present case, supplementation therapy can overcome metabolic disturbances (vascular endothelial injury and consequently altered brain self-regulation)

Disclosure: Nothing to disclose

EPO1323

Hypertrophic pachymeningitis: Report of 3 cases

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Background and aims: Hypertrophic pachymeningitis (HP) is a rare fibrosing inflammatory process of the dura mater. The differential diagnosis of HP includes immune-mediated, malignancies and Infectious conditions but can also be idiopathic. **Aims:** To review 3 cases of HP between 2017-2019.

Methods: Case report.

Results: Case 1: A 38-year-old woman presented with a paroxysmal episodes of language dysfunction and sensitive disturbance of the right hand. MRI revealed a meningeal thickness in the frontoparietal region and meningeal biopsy non-caseating granulomas. She started steroids with neurological improvement. The final diagnosis was neurosarcooidosis. Case 2: A 32-year-old man presented to the emergency department with progressive neck pain followed by left V3 disturbance and left XII palsy. CSF had lymphocytic pleocytosis and hypoglycorrhea. MRI identified HP near magnum foramen with hernation and hydrocephalus for what was put an external ventricular drain. Meningeal biopsy showed few granulomas. IGRA was positive but cultures and PCR study for M.Tuberculosis were negative, he was treated with antibacilars with neurological symptoms resolution. Case 3: A 49-year-old woman was admitted for seizures followed by motor aphasia. Brain MRI showed dural thickening involving mainly the left temporo-occipital region. CSF study was normal. Meningeal biopsy identified diffuse lymphocyte infiltrate. After extensive investigation the final diagnosis was idiopathic HP.

Conclusion: HP is a rare entity and can cause neurological deficits by extension, compression or vascular obstruction. The evaluation of HP includes laboratory investigations of both blood and CSF samples, cross-sectional imaging studies and pachymeningeal biopsy, the latter being useful for differential diagnosis.

Disclosure: Nothing to disclose

EPO1324

Misleading Cavernoma – Occam's razor pitfall

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Background and aims: Wernicke-Korsakoff Syndrome (WKS) is caused by thiamine deficiency. The classic triad of ophthalmoparesis, gait ataxia, and delirium is present in less than 20% of cases at presentation and each particular symptom has a broad differential diagnosis. Alcoholism usually evokes this entity.

Methods: Case Report

Results: A 66-year-old male with a previous history of basal cell carcinoma, came to the emergency department due to sudden horizontal binocular diplopia. Neurological examination showed horizontal gaze-evoked and vertical pendular nystagmus. Brain CT and MRI revealed a small paramedian left pontine cavernoma with recent microbleeding. The patient was treated conservatively. In the following couple of weeks, the diplopia worsened and new symptoms ensued: incoercible vomiting, weight loss, dizziness with gait impairment, and mental confusion. He presented with complete ophthalmoplegia without ptosis, hyporeflexia and severe appendicular ataxia. Repeated brain CT revealed no signs of rebleeding. High doses of IV thiamine were started with improvement of the eye movements in the following day. Despite CSF studies revealing albuminocytological dissociation, the nerve conduction studies were normal and antigangliosides antibodies were negative. Brain MRI showed T2/FLAIR hyperintensity in the periaqueductal grey matter and medial thalamus bilaterally, with diffusion restriction, supporting the diagnosis of WKS. Extensive workup was performed, and gastric adenocarcinoma was diagnosed.

Conclusion: The absence of either history of alcohol consumption or the full classical triad should not keep one from considering WKS. Neoplasms are the main cause of WKS in non-alcoholic patients, so this etiology should be actively investigated. Prompted treatment with thiamine can prevent progression to Korsakoff encephalopathy.

Disclosure: Nothing to disclose

EPO1325

Intravascular lymphoma: A rare cause of longitudinal extensive transverse myelitis

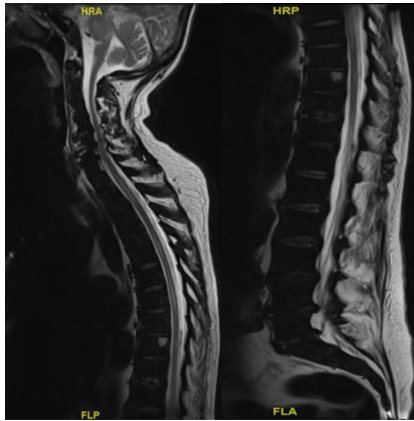
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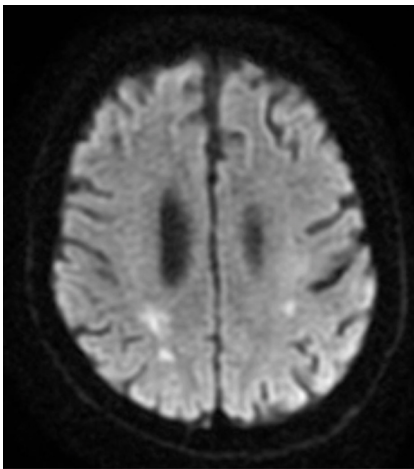
Background and aims: Intravascular lymphoma is a rare entity of large cell lymphoma that proliferates within the lumen of small vessels. It is often presented with central nervous system and skin signs.

Methods: We present a case of intravascular lymphoma, admitted with paraparesis with sensory level and encephalopathy, managed conservatively with steroid and palliation.

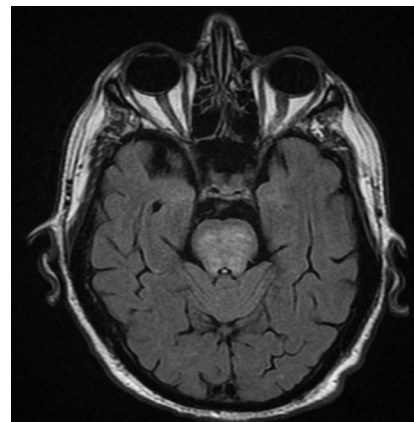
Results: A 72-year-old gentleman with myelodysplastic syndrome (MDS) presented with a subacute onset of paraparesis with sensory level to the umbilicus and intermittent confusion. Spinal MRI showed T2 hyperintensity from T2 to T5 and T7 to T9. Brain MRI showed multiple small foci of diffusion restriction in bilateral cerebral hemispheres. CSF analysis showed lymphocytic pleocytosis with raised protein but no bacterial growth and negative viral PCR. CSF oligoclonal bands, serum NMO and MOG were negative. His other tests including paraneoplastic antibodies, vasculitic screen, CSF cytology and CSF immunophenotyping were negative. PETCT was unremarkable. Despite absence of solid tumour in his cross sectional imaging, the suspicious of a systemic haematological infiltrative or malignant disease remained high in view of his history of MDS, multiple small infarct and abnormal spinal cord signal changes. A random skin biopsy was therefore arranged and confirmed intravascular large B cell lymphoma. He was managed conservatively with IV methylprednisolone with no significant improvement. Decision was made for palliation due to poor performance status and unfit for chemotherapy.



T2-weighted sagittal spinal MR imaging showing multi-segmental T2 hyperintensity of the cord in cervicothoracic region



Brain MRI showing multiple small foci of diffusion restriction in bilateral hemispheres suggestive of new lacunar infarct



Brain MRI demonstrating abnormal FLAIR hyperintensity in the pons

Conclusion: Intravascular lymphoma is often a diagnostic challenge as its symptoms are non-specific. It is prudent to consider this diagnosis in the appropriate settings as this is a potentially treatable condition.

Disclosure: Nothing to disclose

EPO1326

The extensive workup towards building a diagnosis of Neurosarcoidosis without other organ involvement

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Background and aims: Neurosarcoidosis, in the absence of a relevant biopsy is a difficult clinical and neuroimaging diagnosis.

Methods: We present the case of a 67-year-old female patient with a history of multiple cranial mononeuropathies in the last years: diplopia (2008), right hypoglossal paresis and perioral paresthesias (2015), left eye vertical diplopia and blurred vision (january 2018), perioral paresthesias (june 2018), left eye blurred vision and third nerve palsy (july 2018). All these episodes had a duration of 1-2 weeks and were alleviated by corticotherapy.

Results: Initial cerebral MRI showed a fluid accumulation (FLAIR and T2 hyperintense, gadolinium enhanced) in the left sphenoid sinus extending to the left superior orbital fissure and to the cavernous sinus. She was referred to our clinic 1 year later. Neurological examination revealed left eye diminished visual acuity and temporal quadrants. Optical coherence tomography was indicative of bilateral optic atrophy. A repeated brain MRI showed minimal inflammation and atrophy of the left optic nerve. We also performed a spinal tap with normal results (under corticotherapy). The serum ACE had an increased value. The patient was evaluated for other potential infectious, immune and neoplastic etiologies as well as for extraneural sarcoidosis (pulmonary CT, otolaryngology evaluation, cerebral angiography) but the results were negative. The clinical and neuroimaging studies point towards a diagnosis of neurosarcoidosis. The patient was given treatment with Micofenolat Mofetil, preventing further episodes.

Conclusion: Neurosarcoidosis represents a diagnostic challenge in patients without any other organ involvement. The ultimate goal is keeping the disease inactive and maintaining the patient's quality of life.

Disclosure: Nothing to disclose

EPO1327

Looking at the Kidney for Stroke Etiology – A Stroke Case presenting with Microscopic Polyangiitis

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Background and aims: ANCA-associated vasculitis (AAV) is a rare cause of stroke, which consist of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic GPA. In this case report, we describe a stroke patient presenting with MPA.

Methods: Case report

Results: A 65-year-old men presented to our ED with mild right-hand paresis. He was on no medication. His wife noticed slurred speech, discoordination of the right hand and wobbly gait about 10d prior. At that time, he refused to seek medical attention. Vital signs recorded on admission were normal. Neurological examination yielded a right-sided, pure-motor brachiofacial paresis, mild psychoorganic syndrome and gait instability. He declined nasal or oral inflammation and recent infections. Cranial CT showed a parenchymal defect (right temporal lobe) and bilateral bone defects after decompression trepanation and aneurysm clipping after TBI in 1986. Cranial CT (7d after admission) revealed a lacunar infarct in the left capsula interna. Blood test showed elevated creatinine, CRP and ESR. The vasculitis workup was positive for PR3 and MPO antibodies. CSF findings were normal. The kidney biopsy revealed necrotizing glomerulonephritis with fibrocellular crescents. He received high dose steroid treatment followed by rituximab and cyclophosphamide with good treatment response.

Conclusion: CNS involvement in AAV is rare (5-15%). Therefore, early diagnosis can pose a challenge. Ischemic infarctions associated with AAV may present as an isolated lesion or multiple lesions affecting the white matter and are typically unresponsive to antiplatelet therapy leading to recurrent strokes without appropriate immunosuppressive treatment. This case underlines the importance of a systemic approach in stroke evaluation.

Disclosure: Nothing to disclose

EPO1328

Neurological manifestation of medium and large vessel vasculitis

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Background and aims: Neurological manifestations of vasculitis are very diverse and have variable course. Nervous system vasculitis still is diagnostics and management challenge. Nervous system involvement is a common neurological complication, that is why neurologist have an important task to identify patients with systemic vasculitis and diagnose diseases.

Methods: This is a retrospective clinical study of patients with neurological complications of large and medium vessel vasculitis, that were treated and observed in Paul Stradins Clinical University Hospital from 2015 till 2019. Anamnesis and information about the disease evolvment, patients neurological status, patients common condition, treatment, medication and investigations was collected from available previous documentation. Within the framework of this study there was analized patients group and most common medium and large vessel vasculitis neurological complications.

Results: In Paul Stradins Clinical University Hospital from 2015 till 2019 were treated 98 patients with medium and large vessel vasculitis diagnosis. 45 patients with Polyarteritis Nodosa diagnosis, 34 patients had Takayasu arteritis diagnosis and 19 patients had Giant cell arteritis diagnosis. Most often neurological complication was dizziness, which was observed in 48.2% of all patients, the other most spread and serious manifestation was cerebral stroke – 34.3% of all patients and 11.5% had visual disturbance.

Conclusion: Vasculitis neurological manifestations are very diverse. Systemic vasculitis can affect any peripheral or central nervous system structure, causing variable neurological complications. Early neurological symptom identification allows to start treatment on time and improve outcomes. Without correct treatment neurological manifestations might be fatal, rapid diagnostic ant therapy prevents patients from serious disability.

Disclosure: Nothing to disclose

EPO1329

Neurological manifestations of systemic lupus erythematosus

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Background and aims: Neurological manifestations are common in systemic lupus erythematosus (SLE). It may be one of the major presentation and occur in early stages, even before SLE is diagnosed, so early diagnosis and proper recognition is important. The study was made to highlight the pattern of neurological involvement.

Methods: This hospital based retrospective study was carried out from 2015 to 2018. Diagnosed cases of SLE with neurological manifestations were included. Patients with cognitive and psychiatric disturbances were not included due to the type of the study.

Results: In total, from 201 patients, 75 of them had some kind of neurological presentation (37%). 93% were female. The most common age group was from 33-47 years. Peripheral neuropathy was diagnosed in 46 patients (23%), which included sensory motor and also autonomic polyneuropathy and different mononeuropathies. 20% of patients had a history of cerebral infarctions, most often lacunar strokes and transitory ischemic attacks, also large ischemic strokes were found. From retrospective data 10% of lupus patients during the course of the disease were diagnosed with either tension type headaches or migraines, 3 had trigeminal autonomic cephalgias. Less common manifestations were transverse myelitis, central nervous system vasculitis and retrobulbar neuritis.

Conclusion: Neurological manifestation in systemic lupus erythematosus may occur at any time of the disease and be the major presentation. In this study the most common manifestation was peripheral neuropathy and cerebral infarctions.

Disclosure: Nothing to disclose

EPO1330

Tuberous Sclerosis (TS), analysis of a case series

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Background and aims: Analyze systemic symptomatology, especially the neurological one, and characteristic findings in imaging tests of patients with TS in Reina Sofía's Hospital area, Murcia (Spain).

Methods: Digitalized medical records review of patients diagnosed with ST.

Results: 7 patients were included. Average age 44.8 (minimum 30, maximum 60). 57.2% men, 42.8% women. 100% had facial angiofibromas, 71.4% renal angiomyolipomas (AML) and epileptic seizures, 28.5% periungual fibroids, bone abnormalities, lymphangioliomatosis, hepatic AML, retinal astrocytic hamartomas, mental retardation and behavioral disorders (heteroaggressiveness) and 14.3% coffee spots with milk and aneurysm of the interventricular septum. In relation to brain imaging tests, 4 patients had an MRI and 2 had a CT scan, another report was not obtained from another patient. The 3 typical findings of TS, subependymal nodules, cortical/subcortical tuberomas in the cerebral hemispheres (in 1 of the patients also in the cerebellum) and alteration of the white matter (3 with radial migration and 1 with demyelination) were observed in 100% of MRIs. In the 2 patients with CT, subependymal nodules were observed.

Conclusion: The lesions most frequent location was the skin and the central nervous system (since all the patients had findings in the brain imaging tests), followed by the renal one. In most patients, neurological lesions caused epileptic symptoms. It is observed that the data obtained mostly agree with what is described in the bibliography.

Disclosure: Nothing to disclose

EPO1331

Diabetic striatopathy in a patient with hemichorea: a case report

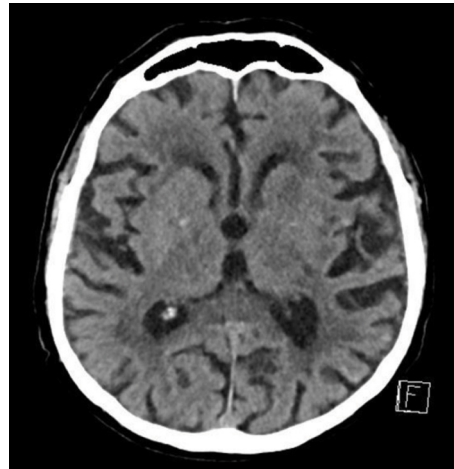
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Background and aims: Diabetic striatopathy is a rare condition characterized by unilateral hemichorea and/or hemiballismus in the settings of uncontrolled nonketotic diabetes mellitus. Imaging studies usually reveal striatal abnormality - subtle hyperdensity on CT and T1 hyperintensity on MRI. Resolution of clinical symptoms is prompt when optimal glycaemic control is achieved.

Methods: We present the case of a 90-year-old male who came to our attention for acute involuntary choreiform movements of his left-sided extremities lasting 2-weeks. Apart from that neurological examination was unremarkable. His medical history included hypertension, atrial fibrillation, previous stroke with no residual disability and poorly controlled type 2 diabetes mellitus on metformin treatment. There was no history of movement disorders or exposure to neuroleptics.

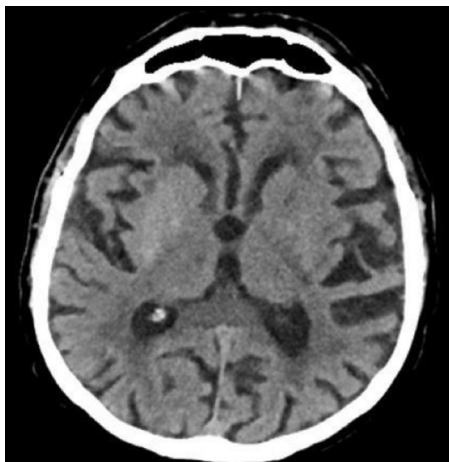
Results: His glucose level on admission was 512.6mg/dL, glycated hemoglobin was 14%. CT scan of the head demonstrated an abnormal increased intensity within the right striatum. Treatment consisted of symptomatic treatment of chorea and improvement of blood glucose control. Tiapride was started with a dose of 100mg 4 times a day. The patient was initiated on intensive insulin therapy which included insuline glargine (Lantus) 10 units every evening and 12 units of insuline glusine (Apidra) 3 times a day with meals. Abnormal movements resolved after normoglycemia was achieved approximately 7 days after admission. Though striatal hyperdensity was still present at follow up CT scan after 10 days, it was less pronounced.



Follow up CT scan

Conclusion: Diabetic striatopathy is rare but treatable disorder and should be considered in patients with poorly controlled diabetes who present with hemichorea.

Disclosure: Nothing to disclose



CT scan of head on admission

EPO1332

The characteristics of 4 patients with ANCA associated vasculitis developing neurological symptoms at the onset

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Background and aims: It is reported that central nervous system (CNS) is affected in less than 15% of patients with ANCA associated vasculitis (AAV). CNS involvement usually presents late in the disease course.

Methods: We experienced 4 patients with AAV who were admitted to our hospital during the period from December 2014 to August 2019, and who developed neurological symptoms at the disease onset. The main characteristics of these 4 patients were compared to those in previous reports.

Results: Mean age was 67 (56-83), and 2 patients were female. 2 patients were affected with hypertrophic pachymeningitis (HP), one developed cerebral infarction, and another patient developed cavernous sinus syndrome (CSS) at the onset. MPO-ANCA was positive in one patient with pachymeningitis, and PR3-ANCA was positive in other 3 patients. No one met the diagnostic criteria of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA). 3 patients excluding a patient with cerebral infarction achieved remission of CNS symptoms with steroid and other immunosuppressive drugs.

Conclusion: As previously reported that HP is the most frequent CNS presentation, our 2 patients developed HP. CNS can be affected late in the disease course and heterogenous neurological symptoms may hinder early diagnosis and treatment of AAV. 3 patients in our cases achieved remission of CNS symptoms probably because ANCA was early detected.

Disclosure: Nothing to disclose

Neuro-ophthalmology/neuro-otology

EPO1333

Cancer of unknown primaries (CUP) invading the jugular vein presenting with unilateral complete ophthalmoplegia: a case report

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Background: Cavernous sinus thrombosis (CST) accounts for 1-4% of cerebral sinus venous thrombosis. Septic CST are due to regional infections draining into the cavernous sinus (CS), aseptic CST are caused by hypercoagulability in malignancies, thrombophilia or pregnancy. Clinical signs include oculomotor palsies because these nerves run through the CS.

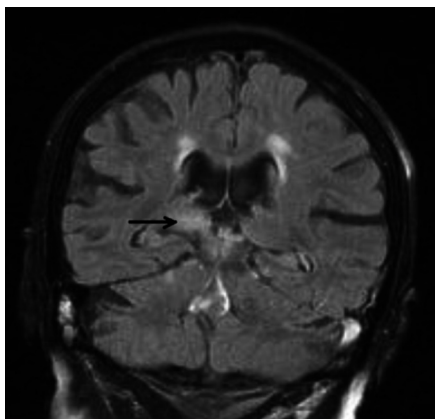
Aims: To present an unusual presentation of CST.

Methods: Case Report: An 84-year-old woman presented with a history of diminished appetite, left temporo-orbital headache and double vision. Neurological examination was normal, the erythrocyte sedimentation rate was 42mm/1h, a cranial CT was normal. Giant cell arteritis was suspected and corticosteroids given. On the following day she had developed a left abducens palsy. A brain MRI showed a hyperintense lesion of the right thalamus and midbrain, MR-spectroscopy was normal. Complete left ophthalmoplegia with ptosis developed within a week and edema of the left arm.

Results: Sonography revealed thrombosis of left axillary, subclavian and internal jugular veins. Another MRI demonstrated thrombosis of the left CS, sigmoid sinus and internal jugular vein, heparin was given. Further examination revealed a thyroid tumor with infiltration of the left carotid artery and jugular vein. Biopsy of pulmonal nodes revealed poorly differentiated epitheloid non-small cell malignancy. The patient deteriorated and died due to pneumonia. Postmortem examination was denied.

Conclusion: Our patient developed progressive unilateral ophthalmoplegia due to CST because of malignant jugular vein infiltration. In retrospect the thalamic and midbrain hyperintensities were due to thrombosis of deep cerebral veins. Our case contributes to unusual cases of CST.

Disclosure: Nothing to disclose



MRI coronar flair image; arrow to thalamic hyperintensity

EPO1334

Spinal medulloblastoma presenting with severe visual loss due to Pseudotumor Cerebri

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Background and aims: Case Report

Methods: A 34 year-old man presented with headache, blurred vision and diplopia. Neurological examination revealed only severe bilateral atrophic papilledema with severe constriction of the visual fields. There was also macular edema with visual visual acuity reduced to 0.2 and 0.3. Colour vision was 0/21. Brain MRI and CT venography were normal. CSF was xanthochromic with a pressure was 50cm water, total protein of 495mg/dl (normal 15-40), glucose of 10mg/dl (normal 40-70), but no white cells, red cells, or malignant cells. After standing for 1 hour the CSF clotted. Tests for tuberculosis, syphilis and cryptococcosis were all negative. Emergency bilateral sequential optic nerve sheath decompressions were done. Spine MRI showed a contrast-enhancing lesion in the lumbar spine, hypermetabolic on PET. Biopsy showed primitive neuroectodermal tumor (PNET).

Results: After 2 months visual acuity, color vision, and visual field remained same, but headaches had gone.

Conclusion: Spinal tumors are a rare but recognized cause of pseudotumor cerebri; we found 2 previous reported cases due to spinal PNET (1,2). The mechanism might be the very high CSF protein causing Froin's syndrome (3).

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Disclosure: Nothing to disclose

EPO1335

Biomarkers of visual deterioration in newly diagnosed Idiopathic Intracranial Hypertension patients

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Background and aims: Idiopathic intracranial hypertension (IIH) is a disorder of unidentified etiology characterized by raised intracranial pressure (ICP) without clinical, laboratory or radio-logical evidence of intracranial pathology. The aim of this work was to determine the visual outcome in newly diagnosed IIH patients.

Methods: The study included 68 IIH patients; 59 responded to medical treatment and 9 needed lumbo-peritoneal shunting (LPS). Patients were submitted to papilledema grading using Frisén Scale, water CSF manometry, brain MRI/MRV, mean deviation of visual field examination (MD-VFE), optic nerve sheath diameter (ONSD), average optic disc optical coherence tomography–retinal nerve fiber layer (OCT–RNFL) thickness and pattern–reversal visual evoked potential (VEP).

Results: Patients needed LPS showed statistically significant increase in baseline papilledema grade, MD-VFE, ONSD, average OCT–RNFL thickness and P100 VEP latency. On the other hand, both studied groups showed statistically non-significant differences regarding the patients' ages and opening CSF pressure.

Conclusion: Newly diagnosed IIH patients' evaluation must be based on multimodality neuroophthalmological assessment where papilledema grade, MD-VFE and OCT–RNFL are valuable biomarkers of PVD while P100 VEP latency delay is a predictor of poor visual outcome and ONSD is an early indicator of elevated ICP regression after LPS surgery.

Disclosure: Nothing to disclose

EPO1336

Bilateral cerebral ptosis in the patient with subdural hemorrhage: A Case Report

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Incheon, Korea, Republic of

Background and aims: Differential diagnosis of bilateral ptosis can be challenging due to multiple etiologies. Although cerebral ptosis is rare, it is known to be frequently associated with the unilateral right hemispheric lesion. We report a bilateral cerebral ptosis case developed after acute right subdural hemorrhage (SDH).

Methods: A 79-year-old woman presented with mild left hemiparesis, bilateral complete ptosis and headache after falling accompanied by loss of consciousness. Computed Tomography of the brain revealed a traumatic right fronto-temporo-parietal SDH without midline shift and there was no evidence of parenchymal lesion in brain Magnetic resonance imaging. She underwent craniotomy with hematoma removal. However, even when she attempted to try opening her eyes, she could not open her eyes at all despite frontalis contraction. There was no evidence of abnormalities in the neuro-ophthalmologic evaluation including pupil reflex, gaze deviation or visual field loss.

Results: Bilateral ptosis was gradually improved with intensive rehabilitation. On neuroimaging, the brain perfusion single-photon emission computed tomography (SPECT) and Diffusion Tensor Imaging (DTI) were conducted. The brain perfusion SPECT revealed hypoperfusion in the left frontal, right temporal regions, and right basal ganglia. The bilateral intact corticospinal tract was visualized in DTI. Bilateral ptosis resolved almost completely and she could walk independently at hospital discharge.

Conclusion: In our case, the brain perfusion SPECT can provide additional information. Right hemispheric hypoperfusion in brain perfusion SPECT implied that lateralization of eyelid control is dominant to the right hemisphere consistent with previous reports. Bilateral cerebral ptosis after the right SDH showed a favorable prognosis of recovery.

Disclosure: Nothing to disclose

EPO1337

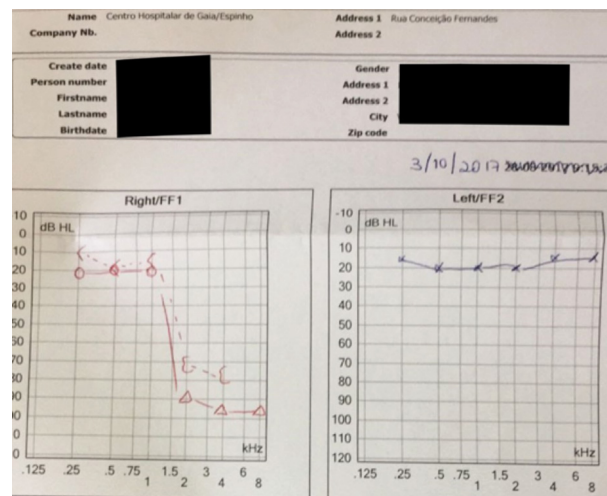
Is the HINTS plus approach in dizziness infallible?J. Costa Novo¹, J. Larangeiro², H. Felgueiras¹

¹Neurology, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal, ²Otorhinolaryngology, Head and Neck Surgery, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

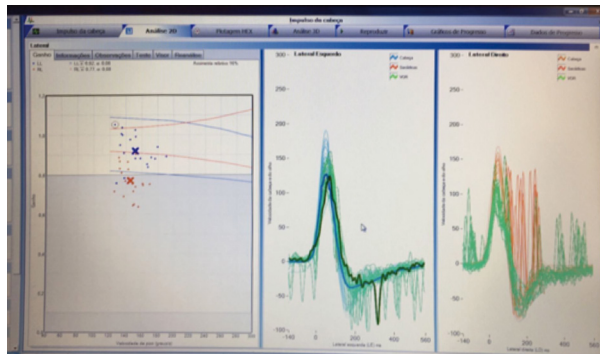
Background and aims: Acute labyrinthitis is characterized by the sudden onset of persistent vertigo, nystagmus, nausea, hypoacusis and head movements intolerance, which may last days to weeks and resolve gradually. Some neurological diseases should be considered in their differential diagnosis (namely stroke and demyelinating diseases of the central nervous system (CNS)).

Methods: Case report

Results: An 18-year-old woman comes to the emergency department for vertigo, right hearing loss, nausea and worsening vomiting in the last 3 days. The clinical examination highlighted: left horizontal-rotatory grade III nystagmus, a positive right-sided head impulse test and absence of skew deviation. The audiogram revealed neurosensory deafness above 1000Hz. Acute labyrinthitis, was assumed. She was hospitalized for treatment with dexamethasone and betahistine, with complete recovery during hospitalization and improvement of the audiogram parameters. For this reason a brain magnetic resonance imaging was ordered, revealing multiple lesions in a typical demyelinating disease topography including 1 in the right middle cerebellar peduncle and in the cerebellar hemisphere white matter. Later, as the study was completed, Multiple Sclerosis (MS) was diagnosed and treatment started.



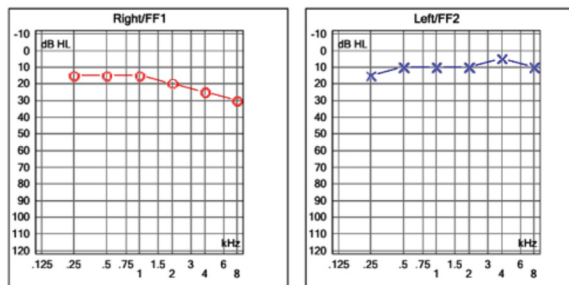
First audiogram



Video Head Impulse Test report

Create date	06-10-2017 14:20	Gender	Female
Person number	[REDACTED]	Address 1	[REDACTED]
Firstname	[REDACTED]	Address 2	[REDACTED]
Lastname	[REDACTED]	City	[REDACTED]
Birthdate	[REDACTED]	Zip code	[REDACTED]

06-10-2017 14:20:31



Second audiogram (three days later)

Conclusion: In this case, the HINTS plus (head-impulse test/nystagmus/test-of-skew, 'plus' new hearing loss) protocol was initially applied and there were no findings suggestive of central etiology. The evidence of rapid hearing recovery was important as it provided the diagnostic clue for CNS disease. Acute vertigo syndrome in young patients is one frequent presentation of MS and should be considered in its differential diagnosis. It is therefore mandatory to follow up these patients.

Disclosure: Nothing to disclose

EPO1338

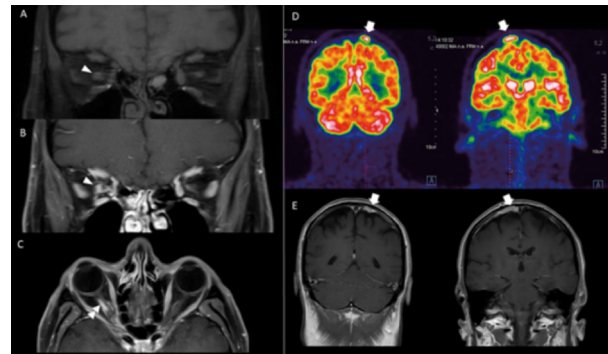
Slowly progressive optic perineuritis as the first clinical manifestation of sarcoidosis

E. Garri¹, F. Rinaldi¹, D. Simonato², M. Margoni¹, P. Gallo³

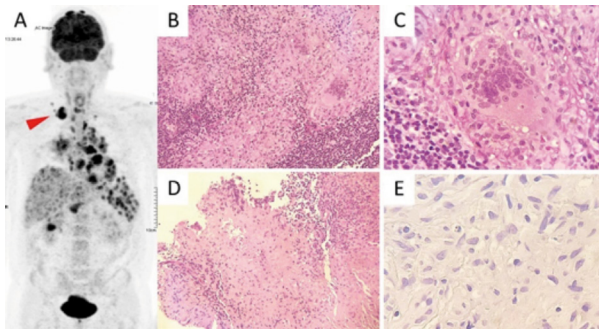
¹Department of Neurosciences, Neurology Clinic, Padua, Italy, ²University of Padua, Padua, Italy, ³Padua, Italy

Background and aims: Isolated involvement of the optic nerve in neurosarcoidosis is a rare event. The inflammation of the optic nerve sheath, i.e., optic perineuritis, is even more rare especially at clinical onset. We report a quite unique case of optic perineuritis, as the first presenting manifestation of sarcoidosis.

Methods: In November 2018, a 56-year-old man developed a painless blurred vision in the right eye with mild photophobia. Neuro-ophthalmological examination and brain-MRI performed at this time were normal. Haematological and immunological screenings were unremarkable. The patient arrived at our attention on April 2018. He reported a further marked reduction in visual acuity. A Brain-MRI disclosed the gadolinium-enhancement with tram track and doughnut signs of the right optic nerve, suggestive of optic perineuritis, while no abnormality in the left optic nerve was detected (Fig. 1 A-C). CSF examination was not significant. ACE was negative in blood and CSF. The patient's visual acuity continued to worsen, and brain and orbit 3Tesla MRI performed in June showed the appearance of two focal areas of dura mater thickening (Fig. 1D). Thus, a whole body combined PET/MRI was performed showing the hypermetabolic signal of the 2 dura mater thickenings (Fig. 1E) as well as multiple widespread hypermetabolic areas. A lymph-node was biopsied disclosing a typical sarcoid granuloma (2 B,C,D,E)



Results: MRI may be unrevealing if performed early in the disease course. Thus, serial MRI scans are recommended.



Conclusion: Whole body ^{18}F -FDG PET/MRI has to be considered since it may provide evidence of a systemic pathology as sarcoidosis.

Disclosure: Nothing to disclose

EPO1339

Functional and structural assessment of the visual pathway increases diagnostic accuracy in several neurological conditions: a case series.

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Department of Neurology and INSPE, Ospedale San Raffaele - Vita-Salute San Raffaele University, Milan, Italy

Background and aims: visual disturbances represent a common complaint in neurological clinical practice. Full-field visual evoked potentials (ff-VEPs) are a widely used tool to document functional abnormalities subtending these symptoms. Sometimes ff-VEPs accuracy may be not sufficient to detect the pathological process going on. In these situations the diagnostic work-up may be completed with other techniques, like multifocal VEPs (mf-VEPs) and optical coherence tomography (OCT).

Methods: case collection showing the usefulness of a neurophysiological evaluation, comprehensive of OCT and mf-VEP, in the presence of normal or non-diagnostic ff-VEPs

Results: mf-VEPs are useful to detect visual pathway involvement in the case of suspected optic neuritis (ON) in the presence of non-diagnostic ff-VEPs and OCT (case 1). Sometimes mf-VEPs can be useful also to characterize the pathological process when ff-VEPs are not informative, as in the case of severe visual loss due to NMOSD with absent ff-VEPs response (case 2). In other cases OCT may support differential diagnosis, as in a MS patient with a visual loss due to central retinal vein occlusion and not to recurrent ON, as initially postulated (case 3). Mf-VEPs also proved to be useful to objectivate visual pathway abnormalities in the case of compressive disorders (case 4) or cerebrovascular conditions (case 5).

Conclusion: these cases exemplify ff-VEPs may fail in identifying abnormalities particularly in the presence of a sectoral involvement of the visual pathway. In the presence of a complaint for visual disturbances and normal ff-VEPs examination, we suggest a multimodal approach, including OCT and mf-VEPs.

Disclosure: Nothing to disclose

EPO1340

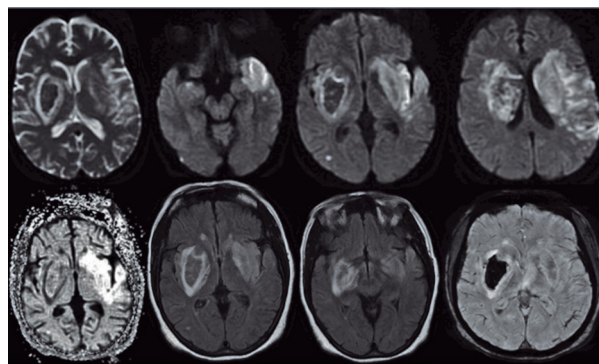
Ping-Pong Gaze: the eyes that look at the injury

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D.E. Barbero Jiménez¹, A. Garcia-Puente Garcia³,
I. López-Zuazo Aroca¹, J. Hernandez Cristobal¹,
A. Yusta Izquierdo¹

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University Hospital, Spain, Guadalajara, Spain, ³Family
Medicine, University Hospital of Salamanca, Salamanca,
Spain

Background and aims: We present an unusual case of bilateral hemispheric Stroke of undetermined cause with atypical clinical presentation Ping-Pong Gaze (PPG).

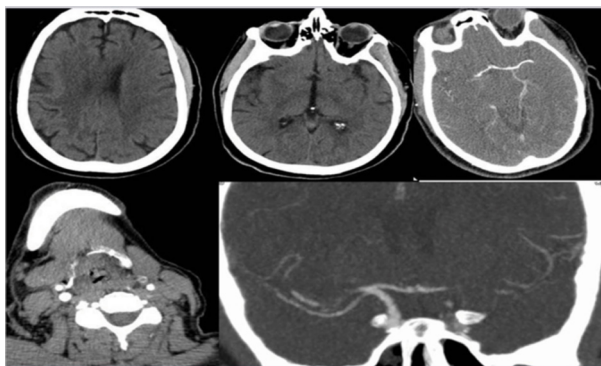
Methods: A 66-year-old woman with a history of schizophrenia, brought to the Emergency Department after being found obnubilated, with the impossibility of language emission and weakness in the left hemibody. Intrahospital stroke code is activated presenting NIHSS 19. Thrombectomy is rejected by RANKIN 3 and IV fibrinolysis is initiated. At the end rTPA she stayed in deep coma (Glasgow 4) accompanied by horizontal alternating Roving movements. Hemorrhagic transformation and intracavitary heart thrombus are ruled out. Brain MRI is performed by diagnosing bilateral hemispheric ischemic stroke.



Brain MRI

Conclusion: We present a rare case of bilateral hemispheric stroke of undetermined cause, probably embolic (ESUS) that led to the death of the patient in less than 6 hours. We also highlight the atypical clinical presentation with PPG, described by Senelick in 1976. In PPG the eyes move horizontally, conjugately, and rhythmically (with a cycle lasting few seconds) in a pendular manner between the 2 extreme positions, without any associated head movements. This occurs as a result of severe bilateral hemispheric injury, or posterior fossa damage with the brain stem intact and, more rarely, drug toxicity (monoamine oxidase inhibitors administered with or without neuroleptics).

Disclosure: Nothing to disclose



Cranial CT and AngioTC

Results: Cranial CT with angioTC is performed presenting ASPECT 10 and thrombus in MI of right ACM and occlusion of CII in its proximal and intracavernous portion. Urgent ecocardiosthoracic without cavity thrombus. Brain MRI ischemic stroke ACMI and in frontal and parietal right territory.

EPO1341

No significant Endolymphatic Hydrops in Vestibular Paroxysmia

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Background and aims: Current studies point to endolymphatic hydrops (ELH) being a pathophysiological syndrome not discriminatory to Menière's disease. Rather ELH seems to be triggering other recurrent dizziness attacks [1] such as in vestibular migraine. However, the data remains scarce.

Methods: Therefore, 18 patients with vestibular paroxysmia (VP; 6 females, mean age 55, range 20-77) – a neurovascular cross-compression (NVCC) of the 8th nerve [2] – were age- and gender-matched to 18 healthy controls (HC; 9 females, mean age 53, range 21-84) and underwent delayed intravenous MRI of the inner ear. ELH was characterized [3,4] and quantified using atlas-based segmentation and local thresholding algorithms. Further diagnostic workup included VOG during caloric stimulation, head-impulse test and audiometry.

Results: As a result, 22% of VP showed an ELH grade I, 39% a mild accumulation of endolymph fluid (ELA) (grade I following Nakashima 2009, grade 0 following Barath 2014) without qualifying as a hydrops and 89% visualized the NVCC. A unilateral ELH in VP was always accompanied by evidence of an ipsilateral NVCC. In comparison, no HC had an ELH, and only 3% showed an ELA ($p > 0.01$). No correlations between electrophysiological data or grade of ELH and duration of illness or number of attacks were found.

Conclusion: In conclusion, for the most part, VP does not seem to entail an ELH in the proper sense. However, VP seems to cause a mild accumulation of endolymphatic fluid when compared to healthy controls, possibly as a sign of disturbance of the inner ear homeostasis by the NVCC.

Disclosure: Nothing to disclose

EPO1342

Acute vertigo: diagnostic concordance after Neurology observation at emergency department

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Neurology Department, Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal

Background and aims: Acute vertigo (AV) is often a challenging condition. Because of its multidisciplinary nature and multiple causes, patients are frequently observed not only by Neurologists, but also Physicians from other areas, such as Internal Medicine and particularly Otorhinolaryngology. We aimed to assess the diagnostic concordance of AV in patients observed by Neurology and other medical specialties.

Methods: Retrospective study with selection of all patients with AV observed by Neurology at the emergency department (ED) of a tertiary centre in 2019, regarding demographic data, imaging studies, diagnosis by Neurology at ED, diagnostic concordance after Otorhinolaryngology observation at ED and after ED discharge by different medical specialties.

Results: 104 patients were identified, 54 (52%) of them females. The mean age was 57.6 years. 45% had a history of AV. 80% underwent imaging studies (CT scan and/or MRI). The most frequent diagnosis established by Neurology was benign paroxysmal positional vertigo, followed by vestibular neuronitis. 58 patients were also observed by Otorhinolaryngology with an overall concordance rate of diagnosis of 45%. 54 patients were observed after ED discharge, mostly in Balance Disorders Outpatient Clinic. Diagnosis by Neurology at ED was not significantly different from observation by other medical specialties after ED discharge ($p = 0.15$) regarding the distinction between peripheral and central causes of AV.

Conclusion: Taking into account diagnosis concordance rate at ED and after discharge, our data suggest that patients with AV should be primarily evaluated by Neurology at ED, avoiding redundant observations and allowing faster patient management.

Disclosure: Nothing to disclose

EPO1343

Superior ophtalmic vein thrombosis.

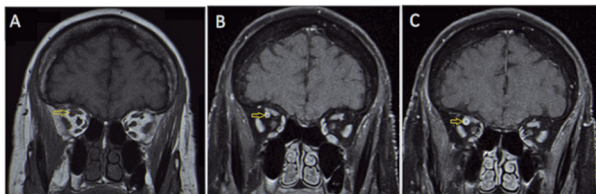
E. Marin Conesa¹, A.M. García Medina¹,
I. Pellicer Espinosa¹, E. Gómez López¹,
M. Martínez Zarco¹, M. Morales de la Prida²,
F.J. Pareja Herrero¹, L. Sanchez Alonso¹,
I. Pena Fernández¹, N. Lacasa Perez³, J. Marín Marín¹,
J.M. Rodríguez García¹, J.A. Iniesta Valera¹

¹Neurology, Hospital General Universitario Reina Sofía, Murcia, Spain, ²Murcia, Spain, ³Hospital General Universitario Reina Sofía, Murcia, Spain

Background and aims: Superior ophthalmic vein thrombosis (SOVT) may present similar to, or occur together with, orbital cellulitis (OC) or cavernous sinus thrombosis (CST). According to a recent review of SOVT, the aseptic etiologies were more frequent than septic ones. Aseptic causes include vascular malformations, autoimmune/systemic diseases, trauma, Haematological diseases, Malignancies or neoplasms, Hormonal Minestrine and others (e.g: diabetes, idiopathic). Septic ones are sinusitis, orbital infections, facial infections and others (e.g: otomastoiditis, Lemierre syndrome).

Methods: We describe a 77-year-old woman with a sudden palsy of 3rd and 4th cranial nerves due to a superior ophthalmic vein thrombosis.

Results: A 77-year-old woman with a history of high blood pressure, diabetes mellitus, obesity, atrial fibrillation in treatment with Rivaroxaban (15mg/24h), obstructive sleep apnea hypopnea syndrome and chronic renal disease, presented a sudden ptosis of right eyelid. At the hospital, a complete 3rd and 4th right cranial nerves palsy was observed. Brain MRI (figure, A-E) revealed right superior ophthalmic vein thrombosis (SOVT). Analyses showed high homocysteine levels. Other possible differentials were excluded. Treatment with Acenocumarol was initiated with an improvement of symptoms.



Brain and orbits contrast MRI scan: T2-FLAIR (A) sequence reveals enlargement of caliber of right superior ophthalmic vein wall (A, arrow). Gadolinium-enhanced fat-saturated T1-weighted imaging (B and C) shows an increase in caliber and abnormal enhancement of right superior ophthalmic vein wall (B and C, arrow).

Conclusion: The patient presented a painless complete 3rd and 4th cranial nerve palsy due to acute isolated superior ophthalmic vein thrombosis. This pathological condition usually accompany cavernous sinus thrombosis, but not this time. Many pathologies can cause this disease, hence an exhaustive study must be done in order to rule out treatable conditions. Aseptic causes are more frequent than septic ones. Whether all complementary tests are normal, idiopathic cause may be considered.

Disclosure: Nothing to disclose

EPO1344

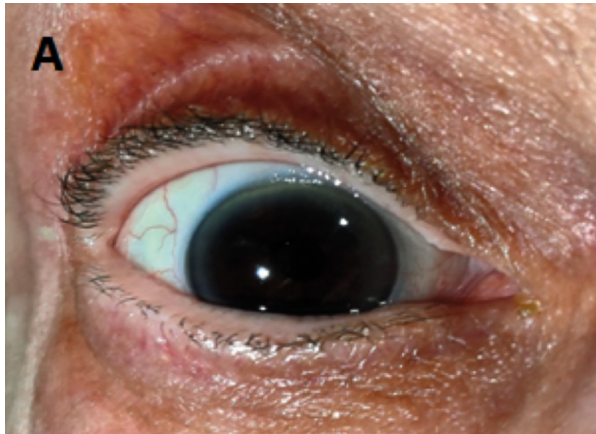
Incomplete third nerve palsy with pupillary involvement following intravitreal anti-VEGF therapy for neovascular age-related macular degeneration: case report and literature review

F. Perez Trapote, J. Gómez Corral, R. Sainz Amo,
A. Celdrán de Castro García, B. Baena Álvarez,
A. Saez Marin, P. Lorenzo Barreto,
E.S. Stiauren Fernandez, N. García Barragán, F.J. Buisan
Neurology, Hospital Universitario Ramón y Cajal, Madrid, Spain

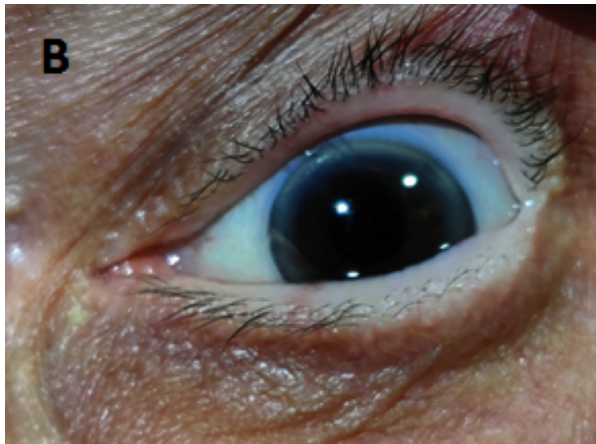
Background and aims: Intravitreal injection of anti-vascular endothelial growth factor (VEGF) has been extended as a useful therapy at neovascular age-related macular degeneration (NVAMD) treatment. Reviewing medical literature suspected adverse systemic events are scarcely described including a sixth and one sparing pupil third nerve palsy .

Methods: A literature review on cranial nerve palsy following intravitreal anti-VEGF was done. Herein we present the 1st case of 3rd nerve palsy with pupillary involvement in a patient on Bevacizumab treatment.

Results: An 85-year-old woman with left NVAMD and mild hypertension presented to the emergency room complaining about dizziness and double vision after the 4th bevacizumab injection given 3 weeks before. On examination she had a marked reduction in adduction and elevation as well as ptosis and mild light reactive mydriasis in the left eye. Angio and brain MRI scan showed no evidence of infarction of any relevant abnormalities of the major cerebral vessels. Based on this we consider a vasculopathic form of oculomotor nerve palsy by occlusion of the small penetrating arteries secondary to the antiangiogenic therapy.



A: Right eye, showing a reactive to light pupil with normal size.



B: Left eye, showing a mild light reactive mydriatic pupil due to parasympathetic fibers damage.

Conclusion: Intravitreal anti-VEGF therapy appeared to be safe and well tolerated. Nevertheless, some severe systemic side effects related to its antiangiogenic activity may show up. As physicians we should be aware of this potential relationship between microvascular damage and anti-VEGF therapy when using this treatment on an elderly AMD population.

Disclosure: Nothing to disclose

EPO1345

Bilateral optic neuritis of immune etiology by nivolumab, an anti-PD-L1 antibody.

A case report.

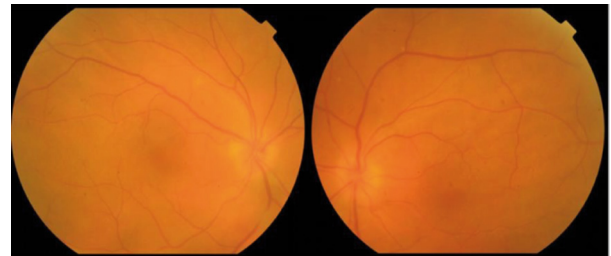
M. Vicente-Pascual¹, K. Rosas-Soto², E.P. Murata-Yonamine³, D. Vázquez-Justes¹, F. Purroy¹, A. Traveset-Maeso⁴

¹Department of Neurology, Arnau de Vilanova Hospital, Lérida, Spain, ²Department of Neurosurgery, Arnau de Vilanova Hospital, Lérida, Spain, ³Department of Oncology, Arnau de Vilanova Hospital, Lérida, Spain, ⁴Department of Ophthalmology, Arnau de Vilanova Hospital, Lérida, Spain

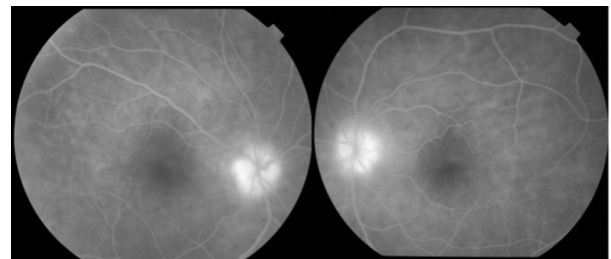
Background and aims: Checkpoint inhibitors have been established as an alternative treatment for various cancers, including renal cancer. Among these drugs are nivolumab, a human monoclonal antibody immunoglobulin type G4 that binds to the programmed death receptor 1. Since these treatments exert their activity by activating the immune system to attack tumor cells, immune adverse reactions are being described.

Methods: We presented a 70-year-old woman with a history of cell renal carcinoma, with nephroureterectomy and subsequent adjuvant chemotherapy with sunitinib. After 2 years it was discontinued due to symptomatic hypothyroidism and neutropenia. Therefore, treatment with nivolumab was started. After the third cycle, a decrease in bilateral visual acuity began.

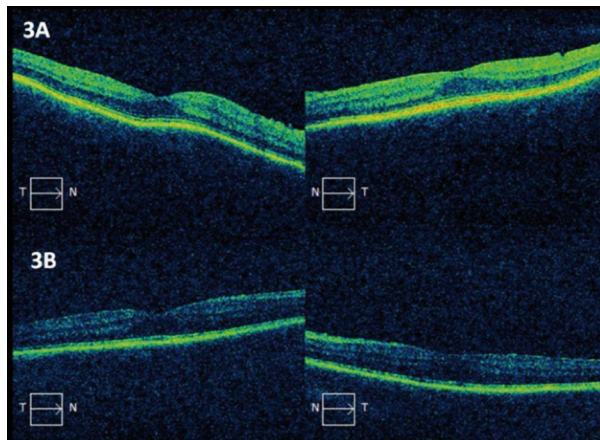
Results: The ophthalmological study showed papillae edema (figure 1), a fluorescein angiography showed bilateral hyperfluorescence (figure 2) and the optical coherence tomography showed thickening of ganglion fibers (figure 3A), all compatible with bilateral optic neuritis. The neurological study was normal. After removing the drug, papillae edema disappeared, without progressing the visual deficit (figure 3A).



Fundus showing bilateral papillae edema. Right eye in the image on the left. Left eye in the image on the right.



Fluorescein angiography shows bilateral papillary hyperfluorescence.



A: Optical coherence tomography (OCT) performed with treatment with nivolumab. It showing thickening of ganglionic fibers. Right eye in the image on the left. Left eye in the image on the right. B: OCT performed after removing the nivolumab. Normal OCT. Right eye in the image on the left. Left eye in the image on the right.

Conclusion: To date 2 cases similar to our patient have been described. 1 of them presents a child with a glioblastoma multiforme, who developed optic neuritis 3 days after the 2nd cycle of treatment. The 2nd is about an adult with lung carcinoma, who presented a left optic neuritis, associated with hypopituitarism. We reported the 3rd case presenting with optic neuritis, which is possibly an immune related adverse event associated with anti-PD-L1 antibody treatment. We concluded that optical toxicity of nivolumab should be considered as a serious and possible adverse event.

Disclosure: Nothing to disclose

Neurotoxicology/occupational neurology

EPO1346

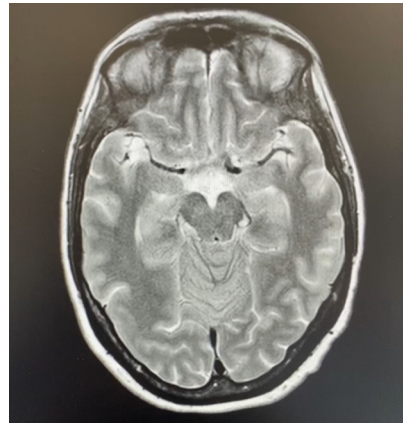
Neurotoxicity after bupivacaine administration: description of 2 cases.

G. Agirre Beitia¹, A. Moreno Estébanez¹,
T. González-Pinto González¹, L. Cabral Martínez¹,
A. Jauregui Barrutia², M. Fernández Martínez¹,
J.J. Zarranz Imirizaldu¹, A. Rodríguez-Antiguedad¹
¹Neurology, Cruces University Hospital, Barakaldo, Spain,
²Neurology, Cruces University Hospital, Osakidetza,
Barakaldo, Spain

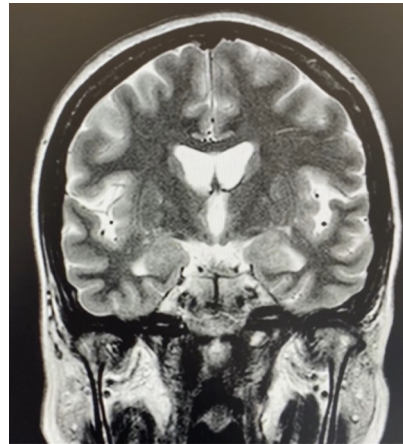
Background and aims: Bupivacaine is a common anesthetic, frequently used in surgical procedures. The use of bupivacaine had not been associated with permanent effects in memory, until now.

Methods: We describe 2 cases of patients with permanent anterograde amnesia, lymphocytic meningitis and bilateral hippocampal lesion following bupivacaine administration.

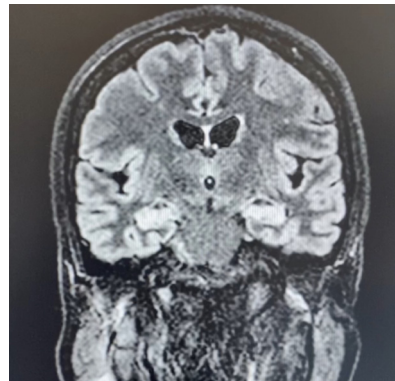
Results: The 1st patient is a 38-year-old pregnant woman who received bupivacaine epidurally during labor induction. 2 hours later, the patient presented confusion, disorientation and anterograde amnesia. The 2nd patient is a 68-year-old woman who underwent renal calculi coral surgery who received spinal anesthesia with bupivacaine. After the intervention, the patient presented disorientation and anterograde amnesia. In both cases, the study of cerebrospinal fluid showed lymphocytic pleocytosis, with a normal biochemical and microbiological study. The cerebral MRI of the patients show a diffuse, bilateral and symmetrical alteration in both hippocampi, without detecting other parenchymal or vascular alterations (Figure 1, 2 and 3). In none of the cases, despite a large study, no other possible precipitant of the condition was found, establishing as a more probable diagnosis the bupivacaine neurotoxicity with bilateral hippocampal involvement.



Axial T2 MRI image



Coronal T2 MRI image



Coronal STIR Flair MRI image

Conclusion: Despite the passage of time, the 2 patients continue with a permanent amnesia of anterograde predominance, with a striking defect in topographic memory. We have not found in the literature any article describing a similar sequence of events. Although infrequent, given the severity and disabling effect it has on patients, we consider it important to describe these cases. The possible adverse drug reaction has been reported to the European pharmacovigilance service.

Disclosure: Nothing to disclose

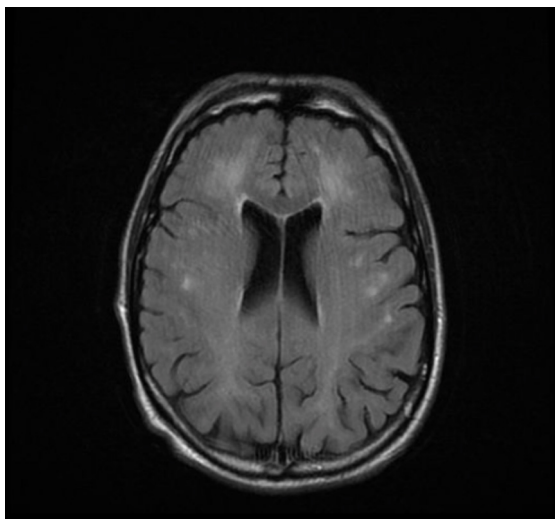
EPO1347

Acute retention of urine as an initial symptom of delayed hypoxic encephalopathy

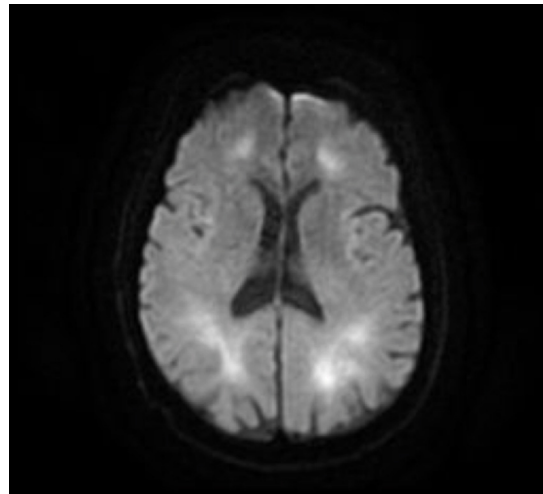
D.E. Barbero Jiménez, G. Carvalho Monteiro, J. Celi Celi, B. Povedano Margarit, J. Hernandez Cristobal, J.M. Fernández Carril, A. Yusta Izquierdo
Neurología, Hospital Universitario Guadalajara, Guadalajara, Spain

Background and aims: Delayed posthypoxic leukoencephalopathy (DPHL) is a demyelination syndrome characterized by the onset of neuropsychiatric symptoms weeks after exposure to low concentrations of oxygen or CO poisoning. It's diagnosed by medical history and diagnostic test, especially magnetic resonance imaging (MRI).

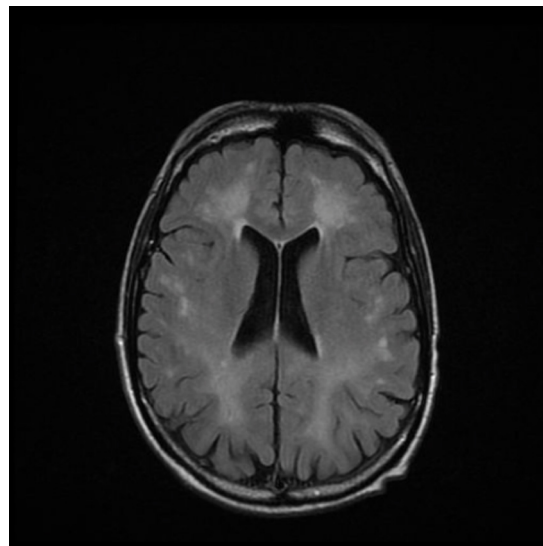
Methods: We present a 63-year-old man who, after climbing in Bolivia at 3600 meters, is found unconscious in his shelter the next day, near a combustion engine. He regained consciousness spontaneously and was diagnosed with altitude sickness. After 10 days, he begins with temporo-spatial disorientation and bradypsychia, in neurological examination appears dysnomia and agrafia with Mini-Mental State Examination of 14/30. EEG demonstrated slow and desynchronized activity in a generalized way. Brain MRI^{1,2} showed demyelinating lesions in bilateral white matter at the frontoparietotemporal level with cytotoxic edema. Brain MRI³ at 7 days showed lesion growth, initiating treatment with hyperbaric oxygen for 25 sessions. MRI was repeated at 5 months with decrease of described radiological findings and almost complete clinical recovery.



Brain MRI1: Extensive involvement of the white, bilateral and symmetrical substance, at the frontoparietotemporal level, with some left occipital lesion, with hypersensal in T2 and FLAIR



Brain MRI2: In diffusion weighted imaging (DWI) hypersensal is observed due to restriction of the movement of free water molecules, translating the presence of cytotoxic edema,



Brain MRI3: The extensive involvement of deep white, periventricular and semioval centers at the frontal, parietal, temporal and occipital, bilateral and symmetric levels, hyperintense in T2 and FLAIR is even more striking than in the previous study.

Results: In DPHL the symptoms that may appear are extrapyramidal syndrome, memory disorders and urinary incontinence, among others. In our patient, draws attention to the appearance of acute retention of urine and the subsequent presentation of cognitive symptoms, with 2 possible pathophysiological mechanisms such as hypobaric hypoxia and poor CO combustion.

Conclusion: DPHL has a variable prognosis, it must be recognized early. The treatment in hyperbaric chambers is discussed, although after the good clinical and radiological evolution of our patient we support the performance of deferred hyperbaric therapy to reduce cerebral edema and increase remyelination.

Disclosure: Nothing to disclose

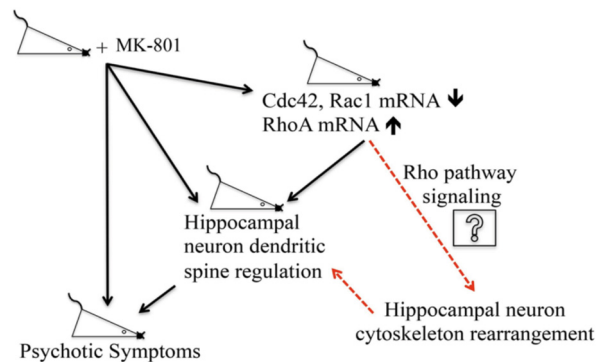
EPO1348

Haloperidol induced behavior rehabilitation and Rho signaling regulation in the brain of dizocilpine rat model of schizophrenia

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Background and aims: The molecular mechanisms for antipsychotic drug (APD) in smoothing psychotic symptoms are still unclear. Dizocilpine, also named MK-801, was mentioned could induce schizophrenia-like psychotic symptoms in various animals. Also, MK-801 was reported that can modulate Rho family proteins mRNA expressions and also the dendritic spines morphology in rat hippocampus. MK-801 induced hippocampal neuron impairments and dendritic spines modulation have been linked to the psychotic symptoms in rats. This study tries to clarify the relations between Rho signaling regulation and MK-801 induced abnormal psychotic behaviors in mice.



MK-801 could induce psychotic symptoms in mice and also could modulate RhoA/Cdc42 expression. The RhoA/Cdc42 were also mentioned could modulate hippocampal neuron post-synaptic dendrite expression related to psychotic symptoms. **We try to verify whether Rho signaling pathway controlled cytoskeleton rearrangement and F-actin condensation are related to hippocampal neuron dendritic spines expression and psychotic symptoms induction in MK-801 psychotic mice model.**

Methods: Hyperactivity in C57BL/6 mice was induced by MK-801 treatment and eased by haloperidol treatment. Open field test was used to determine locomotor activity of mice. Immunoblotting were applied to examine Rho signaling protein regulation in the mice cortex. Cytoskeleton rearrangement and cell migration ability in primary neuron culture will be tested further.

Results: Our data showed haloperidol could rescue MK-801 induced hyperactivity in mice (Figure 1). We also found that MK-801-induced RhoA expression induced would be reduced by haloperidol or clozapine treatment (Figure 2) in mice cortex. Both haloperidol and clozapine might recover MK801 induced Cdc42 reduction in mice cortex (Figure 3). MK-801-induced reduction of PSD95 (post-synaptic density 95 protein) would be recovered by clozapine treatment (Figure 3). Also, PAK1 expression would be

reduced by haloperidol treatment in mice cortex (Figure 2) treated with MK-801.

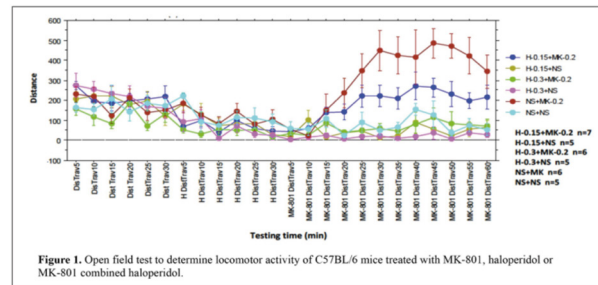


Figure 1. Open field test to determine locomotor activity of C57BL/6 mice treated with MK-801, haloperidol or MK-801 combined haloperidol.

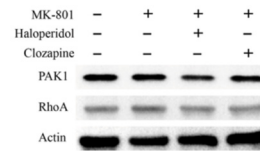


Figure 2. Effects of haloperidol and clozapine on MK-801 induced RhoA and PAK1 modulation.

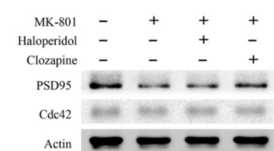


Figure 3. Effects of haloperidol and clozapine on MK-801 induced Cdc42 and PSD95 modulation.

Conclusion: We proposed that APDs might modulate cell biological functions of cortical neurons by regulating Rho signaling to ease the psychotic symptoms or abnormal behaviors induced by MK-801 in mice.

Disclosure: This work was supported by the grant (TCRD-TPE-106-23) of the Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan, Republic of China.

EPO1349

An unsuspected toxic can solve a rare clinical case

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Background and aims: Neurotoxicology is a vast field of study, with a never-ending list of toxics and syndromes. However, recognizing the patterns of the syndromes now considered rare can help us to better diagnose and treat the patients who suffer from them.

Methods: We present the case of a 66-year-old female admitted for dysarthria, paresthesias of the tongue and the limbs, and weakness of the lower limbs, evolving over 3 weeks. As relevant previous history, she denies alcohol consumption. She suffered a car crash in her youth that caused head and hip trauma resulting in right 6th cranial nerve palsy and right hip replacement. The hip prosthesis had to be replaced 3 months prior to her admittance due to prosthetic infection. She was treated with metronidazole since surgery until 2 days before admittance. The neurological examination upon arrival found dysarthria, upbeat nystagmus, weakness of the left leg, hypopalesthesia of the lower limbs, lack of proprioception in hands and feet and ataxia of the left arm, along with a subtle frontal syndrome.

Results: The magnetic resonance showed bilateral red nucleus and olivary nucleus hyperintensity, along with bilateral subcortical white matter hyperintensity (Figure 1). The nerve conduction study disclosed a sensory axonal polyneuropathy. Without metronidazole treatment, the neurological signs significantly improved and the patient was discharged with only mild sensory symptoms remaining.

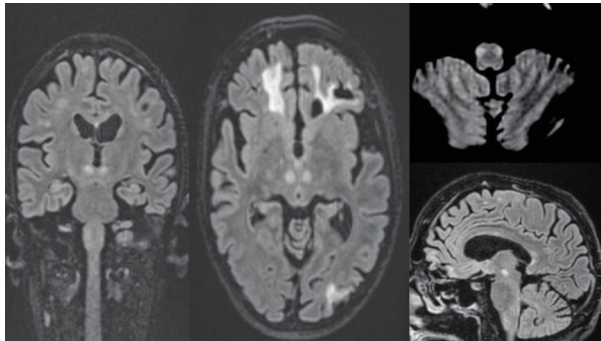


Figure 1. FLAIR sequence cuts (coronal, axial, and sagittal) showing bilateral red nucleus and olivary nucleus hyperintensity, along with bilateral subcortical white matter hyperintensity, besides known lesions secondary to head trauma.

Conclusion: Metronidazole-induced neurotoxicity should be considered in metronidazole-treated patients showing neurological symptoms otherwise unexplained. The magnetic resonance findings are quite specific and help diagnosis. After stopping metronidazole, the majority of patients improve.

Disclosure: Nothing to disclose

EPO1350

Myoneuropathy induced by colchicine toxicity: divergent prognosis for myopathic and neuropathic symptoms.

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Background and aims: Colchicine prevents gout attacks. Its neuromuscular adverse effects are unusual, with only few cases of myoneuropathy published and a prognosis not clearly established.

Methods: A 56-year-old man with stage 5 chronic renal disease and colchicine-treated gout started suffering from distal numbness in all 4 limbs 6 months before admittance. 1 month before consulting, he developed progressive gait instability and weakness in all extremities leading to the loss of independent walking. He had proximal limb weakness with absent muscle stretch reflexes in the legs. Vibration sensation was reduced, and position sensation was abolished in all four limbs. A marked sensory gait ataxia was present.

Results: Laboratory tests showed deterioration of renal function and increase of serum creatine kinase. EMG demonstrated signs of acute sensory motor axonal polyneuropathy. Muscle biopsy showed intracellular vacuoles with basophilic granular material, confirming the diagnosis of vacuolar myopathy induced by colchicine (Figure 1, figure 2). Treatment with colchicine was terminated, resulting in rapidly progressive weakness improvement, consistent with the steady normalization of creatine kinase levels (Figure 3). Numbness and disturbance of vibration and position sensations continued months after discharge revealing that myopathic changes were shortly reversible, not so the neuropathic pathology induced by colchicine.

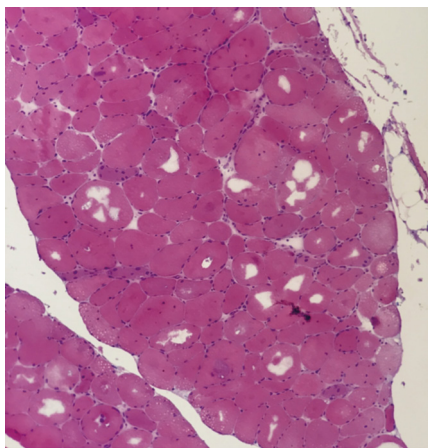


Figure 1- Skeletal muscle with preserved architecture and intracellular vacuoles (H-E, x200)

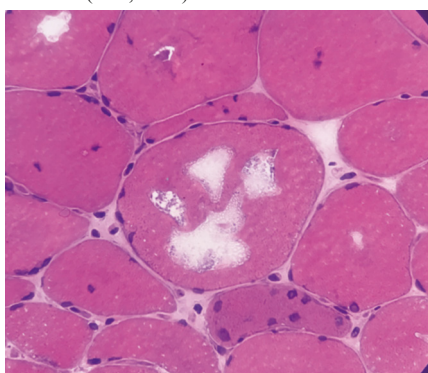


Figure 2- Image of intracellular vacuoles (H-E, x400)

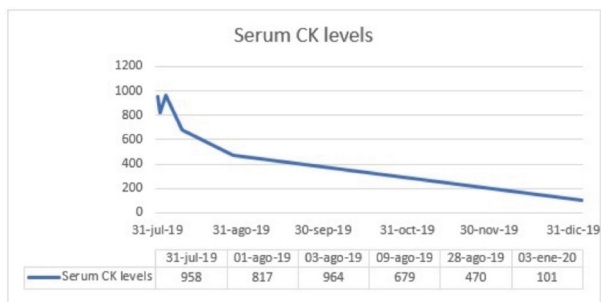


Figure 3- Serum CK levels

Figure 3- Serum CK levels

Conclusion: Colchicine-induced myoneuropathy is characterized by subacute, painless and proximal lower limb weakness. Although uncommon, it should be considered after prolonged colchicine use, even within the usual dose range, especially with risk factors like chronic renal disease or treatments metabolized by the CYP3A4 system. Prognosis seems good for myopathic symptoms, uncertain for neuropathic ones.

Disclosure: Nothing to disclose

EPO1351

Neurological and hematological disturbances joined by the Occam's razor

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Background and aims: Excessive zinc ingestion might cause a decreased copper absorption. It is a possible pathogenic etiology for neurodegeneration of central and peripheral nervous system and hematologic manifestations.

Methods: Case-report.

Results: A 47-year-old male presented a 1-year history of weakness and numbness with a proximally progressive pattern, walking imbalance and urinary symptoms. His previous medical history included a 2-years study of anaemia and leukocytopenia for which he was being investigated by haematology. His examination showed a mild paraparesis with decreased distal pinprick perception to the wrist in the upper limbs and to the hips in the lower limbs; hypopalesthesia to T10 level, hyporeflexia in the upper limbs and lower limbs hiperreflexia, positive Romberg sign and ataxic gait. Analytical study revealed a low serum level of copper and elevated serum and urine levels of zinc. Nerve conduction studies depicted a severe axonal sensorimotor polyneuropathy and spinal cord MRI showed abnormal signal on T2-weighted images confined to the dorsal columns between C2-C6 segments (figure 1). After inquiring for environmental exposures, we found a 5-years daily use of denture fixative containing zinc. He was advised to switch to a zinc-free cream and started on oral copper supplementation with a complete resolution of cytopenias but only a slight improvement in pinprick sensation after 3 months.

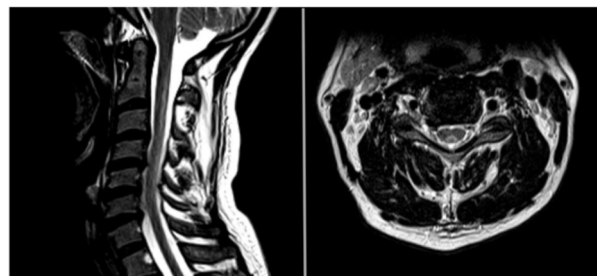


Figure 1. Sagittal (A) and axial (B) T2-weighted MRI demonstrates a contiguous, non-enhancing, increased signal lesion in the posterior columns between the cervical segments C2-C6.

Conclusion: Unexplained cytopenia associated with neurological manifestations should prompt clinicians to look for causes of copper deficiency, namely excessive zinc intake. This case illustrates the diagnostic challenge and insidious clinical manifestations of an unusual cause of myeloneuropathy with a potentially unfavourable outcome.

Disclosure: Nothing to disclose

EPO1352

Posterior reversible encephalopathy syndrome after exposure to disulfiram

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is characterized by acute cerebral endothelial lesion followed by blood-brain-barrier disruption, with predominantly occipito-parietal vasogenic edema. Drug toxicity is among the most common causes, especially chemotherapy agents and immunosuppressants. PRES after exposure to disulfiram is seldom reported.

Methods: Clinical description of a PRES case after exposure to disulfiram.

Results: A 55-year-old male, with a history of chronic alcohol abuse was found unconscious. 3 days prior, he was started on disulfiram 500mg/day. Tonic-clonic seizure was reported during transportation to the emergency department. On admission, blood pressure was 144/92mmHg, 38°C temperature. Neurological examination revealed global aphasia and right hemiparesis. Cerebral CT scan showed bilateral subcortical parieto-occipital hypodensities. Tests for blood alcohol and other drugs were negative. Lumbar puncture showed slightly elevated protein but was otherwise normal. Antiepileptics, benzodiazepines and high-dose thiamine were started and disulfiram was discontinued. Cerebral MRI showed extensive bilateral subcortical occipital T2 hyperintensities with extension to parieto-frontal areas. The patient remained free of seizures for the remaining hospitalization, and fully recovered from the deficits, maintaining amnesia for the events 3 days prior to admission. Infectious and autoimmune testing were negative. A cerebral MRI 3 weeks after admission showed almost complete regression of the hyperintensities.

Conclusion: The pathophysiology and aetiology of PRES are still largely unknown. We describe a case of PRES after a short period of exposure to disulfiram. Some neurotoxic effects of disulfiram are well known and documented, but its association with PRES is still unclear. Disulfiram should be recognised as a potential aetiology.

Disclosure: Nothing to disclose

EPO1353

Neurointoxication with Saxitoxin: "Alimentary, my dear Watson!"

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Background and aims: Paralytic shellfish poisoning (PSP) occurs after ingestion of shellfish contaminated with saxitoxin, a neurotoxin produced by algae. Gastrointestinal and neurological symptoms usually develop within hours after consumption, and rapidly progressive muscle paralysis and respiratory arrest may ensue. Treatment is supportive since there is no available antidote.

Results: A 69-year-old male presented with sudden onset of dizziness, perioral and bilateral hand tingling, myalgia and generalized muscle weakness. Neurological examination revealed flaccid tetraparesis, dysphonia, dysarthria, bilateral peripheral facial palsy, and symmetrical distal limb hypoesthesia. He additionally reported that he and his sister had consumed recreationally harvested mussels a few hours before developing the symptoms. His sister, a 63-year-old female, presented with vomiting, dizziness and perioral tingling starting 30 minutes after consuming the mussels. On neurological examination she had mild tetraparesis, and perioral and distal lower limbs hypoesthesia. Both patients were hospitalized, initially in Intensive Care Unit for close monitoring. It was not possible to analyze a direct sample of the harvested shellfish, but the urine samples were positive for saxitoxin, thus confirming the diagnosis of PSP. They improved gradually and were later discharged almost symptom-free.

Conclusion: We report 2 cases of PSP with different clinical severity. PSP outbreaks have been reported worldwide. Although it seems to be a rare phenomenon in our country, it might be underdiagnosed as mild symptoms may not be recognized. PSP can be fatal without the appropriate management, so it is crucial that healthcare professionals, especially neurologists, are aware of this clinical entity.

Disclosure: Nothing to disclose

EPO1354

An unusual case of ataxia of toxic origin

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Background and aims: Ataxia implies a clinical syndrome of incoordination, which may result from disorders affecting cerebellum and associated pathways. Among the most prominent presentations of ataxia are: dysarthria, nystagmus, gait disturbances and dysmetria. We present an unusual case of subacute ataxia of toxic origin due to phenobarbital exposure.

Methods: Patient J., male, 32 years, had an appointment in our clinic where he complained of slurred speech, vertigo, unsteadiness and “woozy” gait. The symptoms developed gradually in the course of several days with no apparent cofounder.

Results: On examination the patient was responsive, mildly lethargic. Neurologic examination revealed moderate dysarthria, severe horizontal and vertical nystagmus, dysmetria during finger-to-nose test, dysrhythmic tapping of hands. Other signs included kinetic tremor, muscular hypotonia, and hyporeflexia. The gait was unsteady, wide-based. A brain MRI scan was performed which showed no signs of ischemic or degenerative pathology. A more thorough inquiry was performed. It was found out that during the past month the patient had trouble sleeping, which prompted him to use a drug marketed in Russia by the name of “Valocordin”. Subsequent blood and urine tests were performed (Image 1), which demonstrated a marked increase of phenobarbital excretion. This led us to believe that the patient had experienced subacute phenobarbital intoxication with ataxia as the most prominent clinical presentation.

Image 1. Laboratory findings in patient J., 32 yrs

	Value	Reference
Complete blood count		
Hemoglobin	151 g/l	131 – 173 g/l
Red blood cells	5,06 x 10 ¹² /l	4,3 – 5,7 x 10 ¹² /l
Hematocrite	44,3%	39–49%
Platelets	386 x 10 ⁹ /l	180–320 x 10 ⁹ /l
White blood cells	7,29 x 10 ⁹ /l	4,5 – 11,3 x 10 ⁹ /l
ESR	17 mm/h	0 – 15 mm/h
Hemostasis		
APTT	31,9 s	25,1 – 36,5 s
PTI	98%	70 – 130%
Fibrinogen	5,11 g/l	1,8 – 4,0 g/l
Antithrombin III	153%	75–125%
Blood chemistry		
Creatinine	68,0 mcmol/l	62–106 mcmol/l
Glucose	5,0 mmol/l	4,1 – 5,9 mmol/l
ALT	18,6 U/l	<41 U/l
AST	28,3 U/l	<40 U/l
Creatinase	211 U/l	<190 U/l
Bilirubin	3,1 mcmol/l	<24 mcmol/l
C-reactive protein (hs)	83,97 mg/l	<5 mg/l
Uric acid	468,0 mcmol/l	202,3 – 416,5 mcmol/l
Barbiturate detection in urine		
Amobarbital	0,0 ng/ml	0 – 200 ng/ml
Butalbarbital	0,0 ng/ml	0 – 200 ng/ml
Pentobarbital	0,0 ng/ml	0 – 200 ng/ml
Secobarbital	0,0 ng/ml	0 – 200 ng/ml
Phenobarbital	501538,9 ng/ml	0 – 200 ng/ml

Conclusion: A broad spectrum of underlying pathologies is associated with ataxia, sometimes presenting a major difficulty for differential diagnosis. The described case underlines the necessity of a detailed and thorough patient interview.

Disclosure: Nothing to disclose

EPO1355

Lupin bean intoxication: an odd case of dysautonomic symptoms

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Background and aims: Lupinus albus is a traditional bean cultivate in the Mediterranean region, especially popular in Portugal as a snack. We report a case of dysautonomic symptoms after lupin bean consumption.

Methods: Case report description

Results: A 39-year-old man with no past medical history was admitted to the ER complaining of inability to read at nearest distances and blurred vision with bright light, beginning 9 hours earlier, accompanied by dry eyes and mouth, and feeling anxious. He was hemodynamically stable. The neurological examination revealed fixed bilateral mydriasis with no accommodation reflex, xerophthalmia, xerostomia and restless. Lab work and head CT scan showed no abnormalities. Given this clinical picture, the patient was asked about the ingestion or contact with any canned food, medications, drugs, organophosphates but he denied it. He only insisted on the ingestion of a large amount of lupin beans harvested and home prepared, 3 hours before symptoms onset. At the time, this information was not considered relevant to explain patient’s symptoms. During the observation period the patient vomited, including the lupin beans he had eaten earlier. 16 hours after symptoms onset the patient recovered completely, with no further actions required.

Conclusion: Lupinus albus has a quinolizidine alkaloid component which is toxic and associated with anti-cholinergic symptoms if improperly prepared with unprolonged soaking. After some research we found that the patient’s lupin crop was not fully prepared yet, thus explaining the dysautonomic symptoms. This case reminds us that patients often provide the etiology of their condition if we listen them carefully.

Disclosure: Nothing to disclose

EPO1356

A rare cause of Parkinsonism - Manganese toxicity

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Background and aims: 43-year-old male presented with 6 months history of gradual onset and progressive bradykinesia, tremors of upper limbs and imbalance and short shuffling gait. He also had slurring of speech with hypophonia. Neurological examination revealed slow broken saccades, rigidity with cogwheeling, bradykinesia and short shuffling, festinant gait. He had action and postural tremors of upper limbs. Pull test was positive. Thus a diagnosis of Young onset Parkinsonism was considered.

Methods: Occupational history revealed that he worked in blast furnace of a steel plant since past 14 years. He was evaluated with MRI Brain which showed symmetrical hyperintensities involving basal ganglia and subcortical white matter in T2 weighted images. T1 weighted images showed evidence of basal ganglia hyperintensities probably related to mineral deposition. KF Ring, S.ceruloplasmin, Liver function tests and Ultrasound abdomen was normal. Pheripheral smear did not show any acanthocytes. Renal and thyroid function tests were normal.

Results: Anti thyroid antibodies were normal. CSF was normal. In view of occupational exposure and clinical features, a possibility of Manganese toxicity was strongly considered. Serum Manganese was done which was elevated (Twice of upper limit of normal). Patient was started on symptomatic medications like levodopa and trihexiphenidyl. He had stopped working which eliminated occupational exposure to manganese. His parkinsonism gradually started to improve over 3 months period of followup.

Conclusion: Occupational history of manganese exposure is very important in cases of Parkinsonism. Early removal from the work environment can lead to improvement of symptoms and prevent permanent neurological deficits

Disclosure: Nothing to disclose

Peripheral nerve disorders 1

EPO1357

Small fiber neuropathy in the context of cancer before and after oxaliplatin treatment.

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Background and aims: Small fiber neuropathy results in one damage at sensory unmyelinated small neurons or its terminal axons. Oxaliplatin-induced chemotherapy (OIN) produces widespread sensory damage with unclear information regarding large and small fibers' involvement. We aimed to evaluate selectively the sensory profile and also if possible a timeline comparison in patients at risk of OIN.

Methods: 32 patients (between 44-77 ages) mostly with colorectal cancer under oxaliplatin-based chemotherapy regime at least 6 cycles were followed up before initiation and after finishing treatment. At each visit, we recorded symptoms assessment with a neurological and neurophysiological examination based on nerve conduction studies and thermal sensory testing.

Results: Patients complained of sensory symptoms in more than 95% which were referred as pain in less than 15%. Amplitudes of the sural and the cubital nerve were significantly ($p < 0.01$) reduced after treatment in all patients. Elevated warm detection threshold (WDT) at feet was found abnormal in 40% of patients before treatment and in 72% when finished. Cold hypoesthesia and cold allodynia were also present after the treatment (40%). WDT was found at feet clearly abnormal ($p < 0.01$) while there was no significant alteration on hands despite they were symptomatic. No correlation was found with the accumulated dose of oxaliplatin.

Conclusion: Subclinical small fiber damage could reflect a systemic deterioration by cancer itself. OIN is characterized by affecting all sensory nerve fibers in a distance-dependent pattern in which small fibers seem to be more resistant.

Disclosure: Nothing to disclose

EPO1358

Modeling innervation branches and distribution of the femoral nerve in rodents: Biometric analysis of femoral nerve in middle aged male and female C57BL/6 mice.

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Background and aims: Translational research involving peripheral neuropathy is focused on reproducing the functional impact of peripheral nerve disorders or traumatic lesions, and to assess neurorehabilitation strategies. Scarce number of studies address the relationship between the morphology of a nerve and its functional implications. Interestingly, biometrics studies of human femoral nerve have correlated the shape and number of motor branches to quadriceps femoris muscle with patello-femoral pain and cartilage lesions. In the present work we analyze the methodological advantages and limitations encountered in the biometric characterization of the femoral nerve of an aging mouse.

Methods: 25 12-month-old male and female mice with C57BL/6 background were used. Detailed dissection of the femoral nerve was carried out, distinguishing motor branches of the nerve until their penetration in the quadriceps femoris muscle. Nerve length and number of motor points were identified and quantified.

Results: As compared to studies in humans, the characterization of the femoral nerve in mice was facilitated by methodological advantages intrinsic to the use of rodents, such as effortless to reach sample size, higher homogeneity and easier dissection procedures. Besides, we found a simplified innervation and distribution of the nerve in contrast to the complex and diverse patterns that we have previously described in humans. With regards to limitations, the small size of nerves resulted in strong constraints for visual direct observation and quantification of ramifications.

Conclusion: Femoral nerve ramification in mice was simplified as compared to humans, and its biometric characterization can help to provide further understanding of the neurological-functional relationships.

Disclosure: Daniel Alveal-Mellado is recipient of a CONICYT/BECAS CHILE/73200493.

EPO1359

Familial Amyloidosis of the Finnish type: clinical and neurophysiological features of two index cases

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Background and aims: Familial amyloidosis of the Finnish type (FAF) is a rare autosomal dominantly inherited form of systemic amyloidosis, caused by gelsolin gene mutations. The main clinical manifestations are progressive cranial and peripheral neuropathy, corneal lattice dystrophy, and skin changes (cutis laxa). Although it has initially been described in Finland, it was recently reported in Portugal. We hereby describe the clinical and neurophysiological features of the first cases of FAF diagnosed in our Center.

Methods: Clinical cases

Results: Patient 1. A 76 year-old female presented with slowly progressive facial weakness and gait imbalance since her 70s, followed by changes in visual acuity. Her mother and 2 maternal aunts had similar complaints. When examined, she presented cutis laxa, corneal lattice dystrophy, facial diplegia with facial myokymia, hypopallescsthesia and axial and appendicular ataxia.

Patient 2. A 68 year-old male complained of progressive visual loss and facial weakness since the age of 50, with increased of gait difficulties over last years. His familiar history was positive for ophthalmologic problems and facial palsy (maternal grandmother, mother and brother). He presented cutis laxa, corneal lattice dystrophy, facial diplegia, limitation of eye movements, tetraparesis, hyperreflexia and axial and appendicular ataxia.

Gelsolin-gene sequencing revealed the heterozygous c.640G>A mutation in both. The neurophysiological study and clinical features of patients and their relatives are presented.

Conclusion: These index patients are the first cases of FAF diagnosed in our Neuromuscular Outpatient Clinic. Although there was no known Finnish ancestor, FAF should be considered in the differential diagnosis of progressive bilateral facial neuropathy.

Disclosure: Nothing to disclose

EPO1360

Prospective study of autonomic dysfunction in patients with Guillain - Barre syndrome

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Background and aims: Autonomic nervous system can be affected in approximately 2 3rds of patients with Guillain-Barre syndrome (GBS). Autonomic dysfunction may increase mortality in GBS patients. The aim of our study was to prospectively monitor autonomic symptoms in patients with GBS over a 6-month follow-up period.

Methods: Study included newly diagnosed GBS patients hospitalized in 7 tertiary healthcare centers from May 2017 until May 2018. Patients were age- and gender-matched with healthy controls (HCs). As a measure of autonomic function, each subject filled in the SCOPA-AUT questionnaire on day 14 (D14), day 28 (D28), month 3 (M3) and month 6 (M6) from symptom onset.

Results: We registered 74 GBS patients (54% males, 52±16 years old). Mean SCOPA-AUT score was higher in GBS patients vs. HCs on D14 (25.2±11.5 vs. 4.0±4.9, p<0.01), D28 (14.0±12.6 vs. 4.0±4.9, p<0.01) and M3 (6.4±5.9 vs. 4.0±4.9, p<0.01). However, no difference was observed 6 months after disease onset (4.5±4.9 versus 4.0±4.9, p>0.05). Patient with AMAN had more severe autonomic dysfunction compared to AIDP patients subtype on D14 (p<0.01) and M3 (p<0.05).

Conclusion: Significant autonomic dysfunction is present in the acute phase of GBS, and it completely normalizes six months after disease onset.

Disclosure: Nothing to disclose

EPO1361

Guillain-Barré syndrome associated to Hepatitis E virus

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Background and aims: Hepatitis E virus (HEV), previously known as enterically transmitted viral hepatitis, is hyper-endemic in many countries. Neurologic complications as Guillain and Barré Syndrome (GBS) are less known.

Methods: Case report of Guillain and Barré Syndrome associated to Hepatitis E virus

Results: We report a 63-year-old immunocompetent woman who presented acute asthenia with muscle weakness in lower limbs, numbness, and impossibility to walk. Physical examination showed hypotonic motor weakness with areflexia in all limbs, bilateral facial nerve palsy and labored breathing. Cerebrospinal fluid examination and electrophysiological study were in agreement with the diagnosis of GBS associated to a lymphocytic meningitis reaction. Liver function tests showed elevated levels of liver enzymes and Serological study was positive for IgM antibodies for HEV. The patient was treated with intravenous immunoglobulin at a dose of 0.4mg/kg per day for 5 days with good recovery. A month later, liver function was improved.

Conclusion: HEV infection should be strongly considered in patients with neurological symptoms, especially those with elevated levels of liver enzymes.

Disclosure: Nothing to disclose

EPO1362

Guillain-Barré-like onset in young patient with chronic inflammatory demyelinating polyradiculoneuropathy and central nervous system demyelination

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated disease with symmetrical motor and sensory manifestations, specific electromyographic (EMG) characteristics and diverse evolution: progressive, recurrent remissive, monophasic. In up to 1/3rd of cases the disease can manifest with demyelinating involvement of the central nervous system (CNS), and in up to 18% of patients it may have an acute onset as in Guillain-Barre syndrome (GBS).

Methods: We present the clinical case of a patient with acute onset CIDP with CNS involvement.

Results: Male of 27 years, previously healthy, was hospitalized with flaccid tetraplegia, areflexia, pain along the spine and limbs, facial asymmetry. The clinical manifestations evolved over several days. Brain MRI revealed periventricular demyelinating lesions, suggestive for multiple sclerosis. It was initiated pulse therapy with methylprednisolone without any improving. The cerebrospinal fluid (CSF) examination was acellular with increased level of proteins and positive oligoclonal bands. EMG revealed typical signs of demyelination. It was administered plasma exchange (PLEX), subsequently IVIG with partial recovery of motor functions. After 6 months his condition worsened again to the level of tetraplegia. CSF examination showed proteo-cellular dissociation, MRI examination - foci of cerebral and cervical demyelination with gadolinium enhancement. Finally, the diagnosis of atypical CIDP was established. It was applied PLEX and later Prednisolone 1mg/kg/day with rapid regression of symptoms and signs, with almost full recovery 2 months later.

Conclusion: GBS-like onset, brain and cervical spinal cord demyelinating lesions on MRI and CSF positive oligoclonal bands could contribute to the delay of atypical CIDP diagnosis.

Disclosure: Nothing to disclose

EPO1363

Omalizumab Induced Acute Motor Conduction Block Neuropathy: Case report and literature reviewH. Elshony¹, W. Khatir²¹Makkah, Saudi Arabia, ²Neurophysiology, security forces hospital, Makkah, Makkah, Saudi Arabia

Background and aims: Omalizumab is a recombinant, humanized, monoclonal antibody against human immunoglobulin E (IgE). Numerous reports and case series of neurological adverse events due to these biological monoclonal antibodies, specially anti-TNF α blockers, have been reported, including demyelinating conditions, optic neuritis, chronic inflammatory demyelinating polyneuropathy, mononeuritis multiplex, Guillain-Barré syndrome and others, whether literature reviews indicate that there are a limited number of studies investigating the effect of omalizumab on the nerves.

Aim: Report a case with acute motor conduction block neuropathy after 1st dose of Omalizumab, for possible causal association with literature review for monoclonal antibodies induced neuropathy

Methods: We describe a 45-year-old asthmatic patient with acute quadriplegia, 1 week after first dose of Omalizumab, electrophysiological studies, CSF analysis, Serology for antigangliosides, MRI brain and spine were done on admission with follow up after 1 year.

Results: Clinically, patient had acute quadriplegia, happened 1 week after first dose Omalizumab, no sensory, no bulbar or cranial nerve affection. MRI was free, Electrophysiological findings suggested acute motor conduction block neuropathy (AMCBN), CSF show protein 60 and cells 7, negative antigangliosides antibodies. Patient received IVIG with poor response then undergone extensive rehabilitation. After 1 year patient become ambulant and NCS show resolution of the conduction block with decrease CMAP in ulnar and tibial nerves bilaterally with signs of denervation.

Conclusion: Omalizumab considered risk factor for peripheral neuropathy, ranging from merely subclinical electrophysiological changes to GBS like picture with long term disability, by indirect or direct pathological mechanisms, but this conclusion need more studies and long term follow up

Disclosure: Nothing to disclose

EPO1364

The role of vascular endothelial growth factor and its high-affinity receptor in peripheral nerve dysfunction in diabetic polyneuropathy.T. Filimonova¹, Y. Karakulova²¹Perm, Russian Federation, ²Neurology, Perm State Medical University, Perm, Russian Federation

Background and aims: It is little known about potential neurotrophic effects of vascular endothelial growth factor (VEGFA) its high-specific receptor VEGFR2 in diabetic polyneuropathy (DPN).

Aim: to determine a prognostic significance of VEGFA and VEGFR2 in the diagnosis of diabetic polyneuropathy and in prevention of diabetic foot syndrome (DFS).

Methods: 65 patients with DPN were examined with clinical examination, measuring of serum levels VEGFA and VEGFR2 by enzyme immunoassay. The peripheral nerve dysfunction was confirmed by electroneuromyography by measuring nerve conduction velocity (NCV). Control group consisted of 12 healthy persons.

Results: The 1st group included 30 patients with moderate DPN, mean NCV was 35.12 \pm 7.04m/s. Serum level of VEGF-A was 42.44 \pm 12.71pg/ml (versus control 25.13 \pm 2.75pg/ml, p=0.001) and quantitative content of VEGFR2 was 25.14 \pm 4.75ng/ml (versus control 12.58 \pm 1.24ng/ml, p=0.002). The 2nd group consists of 35 patients with severe DPN associated with DFS, the average NCV was 24.81 \pm 6.55m/s. In this group serum content of VEGFA was significantly lower than in the 1st group (24.68 \pm 5.05pg/ml, p=0.001), as well as serum level of VEGFR2 (11.74 \pm 0.84ng/ml, p=0.001). There were revealed correlations between the severity of neuropathy by NCV and the decrease in serum levels of VEGFA and VEGFR2 (R=0.392, R=0.354 accordingly, p<0.01).

Conclusion: The obtained data testify to the important role of endothelial dysfunction in progression of peripheral neuropathy. The high expression of VEGFA and VEGFR2 in serum may be considered as a marker of developing diabetic polyneuropathy and the deficiency of the factors can be a predictor of a diabetic foot syndrome.

Disclosure: Nothing to disclose

EPO1365

Identification of factors influencing severity and activities of daily living in patients with chronic inflammatory demyelinating polyneuropathy

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired progressive or relapse-remitting immune-mediated disease of peripheral nervous system. The diagnosis of CIDP reveals on clinical presentation and electrophysiological data due to EFNS/PNS criteria. The aim of this study was to determine factors influencing severity and activities of daily living (ADL) in CIDP patients.

Methods: Clinical and laboratory assessment was performed to 101 patients with confirmed CIDP diagnosis, whereof 20 were with diabetes mellitus (DM). Neurological deficit was based on Neurology Impairment Scale (NIS) and Medical Research Council (MRC) scales and Barthel index (BI) for ADL.

Results: Statistically significant differences were found between groups of patients with DM and without (table 1). Also there were significant correlations between level of deficit and blood folic acid concentrations (-0.389 (NIS), +0.442 (MRC)) (fig. 1, 2) (p<0.05).

	DM group	Non-DM group	Statistical significance
NIS, points	63,09±6,97	44,45±2,93	p<0,05
MRC, points	45,26±2,24	51,08±0,96	p<0,05
BI, points	78,50±5,76	93,02±1,56	p<0,05

Table 1. Differences in neurological deficit and activities of daily living in patients with diabetes mellitus and without

Table 1. Differences in neurological deficit and activities of daily living in patients with diabetes mellitus and without

Figure 1. Correlations between level of neurological deficit (NIS) and blood concentration of folic acid

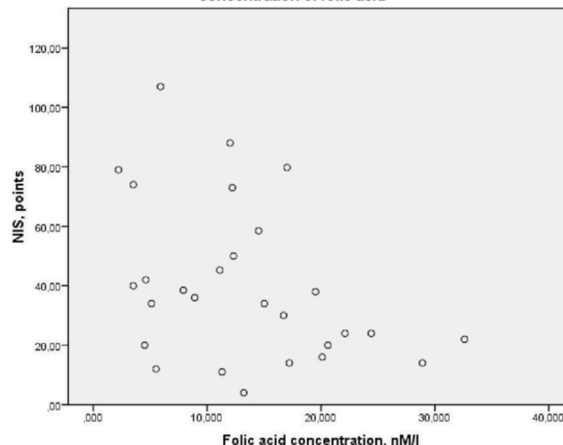


Figure 1. Correlations between level of neurological deficit (NIS) and blood concentration of folic acid

Figure 2. Correlations between level of neurological deficit (MRC) and blood concentration of folic acid

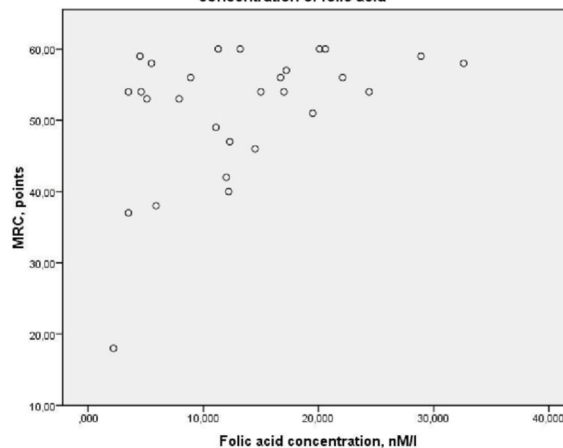


Figure 2. Correlations between level of neurological deficit (MRC) and blood concentration of folic acid

Conclusion: DM is a widespread disease negatively affecting course of many other diseases. Patients with CIDP and DM have greater neurological deficit and lower degree of self-care. The co-existing of DM and CIDP gives an ultimate competition for clinicians to manage status of these patients. Special international recommendations for management and treatment of CIDP in patients with DM are needed to simplify the follow-up of such patients. Folic acid is essential for nucleic acids synthesis, but its role in CIDP wasn't established yet. Our data suggests that level of FA can influence the course of CIDP, so analysis for FA is necessary for assessment patient's condition and subsequent decision of folic acid supplementation to CIDP patients.

Disclosure: Nothing to disclose

EPO1366

Fatigue in patients with chronic inflammatory demyelinating polyneuropathy

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired progressive or relapse-remitting immune-mediated disease of peripheral nervous system. The diagnosis of CIDP reveals on clinical presentation and electrophysiological data due to EFNS/PNS criteria. The aim of this study was to assess the severity of fatigue in CIDP patients and determine relationships between levels of deficit and fatigue in these patients.

Methods: Assessment was performed to 34 patients with confirmed CIDP diagnosis. Neurological deficit was based on Neurology Impairment Scale (NIS) filled by doctor and Rasch Overall Disability Scale (RODS) filled by patient himself and level of fatigue – on Multidimensional Fatigue Inventory-20 (MFI-20).

Results: Statistically significant differences were found between normal MFI-20 sum score (30 points) and CIDP group points (62.11 ± 2.76 points) ($p < 0.05$). Correlations between NIS, RODS and subgroups of MFI-20 are presented in table 1.

	NIS, points	RODS, points
MFI general fatigue, points	0,399*	-0,415*
MFI reduced activities, points	0,449*	-0,457* ¹
MFI reduced motivation, points	0,369*	-0,368* ¹
MFI physical fatigue, points	0,310*	-0,441* ¹
MFI mental fatigue, points	0,255	-0,286 ¹
MFI overall score, points	0,444*	-0,490* ¹

Table 1. Correlations between MFI subscales and level of neurological deficit (* – mark of statistically significant correlations ($p < 0.05$), 1 – Pearson's coefficient was used, in other cases – Spearman's coefficient was used)

Conclusion: Due to trial, fatigue is one of the major symptoms in CIDP patients and it is need to be treated. Treatment includes physical exercises and recommendations for life style modification based on patient's level of disability. Because of correlations between neurological deficit and fatigue subgroups, the relevance of fatigue correction is increased in CIDP patients with high levels of disability.

Disclosure: Nothing to disclose

EPO1367

Clinical-Electrophysiological Correlation of the Hoffmann-Tinel Sign in Carpal Tunnel Syndrome

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Background and aims: A tingling sensation referred distally, produced by tapping over the course of a nerve, has been thought to indicate the nerve regeneration. This test is called Tinel's test. However, Hoffman first described it in March of 1915 as blight percussion of a finger during extension, in October 1915, Tinel described it as application of pressure to an injured nerve trunk induces a sensation of tingling, who called it "le signe de fourmillement."

Carpal Tunnel Syndrome (CTS) is the most frequent compressive neuropathy. History and physical examination, including the Hoffmann-Tinel test (HTT), were considered highly suggestive of the diagnosis.

Methods: We performed a cross-sectional study of patients with positive HTT who were referred for NCS/EMG with suspected CTS. The HTT was made with the percussion of the median nerve in the wrist and was repeated five times. The presence of pain or paresthesia radiating in the median nerve distribution was recorded.

Results: 100 consecutive patients with positive HTT, 55 bilateral, 74 woman with a mean age of 36 years and 26 men with 41 years of mean. We found electrophysiological criteria for CTS in 72 patients, 30 with bilateral CTS.

Conclusion: The HTT test is a clinical indicator of suspected CTS that in our study showed 72% correlation with the electrophysiological evidence of CTS.

Paresthesias in the hands are nonspecific findings and may have several causes, such as other neuropathies, cervical radiculopathy, thoracic duct syndrome and musculoskeletal injuries, such as fibromyalgia. Judgment that relies solely on clinical findings can be misleading.

Disclosure: Nothing to disclose

EPO1368

Coexistence of post zoster myelitis and brachial plexopathy in a patient: A rare complication

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Background and aims: Herpes zoster is characterized by a painful, unilateral vesicular eruption in a restricted dermatomal distribution and results from reactivation of latent Varicella zoster virus. It may be complicated by neurologic disorders such as post herpetic neuralgia, myelitis, plexopathy, meningoencephalitis and vasculopathy. Here we present a case of herpes zoster complicated with both brachial plexopathy and cervical myelitis.

Methods: A 61-year-old immunocompetent male presented with left arm weakness 5 days after a zoster skin lesion affecting the left C3-C7 dermatomes. Neurologic examination revealed paresis (3/5) and hypoactive deep tendon reflexes at left upper extremity, hypesthesia and paraesthesia on C3-C7 dermatomes.

Results: Cervical spinal MRI showed hyperintense lesion at C3-C6 on T2 weighted images. Patient treated with antiviral drug and high dose intravenous methylprednisolone. Weakness did not improve and electromyography and brachial plexus MRI were performed. Electromyography and brachial plexus MRI were consistent with left brachial plexopathy. HIV serology was negative.

Conclusion: Transverse myelitis is a rare complication of herpes zoster and usually occurs within days to weeks following the initial onset of skin lesions. Brachial plexopathy related with zoster infection is also rarely described. These complications should be suspected in presence of post zoster neurologic symptoms. Evaluation of symptoms with both MRI and electromyography can provide useful information about neurologic involvement.

Disclosure: Nothing to disclose

EPO1369

Carpal tunnel syndrome: dynamic of clinical, neurophysiological and ultrasound parameters after single local steroid injection combined with wrist splinting

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Background and aims: Carpal tunnel syndrome is the most frequent entrapment neuropathy. Local injection of corticosteroids is effective for relief symptoms and improvement of nerve conduction, but the duration and point maximum of effect is unclear. Our aim was to evaluate clinical, neurophysiological and ultrasound parameters during 6 month after single local steroid injection in combination with splinting in patients with carpal tunnel syndrome.

Methods: We analyzed 44 patients with mild to moderate single side CTS (in according on classification by Stevens J.C. 1997). Evaluated clinical symptoms (SSS scale of Boston Carpal Tunnel Questionnaire), nerve conduction studies (sensory conduction velocity, distal motor latency, amplitudes of motor and sensory potentials of median nerve) and cross-sectional area of median nerve on entrance to carpal tunnel by ultrasound before injection and after 2, 4 and 6 month. Local injection of betamethasone 7mg and lidocaine 20 mg performed on landmark-guide standart manner. Also we recommended all of patients to use wrist splint for night sleep and hard handwork.

Results: We register significant ($p < 0.05$) improvement all of clinical and instrumental signs 2 months after injection. 4 month after only amplitudes of motor and sensory potentials were significant better than in 2 month, other parameters unchanged. At 4 and 6 month was no difference from 2 and 4 month respectively in all signs. See the details in table 1.

Table 1. Dynamic of clinical, neurophysiological and ultrasound signs after single local steroid injection in combination with wrist splinting in patient with mild to moderate carpal tunnel syndrome

Parameter	Before injection	2 month after	4 month after	6 month after
SSS scale of BCTQ, total points	17,5±8,3	7,7±6,7	9,8±10,8	9,1±9,2
Median nerve sensory conduction velocity, m/s.	33,4±8,3	38,4±6,9	39,2±8,4	39,1±8,4
Median nerve distal motor latency, ms.	5,9±1,7	5±1,3	5,2±1,4	5,1±1,2
Median nerve amplitude of motor response, mV.	6,9±2,8	7,5±2,4	8±3	8,5±3,3
Median nerve amplitude of sensor response, mV.	16,1±13,2	19±13,1	23,2±14,2	22,4±14,9
Median nerve cross-sectional area, sq.mm.	14,8±5,2	13,4±5,5	12,7±5,9	13,3±6,2

Note: Significant changes compared with previous point is red-marked ($p < 0,05$).

Table 1

Conclusion: In case of mild to moderate carpal tunnel syndrome the maximum improvement of clinical, neurophysiological and ultrasound parameters occurred in first 2 month after local steroid injection.

Disclosure: Nothing to disclose

EPO1370

Hysterical and Traumatic Peripheral Nerve Disorder: Immunology Aspects

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Background and aims: There are many causes of peripheral neuropathies. We observed and discussed here traumatic and, as an outcome, inflammatory neuropathy (TIN) on one hand, and peripheral nervous pathology caused by hysterical conversion personality disorder (CPDN), on another. Our goal was to study and compare main immunological involvement in both types of neuropathies including the study of IgG and inflammatory cytokines (IL)-2, IL-6, IL-10, IL-11, IL-17, IL-32, TGF- β , TNF- α , IFN- γ in blood serum of the 26 TIN patients and CPDM patients.

Methods: Control group included 54 healthy donors. All patient's and donor's groups included men and women aging by 17-62 year old. Ig G was detected using diffusion in gel by Mancini. Concentrations of all pro-inflammatory cytokines were measured by ELISA. We used meta-analysis for statistical evaluation of our results.

Results: It was revealed that in 77% of TIN patients IgG and IL-6, IL-10, IL-11, IL-17 serum concentrations were markedly increased. In 48% of CPDN patients serum concentrations of these substances were also increased but in much lower extent. We observed decreased levels of IL-32, TGF- β , TNF- α , IFN- γ in 79% of CPDN patients.

Conclusion: We know that the persons with hysterical personality have markedly higher level of interferon. Contrary to that, concentrations of pro-inflammatory cytokines were not significantly increased on these patients, but in case of traumatic and inflammatory neuropathies IgG and IL-6, IL-10, IL-11, IL-17, was substantially raised, which stressed their pathogenic role namely in these type of peripheral nerve lesions. Our finding will play an important role in future treatment modalities.



Vertebral Column in Traumatic Injury



Spondillitis

Disclosure: Nothing to disclose

EPO1371

Comparison of the effectiveness of platelet-rich plasma and betamethasone in carpal tunnel syndrome

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Background and aims: Compression of the median nerve in carpal canal is a common problem. There is some evidence of platelet-rich plasma (PRP) efficacy. Also, the standard treatment is local administration of betamethasone.

Methods: 18 patients (4 men) with confirmed moderate by nerve conduction study (NCS) and ultrasound diagnostics and do not have concomitant blood diseases not previously treated. After randomization by random numbers, PRP or betamethasone was injected into the carpal tunnel under ultrasound control (the patient was blinded to treatment). Prior to treatment NCS distal latency of compound muscle action potential (CMAP), Boston carpal tunnel questionnaire (BCTQ), visual analog scale (VAS) data were evaluated. After 3 months, the effect was monitored.

Results: in the PRP group there were 10 people, in the betamethasone group 8. The groups were homogeneous in age -46 ± 7 and the severity of CTS. 3 months after treatment, there was a significant improvement in both groups, but there was no significant difference in the PRP and betamethasone groups.

	Before treatment PRP	Before treatment betametason	3 month after treatment PRP	3 months after treatment betametason
N	10	8	10	8
Distal latency	5,44 s.d. 0,68	5,20 s.d. 0,46	4,49 s.d. 0,33	4.26 s.d. 0,25
CMAP			(p<0.05)	(p<0.05)
BCTQ	2,77 s.d. 0,4	2,5 s.d. 0,41	1,52 s.d. 0,33	1,50 s.d. 0,22
			(p<0.05)	(p<0.05)
VAS	5,6 s.d. 0,84	5,12 s.d. 1,12	2,4 s.d. 1,07	1,62 s.d. 1,4
				(p<0.05)

Conclusion: PRP injection may be an alternative to betamethasone. In the future, the selection will be increased.

Disclosure: Nothing to disclose

Spinal cord and root disorders

EPO1372

Tarlov's Cyst: an underestimated cause of Persistent Genital Arousal Disorder. Case report and review.

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Background and aims: Tarlov cyst syndrome is a rare, often asymptomatic disorder, characterized by nerve-root cysts, usually occurring in the sacral spine, near the dorsal root ganglion. The cysts may cause lower back pain, sacral radiculopathy, urinary incontinence, bowel disorders and dyspareunia. The cysts are also reported to produce genital symptoms similar to those described for Persistent-Genital-Arousal-Disorder (PGAD).

Methods: We report a case of a 31-year-old woman with symptoms of persistent, unwanted genital sensations without sexual desire. From early infancy she experienced unpleasant orgasmic-like sensations extremely embarrassing and guilt-inducing, spontaneous or precipitated by mechanical stimuli. A lumbosacral MRI (figure 1) showed sacral Tarlov Cysts with S2-S3 radicular involvement. Neurological examination showed diffused hyperesthesia, bilateral radicular S2-S3 pain and hyperactive symmetrical deep tendon reflexes in the lower limbs.

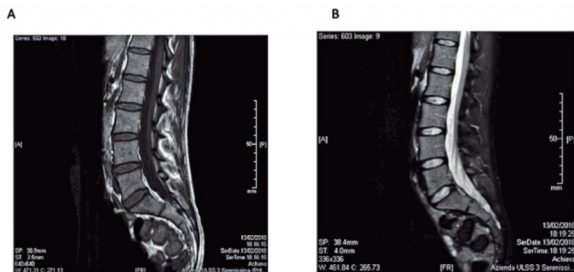


Figure 1. Sagittal T1 (A) and T2 (B) weighted images of the same cyst at S2-S3.

Results: PGAD is a rare syndrome of unremitting sexual arousal in the absence of conscious feelings of sexual desire. The arousal does not resolve with ordinary orgasmic experience, which is distressing and intrusive. Tarlov cysts have a prevalence of 66.7% in PGAD population, much higher than in the general one (up to 9%). The shame and embarrassment attached to the symptoms has contributed to the absence of reliable epidemiological data of PGAD and its underestimation. Surgical decompression of the cyst can lead to elimination or improvement of PGAD symptoms.

Conclusion: It is reasonable to recommend lumbar MRI in patients with PGAD. Future research are necessary to clarify the relationship between PGAD and Tarlov cysts in order to establish an appropriate and effective therapeutic management.

Disclosure: Nothing to disclose

EPO1373

Pallister-Killian syndrome associated to Froin's syndrome

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Background and aims: Pallister-Killian syndrome is a rare chromosomal duplication disorder caused by additional copies of the short arm of chromosome 12. It is characterized by craniofacial dysmorphism with fronto-temporal alopecia, hypertelorism, low-set ears, kyphoscoliosis, intellectual disability, epilepsy, and abnormal muscle tone. Neurological abnormalities common to PKS include cerebral volume loss, malformations of cortical development, corpus callosum dysgenesis, craniofacial malformations, hypotonia and hyporeflexia.

Methods: Data obtained through review of medical records, after evaluation and authorization of the patient and photographic record of the diagnostic methods to which the patient was submitted and literature review.

Results: A 19-year-old young adult with KPS was admitted to the emergency department of our institution referring recurrent episodes of seizures, followed by inappetence, horizontal nystagmus, hypertonia and global hyperreflexia. At the admission, the patient's laboratory exams were normal. The spinal tap showed xanthochromia with high protein level of cerebrospinal fluid (3,114.5mg/dl). Magnetic resonance imaging and computed tomography scans of the brain/spine showed multiple abscesses at the posterior fossa and spinal cord, at the thoracic and lumbar level determining mass effect and obstruction of the spinal canal.

Conclusion: The neurological symptoms were associated to the Froin's syndrome, that is characterized by marked cerebrospinal fluid (CSF) xanthochromia (yellow discoloration of the CSF) and hypercoagulability due to increased protein content. Pseudo-Froin's syndrome has also been described as stagnation of the CSF distal to a spinal block due to spinal disc bulging or tumor. In our case, the spinal obstruction was determined by multiple abscesses at the spinal cord.

Disclosure: Nothing to disclose

EPO1374

Intramedullary spinal-cord tumor-like lesions

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Background and aims: Isolated intramedullary lesions present a diagnostic challenge for the neurologist, particularly when they display tumor-like features. The most common etiology of these lesions are primary demyelinating, other inflammatory diseases, vascular and infectious. The real challenge when approaching these lesions is differentiation the tumors from the tumor-like lesions.

Objectives: Describe our population of “tumefactive” spinal-cord lesions.

Methods: We collected data from clinical database and spinal-cord MRI’s from January 1st 2010-December 31st 2018 using the keywords “tumefactive”, “medullary expansion” and “edema” and included patients which met the following definition of “tumefactive”: spinal-cord lesion with diameter >2cm and causing medullary expansion, mass effect or edema. We excluded patients with concurrent brain lesions or extramedullary lesions.

Results: We included 21 patients with a median age at presentation of 53.6 years (range 23-78 years), 13 men (61.9%). 4 (19%) had NMOSD, 1 (4.8%) had neurosarcooidosis, 1 (4.8%) had syringomyelia, 5 (23.8%) had idiopathic myelitis and 10 (47.6%) had a tumour. Comparing inflammatory pseudo-tumoral with tumoral etiologies, there were significant differences in: sphincter involvement; T1 hypointensity/isointensity and T1 signal heterogeneity; T2 hyperintensity and T2 signal heterogeneity. There were no significant differences in other clinical features, gadolinium enhancement, number of vertebral segments affected, location of lesions and CSF characteristics.

Conclusion: Clinical features, other than sphincter involvement, and CSF characteristics do not appear to help in the distinction between tumors and tumor-like lesions. MRI’s T1 and T2 signal pattern appear to be the most helpful in the differential diagnosis of tumors and tumor-like lesions.

Disclosure: Nothing to disclose

EPO1375

Malignancy in low back pain – clinical and paraclinical features

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Background and aims: It is estimated that up to 84 percent of adults have low back pain at some time in their lives. Malignancy is rare as a cause of low back pain. In patients with low back pain presenting to primary care, less than 1% have malignancy as underlying cause. According to previous studies the most useful feature is previous history of cancer. To find other important red flags we performed retrospective study between January 2012 to December 2018 among all patients with persistent low back pain (VAS>8) and signs or symptoms of spinal stenosis hospitalized in neurological clinic of Tokuda Hospital Sofia. The age of the patients were between 18 and 95 during the hospitalization.

Methods: Somatic and neurological status, laboratory tests, magnetic resonance tomography (MRI) and computed tomography of lumbar spine (CT).

Results: Our study included 236 patients (138 female and 98 male). We found malignancy in 28 (11.86%) of patients (11 female and 17 male). The most common malignancies were: lung carcinoma - 9, prostate carcinoma - 5, breast carcinoma - 5, melanoma malignum - 3; other - 6. The most common red flags are: decreased hemoglobin values (85.7%), slightly increased C-reactive protein (96.4%), history of malignancies (71.4%); refractory to analgesia pain increased from the beginning (92.8%), autonomic symptoms (17.8%); weight loss (25%); Age between 45-65 (64.2%).

Conclusion: According to our study malignancy is not a rare cause for back pain probably because of different defined inclusion criteria. It seems that the patients who failed to respond to conservative management are more likely to have malignancy.

Disclosure: Nothing to disclose

EPO1376

Prognostic factors of spinal cord decompression sickness

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Background and aims: Spinal decompression sickness (DCS) is 1 of the most serious forms of diving related injuries. Its pathophysiology isn't completely understood. Our aim was to describe clinical and paraclinical features of patients having spinal DCS, to identify its risk factors, the therapeutic procedures and the clinical outcome.

Methods: We performed a retrospective study that included patients having spinal DCS treated between 2009 and 2018.

Results: We included 32 males. The mean age was 33.7±9.5 years. Factors favouring the occurrence of DCS were diving procedure errors, cold weather, addictive behaviours, working time at the bottom >20 minutes, cervico-osteoarthritis, and the presence of a patent foramen ovale. A severe motor deficiency at onset (paraplegia or tetraplegia) was noted in 28% of cases. Bladder dysfunction was noted in 48% of cases. MRI demonstrated increased signal intensity in the spinal cord on T2-weighted images in 41% of cases. The poor prognostic factors were an age greater than 40 years, a depth greater than 60 meters, a consultation time of more than 24 hours, and an extensive myelitis. The treatment was based on recompression in hyperbaric chamber, rehydration and acetylsalicylic acid in all cases. Half of patients had a complete resolution after one month while 25% of patients had neurologic sequelae.

Conclusion: The diagnosis of spinal DCS is based on clinical signs and should be suspected in any person with neurological symptoms and a recent history of diving. The outcome is unpredictable with a high risk of incomplete recovery whatever the treatment undertaken.

Disclosure: Nothing to disclose

EPO1377

Trends in traumatic spinal cord injuries in Estonia during 22 years

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Background and aims: To investigate trends in the incidence and causes of traumatic spinal cord injuries (TSCI) in Estonia from 1997 to 2018.

Methods: Medical records of patients with TSCI from Estonian regional hospitals from 2008 to 2018 were retrospectively reviewed. The new epidemiological data were compared with the data from the previous period 1997-2007.

Results: A total of 383 new patients with TSCI were identified. The average annual incidence rate (standardized to the Estonian population by age and gender) decreased significantly from 39.3 per million population (95% CI 36.2-42.5) at the 1st period (1997-2008) to 26.2 per million population (95% CI 23.6-28.8) during the 2nd period (2008-2018) (incidence rate ratio (IRR) 0.63 (95% CI 0.57-0.75), $p < 0.0001$). The mean age at injury increased from 39.0 (±17.0) years to 46.6 (±19.9) years, $p < 0.0001$. The male to female ratio decreased from 5.5:1 to 3.8:1 ($p = 0.04$). Falls were the leading cause of injury during both periods followed by traffic accidents and sports injuries. Still, the percentage of traffic accidents decreased significantly (from 29.7% to 20.6%, $p = 0.002$) and falls increased (from 41.4% to 59.5%, $p < 0.0001$) during the 2nd period. Alcohol consumption prior to injury also decreased significantly from 65.6% to 55.1% ($p = 0.007$).

Conclusion: Estonia has become more similar to other European countries during the last decade: TSCI incidence has significantly decreased, the mean age at injury and the percentage of falls have increased. In addition to increased alcohol taxes, better preventive measures probably have important role in the decreased burden of TSCI in Estonia.

Disclosure: Nothing to disclose

EPO1378

Efficiency of application of various schemes of treatment of neuropathic pain in cervical radiculopathies

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Background and aims: To evaluate the effectiveness of various regimens for the use of lornoxicam, tolperisone and gabapentin for the treatment of acute pain in patients with cervical radiculopathies

Methods: 62 patients with cervical radiculopathy were examined. All patients were divided into 2 groups. The 1st group included 31 patients, 2-31. The examination was carried out twice: before and after treatment. In different groups, 2 treatment regimens were compared: the use of lornoxicam in combination with tolperisone, in the 2nd - the use of dimensions in combination with lornoxicam. Investigated serum levels of IL-6 in patients before and after treatment

Results: According to the VAS scale, a decrease in pain from 9 points to 3 points was evaluated in patients of group 2, compared with group 1, which also showed a slight decrease from 9 points to 7 points. The level of IL-6 in patients of group 1 before treatment was 14.9pg/ml, after treatment it was 10.6pg/ml. In patients of group 2, the cytokine level before treatment was 13.1pg/ml, after - 6 pg/ml ($p < 0.001$)

Conclusion: As a result of the study, it was found that the use of gabapentin in combination with lornoxicam has a positive effect in reducing pain, compared with the results of patients who received lornoxicam in combination with tolperisone. Patients with pain in cervical radiculopathies are recommended to use this scheme to reduce neuropathic pain

Disclosure: Nothing to disclose

EPO1379

Cervical and Thoracolumbar Traumatic Spinal Cord Injury and the impact on Quality Of Life: A Comparative Study

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Background and aims: Traumatic Spinal Cord Injury (TSCI) may be the most traumatic and devastating event in one's life and can significantly compromise one's Quality Of Life (QOL).

Methods: Cross-sectional study conducted at the Catarinense Rehabilitation Centre (CRC) population, Southern Brazil, to verify the impact on QOL according to injury level and time since injury and associated factors in SCI patients older than 18 years old who have suffered TSCI and were undergoing rehabilitation. The WHOQOL-bref instrument was chosen to measure patients' QOL after SCI. Analysis was made in the SPSS 18.0 where there were compared average scores from the WHOQOL-bref, t-student test was used in independent samples ($p < 0,05$). Questionnaire analysis was carried out without any particularities or adjustments to the subject under study, t-Student test and $p \leq 0,05$. The study was approved by the Ethics Research Committee (ERC) of the Institution.

Results: Prevalence of young men between 30 and 50 years old (30.5%) who suffered traffic accident (33.3%). There were differences in QOL scores between paraplegic and tetraplegic patients, mainly in physical (64.45x45.47) and psychological areas (70.2x60.0). There was predominance of injuries older than 6 months (94.4%) and rehabilitation time also lasting more than 6 months (77.7%).

GRAPHIC 1

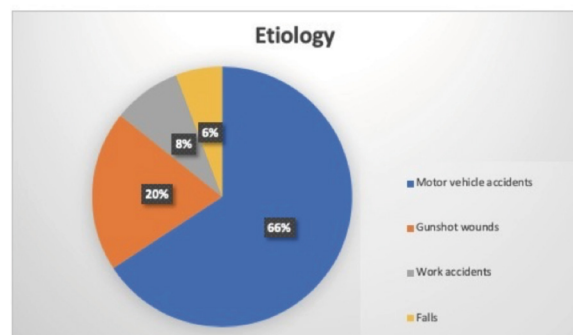


Table 1 – Analysis of the population sociodemographic characteristics

Variables (n = 36)	Cervical n (%)	Thoracolumbar n (%)
Gender		
Male	13 (36,1)	19 (52,7)
Female	2 (5,5)	2 (5,5)
Age		
18 – 30 years old	6 (16,6)	6 (16,6)
30 – 50 years old	8 (22,2)	13 (36,1)
≥ 50 years old	1 (2,7)	2 (5,5)
Injury Time		
< 6 months	1 (2,7)	1 (2,7)
> 6 months	17 (47,2)	17 (47,2)
Rehabilitation Time		
< 6 months	3 (8,3)	5 (13,8)
>6 months	12 (33,3)	16 (44,4)

Source: Author elaboration.

Table 2 – Association between injury level and quality of life domains

Variables	Physical	Psychological	Social Relations	Environment
	Average (SD) <i>p</i> value	Average (SD) <i>p</i> value	Average (SD) <i>p</i> value	Average (SD) <i>p</i> value
Injury Level (n=36)				
Cervical (n=15)	45,47 (13,8)	60,0 (10,0)	61,11 (20,0)	61 (14,2)
Thoracolumbar (n=21)	64,45 (12,4)	70,23 (10,3)	69,44 (23,3)	65,47 (15,7)
	<i>p</i> <0,001	<i>p</i> <0,01	<i>p</i> =0,27	<i>p</i> =0,39

Source: Author elaboration.

Conclusion: Predominance of young men victims of traffic accident who became paraplegic. Lower QOL scores were obtained mainly in the physical and psychological domains. The main factors associated with TSCI are male, youth, traffic accidents, paraplegia, physical and psychological losses.

Disclosure: Nothing to disclose

EPO1380

Gender, age-related features and frequency of spine surgery in patients with large lumbar disc herniation

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Background and aims: The most common cause of spinal roots compression in intervertebral foramen is disc herniation. Clinically significant changes are mostly seen in patients with large disc herniation. Study aimed to analyze gender, age distribution and frequency of spine surgery in patients with large lumbar disc herniation (LLDH).

Methods: Study recruited adults with signs of compression of spinal roots of lumbar localization that required hospital admission. Clinical, neuroimaging data were evaluated. Patients were divided into 2 groups - with LLDH (≥ 8mm) and smaller lumbar disc herniation (SLDH) (<8mm). Standard statistical tools were applied, *p*-value <0.05 was considered statistically significant.

Results: Altogether 90 patients were enrolled. LLDH was diagnosed in 31 patients (34%; 18/31 female, mean age 47±2.7 years old), SLDH – 59 patients (66%; 41/59 female, mean age 59.5±2.0). Patients with LLDH were younger (*p*<0.05), there was no significant difference in gender between groups (*p*>0.05). Surgical treatment was much frequently performed in patients with LLDH as compared to SLDH (32% vs 14%, *p*<0.05).

Conclusion: Formation of LLDH doesn't depend on gender but is much more common in younger patients. Surgical treatment is more often applied in patients with LLDH as compared to SLDH.

Disclosure: Nothing to disclose

EPO1381

Spontaneous Spinal Cord Infarction – retrospective cohort of a tertiary center

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Background and aims: Spontaneous Spinal Cord Infarction (sSCI) is uncommon but often very disabling. Differential diagnosis is sometimes difficult, leading to diagnostic delay and compromising acute phase treatment. Our goal is to describe patients diagnosed with sSCI in our center and retrospectively to apply Nicolas Zalewski and colleagues (2018) diagnostic criteria.

Methods: Retrospective review and descriptive analysis of sSCI cases admitted in a 10-year period.

Results: We included 18 patients, 72% male, median age 60 years (IQR:22.5); 78% with previous mRS ≤ 1 . 72 percent reached the neurological deficit nadir within 12 hours (median: 3h; IQR:17.3). 2 patients had contraindication to MRI; of the remaining, 75% had spinal cord hypersignal and 29% had diffusion restriction. Of the 14 patients who underwent AngioCT/AngioMRI, 2 had aortic dissection, 2 had occlusion of intercostal arteries, and 1 had segmental artery occlusion. CSF study (performed in 10 patients), showed pleocytosis (22 cells) in 1 and increased protein in 3. No patient underwent revascularization treatment. At 3 months, 50% of patients had functional disability (mRS ≥ 3); at 12 months this percentage was similar (46%). According to the criteria proposed by Zalewski et al., 5 patients met criteria for definitive sSCI and 8 for possible (of these, 2 without MRI and 4 without CSF study).

Conclusion: Our results agree with previous published data regarding the delay of sSCI diagnosis, limiting the possibility of a proper acute phase treatment, and leading to poor functional prognosis. A more timely and complete diagnostic study is warranted to reverse these results.

Disclosure: Nothing to disclose

EPO1382

Objective evaluation of paresis in patients with lumbar disc herniation

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Background and aims: Motor disorders of the lower extremities caused by compression radiculopathy at the lumbar level are the main disabling factor. The number of decompressive operations of the lumbar spine is increasing, but the problem of restoring paresis of the lower extremities is still relevant.

Methods: The analysis of 26 patients was performed, including 16 patients with L4-L5 disc herniation with L5 compression radiculopathy, 11 patients with L5-S1 disc herniation with S1 radiculopathy. Compression of the spinal root was detected on an MRI. In order to detect paresis was used a standard paresis scale and a test was performed on an isokinetic dynamometry device (Humac Norm). The strength of the lower leg muscles on the affected side was compared with a healthy limb. This examination was performed before surgery, 14 days after microdiscectomy, and 3 months later.

Results: The following parameters were obtained m. Gastrocnemius of the affected side: eccentricity: PT (before surgery vs 90 days after surgery) 42Nm vs 57Nm; concentricity: PT 34Nm vs 39Nm; M. Gastrocnemius of the healthy limb: eccentricity: PT 52Nm vs 46Nm; concentricity: PT 42Nm vs 43Nm. In the antagonist muscle-M. Peroneus Long. of the affected limb: eccentricity: PT 19Nm vs 22Nm; concentricity: PT 14Nm vs 23Nm. M. Peroneus Long. of a healthy limb: eccentricity: 23Nm vs. 24Nm; concentration: 22Nm vs. 2 Nm.

Conclusion: Isokinetic dynamometry is effective in objectively assessing the dynamics of motor disorders in patients after decompression of the lumbar spine root.

Disclosure: Nothing to disclose

EPO1383

Spinal Epidural Lipomatosis in a Patient with Chronic Alcoholism: Case ReportV. Stefanova¹, B. Benishev², M. Dimitrova¹¹Neurology, UMHATEM "N.I. Pirogov", Sofia, Bulgaria,²General and Endoscopic Surgery, UMHAT "SV. Ivan Rilski", Sofia, Bulgaria

Background and aims: To present a rare case of spinal epidural lipomatosis (SEL) with slowly progressing neurological symptoms in patient without other risk factors except chronic alcoholic abuse. SEL is described as the accumulation of fat in the extradural territory and observed in patients receiving long-term exogenous steroid therapy, obesity, endocrinological disorders and rarely in chronic alcoholism. The hypertrophy of the epidural adipose tissue causes a narrowing of the spinal canal and compression of neural structures. Patients present with progressive myelopathy, but radicular symptoms are also common. Conservative treatment - weaning from alcohol, steroids or weight loss - can reverse the hypertrophy and relieve the neural compression. Failing conservative management indicates surgery.

Methods: A 41-year-old man, non-obese, experienced low back pain, numbness and lower limbs weakness, bladder and sexual dysfunction with progressive deterioration over 1 year. Objectively we found bilateral peroneal and tibial paresis. MRI demonstrated fat tissue overgrowth in the epidural space with compression of the dural sac, incipient degenerative disc disease L2-S1. The patient had no history for long-term exogenous steroid therapy, no endocrinologic disorders, only over 2 bottles of alcoholic drinks/day for one decade. The patient was treated conservatively with simultaneously weaning from alcohol.

Results: A significant improvement in the patient's neurological status is recorded. The patient remained under observation.

Conclusion: There is relationship between alcohol and fat deposition in several studies, since SEL and metabolic syndrome share many components. Etiological mechanism is assumed to be a malfunction in fat metabolism due to mitochondrial DNA. Some studies have shown the role of alcohol on the development of metabolic syndrome.

Disclosure: Nothing to disclose

EPO1384

Spontaneous spinal epidural haematomas in the era of anticoagulant treatmentI. Štětkářová¹, E. Ehler², K. Brabec¹, L. Jelínková¹, T. Peisker¹¹Prague, Czech Republic, ²Pardubice, Czech Republic

Background and aims: Spontaneous spinal epidural haematomas (SSEH) are rare nosological units wherein acute collections of blood develop in the spinal canal with no clear traumatic or iatrogenic cause, usually after a sharp increase in intra-abdominal or intra-thoracic pressure. Further risk include anticoagulant or antiplatelet therapies. SSEH are usually manifested by sudden severe back pain, which is accompanied by the development of neurological symptoms. Although surgical treatment remains the gold standard, conservative management may be also chosen in cases with minor neurological deficits.

Methods: Between 2012 and 2019, we examined 14 patients (age range 17–89 years, 10 women) diagnosed with spontaneous spinal epidural haematomas. 9 cases were patients using anticoagulant therapy (7 warfarin, 1 dabigatran, 1 apixaban). The exact localisation and extent of changes was determined from acute magnetic resonance imaging. 4 people using warfarin had INR higher than 3.0 at the time of their diagnosis.

Results: In 7 patients SSEH were localised in the cervical spine, in 3 patient in the middle thoracic spine, and in 4 patients in the thoracic/lumbar level. 6 patient underwent acute surgery due to rapidly developing spinal cord compression. The clinical condition was favourable in the other patients and a conservative approach was chosen.

Conclusion: 1 of the serious risk factors for the development of SSEH is the use of anticoagulant therapy. Early decompression in cases with severe clinical symptoms is an important therapeutic approach to SSEH, but it is also possible to choose conservative management in cases with minor neurological involvement.

Disclosure: Nothing to disclose

EPO1385

An uncommon cause of subacute myelopathy misdiagnosed as transverse myelitis

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Background and aims: The differential diagnosis of subacute myelopathy is broad and includes mainly inflammatory and infectious etiologies. Metabolic etiologies, intramedullary tumors, and spinal dural arteriovenous fistula should also be considered.

Methods: Case report

Results: A 67-year-old male with history of focal epilepsy and multiple brain cavernomas, presented with subacute paraparesis. 1 year prior to presentation, he had an episode of acute bilateral lower extremity weakness, bowel and bladder incontinence. At another facility, he was found to have a T8-T9 spinal cord lesion diagnosed as transverse myelitis. After treatment with high-dose intravenous steroids he nearly completely recovered. Over 2 months, the patient noticed gradual difficulty walking. He then developed acute lower back pain and lower extremity weakness while changing car tires. Within days, he was wheelchair bound, had constipation and inability to urinate. Neurological examination revealed flaccid paresis of the right lower extremity proximally worse than distally, and mild weakness of left hip flexion. Plantar responses were equivocal bilaterally. Lower extremity vibration and position sense were absent distally. He had urinary retention of 875 cc. Spine MRI showed increased T2 signal from T7-T8 to T11-T12, with regions of T2-hypointensity suggesting hemosiderin deposition, with heterogeneous enhancement and cord expansion. CSF was normal. Aquaporin-4 antibody was negative. The lesion was surgically resected, and histopathology revealed a benign vascular lesion consistent with cavernoma.



Figure 1: MRI of the thoracic spinal cord, sagittal T2-weighted (A) and post-contrast T1-weighted (B) images. Increased T2 signal from T7-T8 to T11-T12, with regions of T2-hypointensity suggesting hemosiderin deposition. There was also a central cystic component of the mass (A) with heterogeneous enhancement and moderate cord expansion (B).

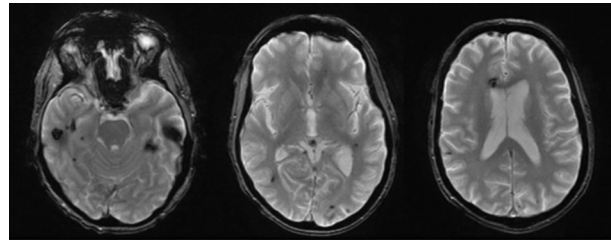


Figure 2: Brain MRI, axial gradient echo sequences, showing multiple small cavernomas scattered in the cerebral hemispheres

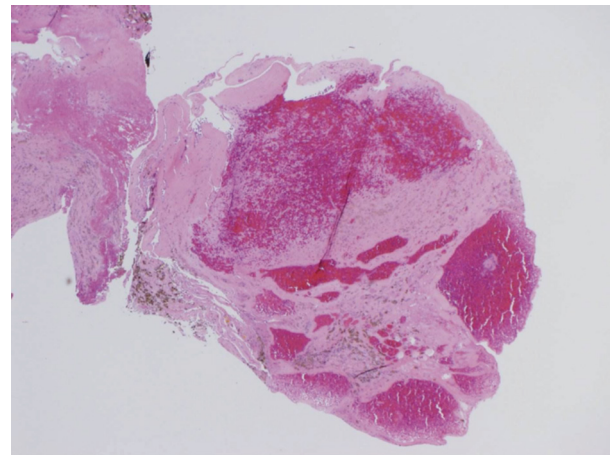


Figure 3: Biopsy specimen. Hematoxylin and eosin stain. The lesion consisted of an aggregate of irregularly-shaped vascular spaces filled with blood. Hemosiderin-laden histiocytes were seen in the surrounding connective tissue.

Conclusion: Spinal intramedullary cavernomas are rare vascular malformations. Clinical presentation and imaging characteristics can be confused with inflammatory processes and neoplasms. This diagnosis should be considered especially in patients with brain cavernomas.

Disclosure: Nothing to disclose

EPO1386

Mass media and Movement disorders: a study of the effects of media on mass psychogenic illness

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Background and aims: This study presents clinical data from a rare case of Mass Psychogenic Illness (MPI) involving movement disorders and explores how symptom exacerbation was influenced by media coverage.

Methods: A retrospective study evaluated clinical histories, precipitating events, treatment strategies, severity and duration of illness for the 16 patients seen at DENT Neurologic Institute. Publications, broadcasts, and other forms of public documentation regarding the affected patient cohort were retrospectively collected. A timeline of patients' encounters and media reporting was developed to examine the evolution of the MPI event and factors which may have prolonged symptomatology.

Results: The completed timeline displays a relationship between mainstream media and the exacerbation of patients' symptoms. Noticeable increased frequency in tics, syncopal episodes, and psychogenic seizures coincided with media attention. When public attention on the case ceased, symptoms resolved in sixteen patients and improved in one patient. There were 14 instances of media attention and 13 reported incidents of exacerbations amongst the patients. Patients reported from 0 to 5 exacerbations. Observed worsening of symptoms occurred within 72 hours of a media event for these reported exacerbations.

Conclusion: There is a possible relationship found between media attention/events and exacerbation of symptoms of MPI in this cohort. These findings may give researchers and clinicians more insight into the symptomology and demonstration of MPI in a modern setting. Occurrences of MPI may be affected by media involvement and clinicians should be aware of the possible associated risks.

Disclosure: Nothing to disclose

ePoster Sessions

Sunday, May 24 2020

Ageing and dementia 2

EPO2001

Epilepsy in early onset Alzheimer's disease

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Background and aims: Epilepsy seems to be an important comorbidity in patients with Alzheimer's disease (AD), especially in young onset AD (<65 years old). At this time, epileptic seizures are still underestimated in this population. However, seizures may interact with AD evolution with possible acceleration of cognitive decline. This study aims to determine the prevalence of the epileptic comorbidity in patients with early onset AD. Secondly, it will extract characteristics of AD patients at higher risk of epilepsy.

Methods: All patients diagnosed as early-onset AD between 2013 and 2019 and followed at the University Hospital of Nancy were selected. The usual follow-up was extended with a prolonged EEG and a consultation with an epilepsy expert. Based on this interrogation and EEG results, patients were classified as epileptic or non-epileptic. We collected demographic data and information on epilepsy and AD disorders.

Results: Among the 22 included patients, 10 were classified as epileptic with a prevalence of 45%. Considering seizure types, patients presented generalized seizures (n=4), typical temporal seizures (n=4), myoclonus (n=1) and extratemporal seizures (n=1). Epileptic patients presented a more severe cognitive decline than patients without seizures (MMSE 8.4±6.9 versus MMSE non epileptic 20.9±5.45). 100% of patients with a MMSE <10 were epileptic.

Conclusion: Epilepsy appears to be a frequent comorbidity in early onset AD patients and seems to be a marker for severe AD. The role of the epileptic disorder in the acceleration of cognitive decline as the positive impact of antiepileptic drugs still need to be determined.

Disclosure: Nothing to disclose

EPO2002

Abstract withdrawn

EPO2003

Improvement of long-term care requirements one year after surgery for idiopathic normal pressure hydrocephalus

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Background and aims: Idiopathic normal pressure hydrocephalus (iNPH) is well-known as “treatable dementia”. However, in contrast to evident improvements in gait disturbance, improvement of the dementia is ambiguous, although previous studies have reported improvements in the results of cognitive tests such as the mini-mental state examination. In this study, changes in long-term care (LTC) requirements for physical disability and dementia were studied using data from a cooperative study of iNPH in Japan (SINPHONI-2 [UMIN000002730]).

Methods: SINPHONI was designed for a 1-year follow-up with after treatment of lumbo-peritoneal shunt surgery. Among 83 participants, 69 participants with data available on the severity of disability and dementia with respect to LTC requirements were analyzed in this study. In the LTC insurance system in Japan, disabilities in elderly people are categorized into 5 major grades (9 levels including subdivisions) and dementia is divided into 6 major grades (8 levels). Postoperative changes at 12 months were classified as improved, unchanged, or worse. Comparisons between pre- and post-operative states were studied using the Brunner-Munzel analysis for ordinal scales

Results: Out of the 69 patients who underwent surgery, improvement in disability and dementia 1 year after surgery was observed in 53.6% and 47.7%, respectively. Statistical analysis revealed that both were significant improvements (p<0.05).

Conclusion: The present study revealed a reduction in the LTC requirements for both disability and dementia one year after surgery for iNPH. Thus, it was confirmed that iNPH is a “treatable dementia” from the viewpoint of LTC.

Disclosure: Nothing to disclose

EPO2004

Transdermal Opioid Use among Elderly with Dementia

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Background and aims: A recent study reported that transdermal opioid use was frequent among elderly with dementia and has been increasing (Jensen-Dahm 2019). Long-acting opioids, such as transdermal fentanyl, have been associated with severe adverse events. To determine possible factors contributing to the high consumption of transdermal opioids, we aimed to investigate potential geographical differences, which might reflect variances in clinical practice.

Methods: Register-based cross-sectional study of the entire elderly (≥ 65 years) population of Denmark in 2015. Data included place of residence (region; municipality; home-living or nursing home), prescriptions, and discharge diagnosis from hospital contacts. Transdermal opioid (buprenorphin and fentanyl) use among elderly patients with dementia ($n=36,014$) and without dementia ($n=1,011,787$) was compared across 98 municipalities.

Results: Across the 98 municipalities transdermal opioid use among home-living elderly with dementia ranged between no use and 12% (36% of total opioid use), whereas it ranged between 0.6% (4% of total use) and 1.9% (11% of total use) for home-living elderly without dementia.

Among nursing home residents transdermal opioid use varied from 6.7% (22% of total) to 29.1% (56% of total) among elderly with dementia and from 5.8% (16% of total) to 27.5% (47% of total) among elderly without dementia.

Conclusion: Transdermal opioid use in elderly with dementia was frequent despite concern about serious adverse events associated with the drugs. The large difference across municipalities, particular among elderly with dementia, suggests variance in how chronic pain is treated in primary care. Our study suggests that more guidance on how to treat pain in elderly with dementia is needed.

Disclosure: Nothing to disclose

EPO2005

Expanding the clinical phenotype spectrum of Prion Protein Gene polymorphism p.met129val: a Greek family with a clinical phenotype of Primary Progressive Aphasia-Motor Neuron Disease

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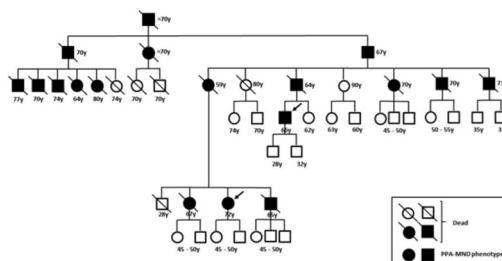
Background and aims: Frontotemporal Dementia (FTD) and Motor Neuron Disease (MND) represent a spectrum of overlapping clinical entities. The behavioral variant of FTD (bvFTD) is considered the most common case and Primary Progressive Aphasia (PPA) is often underrecognized. Prion protein gene (PRNP) mutations and single nucleotide polymorphisms (SNPs) are considered to play a key role apart from Prion Diseases in many Neurodegenerative Diseases, with ongoing field research.

Methods: We evaluated a Greek family with a clinical phenotype of PPA-MND.

Results: 18 family members presented progressive speech (3 of them subtle) and motor disorders around the 6th decade of their lives (PPA-MND spectrum). 16 died, most of them after 5-10 years since symptom onset. 2 members are still alive and underwent genetic testing. 1st patient is a 66-year-old male with progressive speech and upper/lower motor neuron disorders since the age of 57. PPA diagnosis is supported by neuropsychological evaluation and ^{99m}Tc-HMPAO brain SPECT. Whole exome sequencing revealed an heterozygous SNP in PRNP [c.385A>G/p.Met129Val]. 2nd patient is a 72-year-old female with progressive upper/lower motor neuron disorders since the age of 60. Speech disorders appeared only recently and are subtle. Targeted genetic testing revealed an homozygous SNP in PRNP [c.385A>G/p.Met129Val].

Conclusion: This Greek family (1st description in the literature) represents a rare clinical phenotype of PPA-MND spectrum with strong evidence of genetic background. Unfortunately, only 2 members underwent genetic testing. Hence, the exact genetic association is open to further investigation such as the hypothesis that Methionine/Valine heterozygosity predisposes to a prominent PPA phenotype.

Disclosure: Nothing to disclose



A Greek family with eighteen members presenting a clinical phenotype of PPA-MND

EPO2006

Muscone promotes Abeta clearance and ameliorates cognitive deficiency in APP/PS1 mice through HDAC2 degradationY. Liu¹, X. Cao¹, S. Shu¹, Y. Xu¹, J. Chen²¹Department of Neurology, Nanjing Drum Tower Hospital, Nanjing, China, ²Department of Neurology, Drum Tower Hospital of Nanjing University Medical School, Nanjing, China, Nanjing, China

Background and aims: In the pathology of Alzheimer's disease (AD), Abeta deposition causes degeneration of synaptic plasticity, leads to memory loss and cognition impairment. Histone deacetylases 2 (HDAC2) has been shown to promote the pathologic alterations. Muscone (Mus), 1 of the simplex ingredients of traditional Chinese medicine, has been discovered neuroprotective effects on cerebral ischemia models. It is aimed to finding new drug targets for the treatment of AD.

Methods: Mus was intraperitoneally (i.p.) injected into the 6-month-old APP/PS1 or WT mice every day. 20 days later, Novel object recognition test (NOR) and Morris water maze (MWM) test were performed to evaluate spatial reference and working memory. Enzyme linked immunosorbent assay (ELISA), Immunofluorescence, Golgi staining and long-term potentiation (LTP) were used to measure the Abeta clearance and synaptic morphology. Western blot was conducted to detect the expression of target proteins.

Results: Behavioral results showed that the APP/PS1 mice with Mus treatment has a longer exploration time for NOR and more crossing platform times for MWM compared with APP/PS1 mice without it. The expression of Abeta was decreased and synaptic plasticity was rescued by administration of Mus in ELISA, Immunofluorescence, Golgi and LTP results. It also decreased the protein levels of HDAC2 in the brain tissues compared with APP/PS1 mice.

Conclusion: Our results indicated that Mus exhibited a protective effect against Abeta and synaptic plasticity via degradation of HDAC2 in APP/PS1 mice. These results provided evidences for the novel and potential application of Mus for the treatment of AD.

Disclosure: Nothing to disclose

EPO2007

Could in vivo measured cerebral tissue pH be an indicator of neurodegenerative diseases associated with age and pathological protein aggregation?E.E. Lyros¹, A. Ragoschke-Schumm¹, P. Kostopoulos², A. Sehr¹, M. Backens³, S. Kalampokini¹, Y. Decker⁴, M. Lesmeister¹, Y. Liu¹, W. Reith⁵, K. Fassbender¹¹Neurology, Saarland University Medical Center, Homburg, Germany, ²Medical Park Bad Camberg, Bad Camberg, Germany, ³Neuroradiology, Saarland University Medical Center, Homburg, Germany, ⁴Neurology, Saarland University Medical Center, Homburg, Germany, ⁵Neuroradiology, Saarland University Medical Center, Homburg/Saar, Germany

Background and aims: There is in vitro evidence that low pH can enhance the pathological aggregation of proteins such as amyloid peptide and alpha-synuclein. The clinical relevance of these experimental findings is however largely unknown. We recently showed in vivo that Alzheimer's disease (AD) patients have lower pH than controls in the periventricular white matter (WM).

Methods: We extended our study to 12 patients with idiopathic Parkinson's disease (PD) who underwent proton spectroscopy after oral administration of histidine. We compared pH measurements from 3 brain regions (periventricular WM, hippocampus and cerebellum) of PD patients to those of 30 controls by means of ANCOVA to adjust for variation in age and scanner used.

Results: ANCOVA revealed a trend toward lower WM pH in PD patients than in controls (6.87 ± 0.04 vs 6.91 ± 0.06 , $p=0.06$). The difference in cerebellar pH also approached statistical significance ($p=0.08$) with lower values in PD, whereas the comparison of hippocampal pH revealed no trend ($p=0.36$). Within all participants, worse visuoconstructive task performance (figure drawing) correlated with lower WM pH ($r=0.44$, $p=0.004$).

Conclusion: These preliminary results demonstrate a tendency towards a more acidic brain pH also in PD and complement our recently published data in normal brain aging and AD. We thus raise the plausible hypothesis that alterations in cerebral tissue pH may be involved in the initiation and progression of neurodegenerative diseases characterized by pathological aggregation of either amyloid beta or alpha-synuclein and appearing more frequently with increasing age. Consequently, targeting pH warrants investigation as a therapeutic approach for tackling these diseases.

Disclosure: This work was supported by Grants to K.F. and Y.L. from SNOWBALL, an EU Joint Programme for Neurodegenerative Disease (JPND) (01ED1617B).

EPO2008

Cholesterol content in peripheral blood cells of patients with Alzheimer's disease

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Background and aims: Alzheimer's disease (AD) is the most frequent degenerative dementia, with a prevalence expected to increase in coming years. Deposits of amyloid and hyperphosphorylated TAU protein constitute the characteristic pathological findings of the disease, although its etiology in sporadic cases is still unknown. Cholesterol metabolism has been related to AD through multiple evidences. Filipin is a macrolide that binds to cholesterol and allows its quantification. We consider assessing whether there are differences in cholesterol content determined by Filipin's fluorescence (FF) in peripheral blood mononuclear cells (PBMCs) of patients with AD and healthy controls.

Methods: Cross-sectional study. Patients diagnosed with AD at different stages with support of biomarkers in cerebrospinal fluid (CSF) and cognitively healthy controls were included. PBMCs obtained from whole blood were co stained with Filipin and antibodies for several leucocyte subpopulations (CD8, CD4, CD11b, CD19, CD14 and CD16). FF was measured by flow cytometry in PBMCs and in different subpopulations

Results: N=61 (51AD, 10 controls). When the whole PBMCs were compared, no significant differences in filipin fluorescence among diagnostic groups were observed (AD 1280, controls 1218.9; $p=0.65$). However, subpopulation analysis revealed significant decrease in cholesterol content in CD14+ cells of patients with AD (AD 2623.9, controls 4433.2; $p=0.007$). Differences in cholesterol content in this CD14+ subpopulation were also significant in ApoE4 carriers (2427.1 in carriers, 3130.43 non-carriers, $p=0.017$)

Conclusion: Cholesterol content of CD14+ peripheral blood mononuclear cells could be a neurodegeneration biomarker and it could be related with AD, which supports the involvement of cellular cholesterol homeostasis in the pathophysiology of the disease.

Disclosure: This research has been granted by Economy Ministry of Spain (institutional support)

EPO2009

Clinical and imaging characteristics of high amyloid-producing Alzheimer's disease patients

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Background and aims: In 2018, the ATN criteria recognized CSF A β 42/40 ratio as a surrogate biomarker of amyloid deposition in Alzheimer's disease (AD) when CSF A β 42 is in the normal range. Pathological A β 42/40 ratio yet normal A β 42 is a situation commonly seen in high amyloid-producing patients (HAP), where there is a relative decline of A β 42 that remains in the normal range.

We aim to compare the clinical, biochemical and neuroimaging profile of HAP AD patients (A+T+N+, A positivity being determined with the A β 42/40 ratio) as compared to low amyloid-producing patients (LAP).

Methods: Among the 547 A+T+N+ patients that attended our memory clinic since 2011, 402 were LAP and 146 were HAP. Analysis of the cognitive profile was performed in the 215 (138 LAP and 77 HAP) patients that had a MMSE >20 at baseline. VBM analysis was performed on a subset of 80 patients paired by age and MMSE (38 HAP and 42 LAP) with both MRI and FDG-PET scans available.

Results: HAP are older have a higher MMSE score at baseline than LAP (72y \pm 9 vs 69y \pm 8 and 20 \pm 6 vs 19 \pm 6).. However, the cognitive profile at baseline was identical in patients with a MMSE >20. CSF Tau biomarkers are not statistically different between the 2 groups ($p=0.27$). VBM analysis did not show any significant difference on brain atrophy nor FDG metabolism.

Conclusion: Our study reinforces the use of the A β 42/40 ratio when A β 42 is normal since there are no cognitive, biochemical and neuroimaging point of view. Analyses of ApoE genotype and MMSE progression are currently undergoing.

Disclosure: Nothing to disclose

EPO2010

Functional connectivity in patients with Alzheimer's disease as a biomarker of cognitive decline

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Background and aims: Alzheimer's disease (AD) is 1 of most frequent neurodegenerative disorder. EEG-coherence is a sensitive marker of connectivity in brain, whereas fMRI detect activation patterns, which could be coupled. The aim of this study was to correlate fMRI activation patterns and EEG-coherence in AD, mild cognitive impairment (MCI) and age-matched healthy controls, investigating differences of connectivity between groups.

Methods: 53 patients with AD, 45 patients with MCI were included in the investigation according to diagnostic criteria of DSM V and MKB 10. The control group includes 45.

We performed fMRI (3 Tesla ,TRIO, Siemens, Erlangen, Germany) and resting EEG-recordings (NeuroScan Synamps System). EEGs were recorded in a wakeful resting state with eyes closed using a standard protocol and montage. Coherences between regions of interest, based on fMRI activation patterns, were calculated.

Results: We found significant differences between AD and MCI - theta band coherences, between anterior cingulate and left temporal gyri ($p < 0.05$), (fig3); between AD and control subjects for theta -anterior cingulate and right temporal gyri, anterior cingulate gyrus and left hippocampus ($p < 0.01$), (fig2). Theta coherence was significantly lower in patients with MCI compared with controls between anterior and posterior cingulate gyri, anterior cingulate and left/right temporal gyri, posterior cingulate and superior frontal gyri ($p < 0.01$), and between right and left temporal gyri ($p < 0.05$), (fig1).

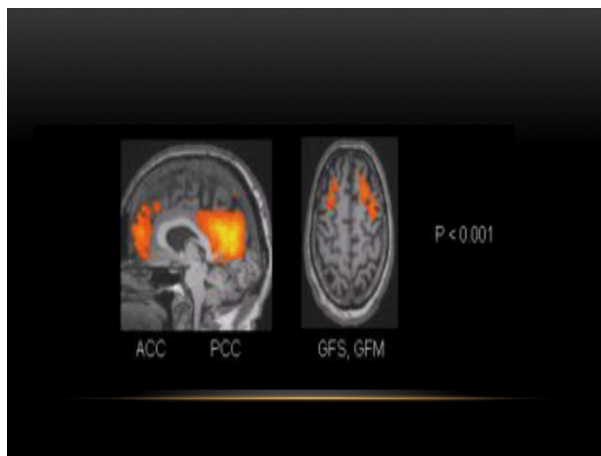


Fig.1 Comparison of healthy elderly subjects vs. MCI patients. fMRI activations ($p < 0.001$) Correspondence in frontal, but not in posterior regions

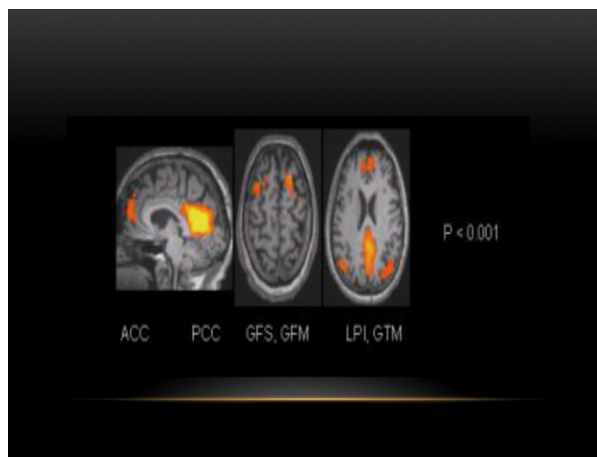


Fig.2 Comparison of healthy elderly subjects vs. AD patients. fMRI activations ($p < 0.001$). Correspondence in frontal, but not in posterior regions



Fig.3 Comparison of MCI and AD patients. fMRI activations ($p < 0.001$).

Conclusion: EEG coherence could serve biomarker of AD and help in the early detection of the neurodegenerative disease.

Disclosure: Nothing to disclose

EPO2011

A systematic review of QEEG as a tool for differential diagnosis of Alzheimer's disease with other forms of dementia

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Background and aims: The differential diagnosis of Alzheimer's disease (AD) with other dementias is often difficult. The literature of the past 30 years suggests the presence of certain QEEG alterations associated with cognitive impairment. This systematic review aims at offering a comprehensive analysis of possible QEEG patterns which might improve the differential diagnosis of AD.

Methods: The systematic review process was performed in compliance with the PRISMA statement and checklist. PubMed, Embase and PsycNet databases were queried using equivalent combinations of 'quantitative EEG' and 'Alzheimer'.

Results: 10 articles were selected after title, abstract and full-text screening of 667 search results. The most often used QEEG parameters in differential diagnosis were absolute power, relative power and coherence. Diffuse alterations are found in the δ and θ frequency bands in AD, with reduction of α -central activity, but the enhancement of the slow global activity is more pronounced in dementia associated with Parkinson's disease. The reduction of coherence in frontal and central areas appears specific in AD in contrast to vascular dementia. 2 studies integrated QEEG parameters into classification algorithms based on machine learning, increasing the precision of algorithm by 8%.

Conclusion: This review is among the 1st in the literature to propose an assessment of the role of QEEG in recognizing AD and discriminating between other forms of dementia. In this problematic process, QEEG may serve as an alternative technique for a more accurate diagnosis. Further research should explore this topic through comparable quantitative approaches.

Disclosure: Nothing to disclose

EPO2012

Metabolic failure of right inferolateral frontal cortex impairs prospective memory (PM) in MCI due to Alzheimer's disease (MCI-AD)

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Background and aims: Prospective memory (PM) involves executive processes such as forming and maintaining an intention in memory over time while performing another task. Prefrontal regions could be involved in PM although little is known in early Alzheimer's disease (AD). We investigated the brain metabolic correlates of PM in patients with MCI-AD compared to healthy controls (HC).

Methods: 18 patients (10 males, age: 74±4.9; MMSE score: 27.7±1.6) with intermediate (FDG-PET, 6 patients) or high (plus a positive amyloidosis biomarker, 12 patients) likelihood of MCI-AD were enrolled. In 10 patients the diagnosis of AD dementia was made 2.7 years later (range: 0.8-3.4) while eight patients are not converted after 3.4 years (range: 0.25-6.9). HC included 23 subjects (11 males, age: 71.5±5.7) undergoing FDG-PET and neuropsychological evaluation. PM was evaluated with the Ungvari et al (Arch Clin Neuropsychol. 2008; 23:613-622) paradigm test. Brain metabolism was compared between MCI-AD and HC (SPM-12) and correlated with the PM score in all the 41 subjects, then in HC and in MCI-AD groups separately, with age and education as nuisance variables.

Results: In MCI-AD group significant hypometabolism was found in the precuneus/posterior cingulate (PC/PCC) region. PM score was positively correlated (uncorrected $p < 0.001$) with the same PC/PCC region in all subjects, with right inferior frontal and orbitofrontal gyri (uncorrected $p < 0.005$, $p < 0.05$ FWE-corrected at cluster level) in MCI-AD patients (Fig. 1); no correlation was found in HC.

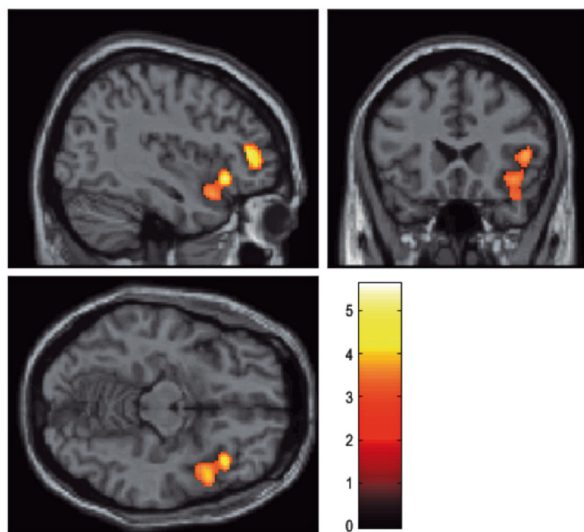


Fig.1

Conclusion: Progressive impairment of brain function in right inferolateral frontal cortex is responsible for loss of PM in early AD.

Disclosure: Nothing to disclose

EPO2013

A rare case of adult onset neuronal intranuclear disease

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Background and aims: Adult onset neuronal intranuclear inclusion disease (NIID) is a rare and slowly progressive neurodegenerative disorder that can be sporadic or familiar in onset. The clinical manifestations are highly variable but patients have been reported to present with dementia or encephalitic episodes. It is characterised by eosinophilic intranuclear inclusions in the nervous system and visceral organs.

This case study aims to increase awareness and deepen other clinicians' understanding of this disease.

Methods: 59-year-old lady presented to ED with 3 days of profound expressive dysphasia and worsening confusion on background of gastrointestinal symptoms and episodic migraines with left sided hemispheric dysfunction since 2012.

Results: There was progressive cortical thickening and signal hyperintensity on MRI with hypometabolic change on PET-CT in left temporal, parietal and occipital region with EEG consistent with moderate to severe encephalopathy resulting in commencement of steroids and Levetiracetam. Ongoing debilitating symptoms led to a brain biopsy from the left temporal region that revealed intranuclear eosinophilic inclusions. She received multidisciplinary team input and had slow improvement in ability to perform activities of daily living.

Conclusion: This case was a diagnostic challenge and was academically stimulating. It reminds us of the importance of keeping broad differentials in mind when dealing with encephalopathy. NIID is increasingly recognised as an under diagnosed entity and an important differential diagnosis of leukoencephalopathy and neuropathy.

I will be presenting an overview of NIID and discuss when to suspect this disease and the use of skin biopsy, which is a reliable and practical diagnostic method.

Disclosure: Nothing to disclose

EPO2014

Perspective taking abilities in Alzheimer's disease

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Background and aims: There is an increasing effort to find simple and reliable tests for the early diagnosis of Alzheimer's disease (AD). Spatial orientation deficits are present early in AD and could thus serve as an early cognitive marker of the disease. We aimed to evaluate the potential of perspective taking tests to identify individuals with early AD and to differentiate them from those with cognitive deficit of other etiology.

Methods: 57 participants with amnesic mild cognitive impairment (aMCI) and positive AD-biomarkers (aMCI due to AD, n=14), aMCI and negative biomarkers (aMCI AD-negative, n=12), mild AD dementia (n=12) and cognitively normal (CN) older adults (n=19) underwent clinical and neuropsychological evaluation, MRI brain scan, amyloid PET imaging, cerebrospinal fluid biomarker assessment and 2 perspective taking tasks: Standardized Road-Map test of Direction Sense (RMTDS) and Perspective Taking/Spatial Orientation test (PTSOT). In the RMTDS, the participants followed a pathway on a city map indicating a direction of turning (left or right) at each intersection. The PTSOT included pictures of arrays of objects and participants indicated direction between selected objects.

Results: The aMCI due to AD and mild AD dementia groups had lower scores in the PTSOT compared to the CN ($p<0.05$) and aMCI AD-negative ($p<0.05$) groups. There were no differences between CN and aMCI AD-negative groups in the PTSOT. All groups had similar performance in the RMTDS.

Conclusion: The PTSOT reliably detects spatial orientation impairment typical for early stages of AD. This test can differentiate aMCI participants due to AD from those with non-AD etiology.

Disclosure: Supported by: Grant Agency of Charles University grant no. 693018

EPO2015

H.pylori infection and cortical thinning in cognitive normal individuals

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Background and aims: Helicobacter pylori (H.pylori) is a well known bacteria for development of stomach cancer and chronic inflammation. However, H.pylori's contribution to the neurodegeneration remains largely unknown. We aimed to evaluate the association between H.pylori infection and brain cortical thickness in cognitively normal individuals.

Methods: Total 3996 participants (age \geq 45 years) were recruited from Health Promotion Center in Samsung Medical Center from September 2008 to December 2014. After excluding participants with missing variables, 1,594 were selected in final analysis. Participants underwent brain magnetic resonance images including 3-dimensional volume images. We measured cortical thickness using the standard Montreal Neurological Institute image processing tool CIVET. H. pylori infection was defined pathologically with esophagogastroduodenoscopy biopsy. Multiple linear regression analysis was done to evaluate the relationship between H.pylori infection and brain cortical thickness after controlling for age, intracranial volume, CRP.

Results: In male, H. pylori infection was associated with cortical thinning in the bilateral lateral temporal, lateral frontal, and right occipital areas after adjusting for age, intracranial volume, CRP. However, in female, H. pylori infection was not associated with cortical thickness.

Conclusion: Our findings suggest that H.pylori infection is associated with neurodegenerative changes in cognitive normal male, regardless of chronic inflammation.

Disclosure: Nothing to disclose

EPO2016

Serum neurofilament light chain levels and disability milestones in Lewy body diseases

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Background and aims: Blood and CSF neurofilament light chain (NfL) levels have been proposed as a marker of neurodegeneration. Several studies show NfL levels could be used to discriminate between Parkinson's disease (PD) and atypical parkinsonism. Aim of the study was to evaluate the correlation between NfL and milestones of disability in Parkinson's disease (PD) and dementia with lewy bodies (DLB)

Methods: Plasma NfL concentration was measured using Single molecule array technology in a cross-sectional study including patients with PD, n=92 and DLB, n=27. We evaluated the correlation between NfL concentrations and motor, non-motor symptoms, cognitive and behavioral abnormalities in PD and DLB. All analyses are corrected for age, sex and disease duration.

Results: Plasma NfL correlated with age and age at onset in the cohort; PD showed lower NfL levels compared with DLB patients (p=0.001). In PD, higher NfL correlated with hyposmia (p=0.01), total UPDRS-II and UPDRS-III scores (p=0.001), gait speed (p=0.04) and several disability milestones, including cognitive impairment (p=0.001), symptomatic dysautonomia (p=0.001), loss of independency in activities of daily living (p=0.01) and instrumental daily living (p=0.001). In DLB, NfL correlated with disease duration, hyposmia and neuropsychiatric symptoms, but not with motor function assessed by UPDRS-III. At follow-up, NfL was the best predictor of motor progression in PD, beyond the classification of malignant phenotype.

Conclusion: Elevated plasma NfL levels are associated with disability milestones in PD patients and neuropsychiatric abnormalities in DLB. Further longitudinal investigations are warranted in order to evaluate NfL as a predictive biomarker of disability progression in Lewy bodies disorders.

Disclosure: Nothing to disclose

EPO2017

Extrastriatal dopaminergic and serotonergic pathways in Alzheimer's disease: a 123I-FP-CIT study

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Background and aims: Pathological reports suggest that dopaminergic and serotonergic pathways are early involved in Alzheimer's disease (AD). 123I-FP-CIT SPECT imaging allows the evaluation of both dopamine transporter (DAT) and serotonin transporter (SERT) in several brain regions. Aim of the study was to evaluate extrastriatal dopaminergic and serotonergic pathways in AD patients by using a 123I-FP-CIT SPECT imaging.

Methods: 69 subjects with AD were included in a multicenter study and underwent neurological examination, structural and functional imaging or CSF, in order to reach a biomarker diagnosis of AD (i.e. A+T+N+). Each individual underwent 123I-FP-CIT SPECT imaging. The occipital-adjusted binding (SBR) in extrastriatal regions were compared between AD subjects and controls, adjusting for the effect of age, sex, disease duration and serotonergic/dopaminergic treatment.

Results: 52 AD subjects A+T+N+ and 75 controls entered in the study. AD patients (n=35) showed lower 123I-FP-CIT SPECT SBR in the cingulate gyrus (p=0.001) and temporal lobe (p=0.007) as well as in the insula (p=0.01) and thalamus (p=0.025) compared to controls. When dividing AD subjects according to severity, MCI due to AD (n=17) showed significantly lower parietal SBR compared to controls (p=0.002) and significantly higher SBR in the insula (p=0.01), thalamus (p<0.001) and temporal lobe (p=0.008) compared to AD dementia cases.

Conclusion: We demonstrated extrastriatal dopaminergic and serotonergic impairment in Alzheimer's disease and from the prodromal phase and become widespread during disease course. Longitudinal studies will be necessary in order to evaluate the clinical value of extrastriatal 123I-FP-CIT SPECT assessment in AD patients.

Disclosure: Nothing to disclose

EPO2018

“Don’t know” sign: description and evaluation of its diagnostic accuracy for cognitive impairment, comparing to other observation based signs

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Background and aims: In neurology clinic, sometimes patients do not know the main complaint or the reason for the consultation. We have called this circumstance “don’t know” sign (DKS). Our objective is to define this new sign and its modalities and to evaluate its prevalence and diagnostic accuracy for cognitive impairment (CI), comparing with other observation based signs.

Methods: Cross-sectional, prospective study, which includes all new patients evaluated by authors in outpatient settings, during 5 months. We recorded the presence of DKS during the consultation. We used global deterioration scale (GDS) to assess cognitive status, using clinical history, caregivers’ interview and cognitive tests. We considered CI if GDS \geq 3. We analyzed prevalence and diagnostic accuracy of DKS, “head turning sign”, “attending with” and verbal repetition, by calculating their Sensibility (Se), Specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV).

Results: We included 673 patients (62% female), with a wide range of age (14-97 years old; 59.3 \pm 20.2 (average \pm sd)). DKS was positive in 14% of the sample and its presence was strongly associated to GDS. DKS has Se 0.41, Sp 0.98, PPV 0.89 and NPV 0.79. Remarkably, “attending with” sign has Se 0.97, Sp 0.34, PPV 0.39, and NPV 0.96.

Conclusion: DKS is common in neurology outpatient; its Se is low but it is very specific for CI, and it has high PPV. It does not cost any extra time and we recommend its use in combination with other signs based on observation (particularly “attending with” sign).

Disclosure: Nothing to disclose

EPO2019

Metabolic connectivity alterations of dorsal attention, ventral attention and limbic networks are associated with visual hallucinations in Lewy Body Dementia (DLB): a FDG-PET/MRI study

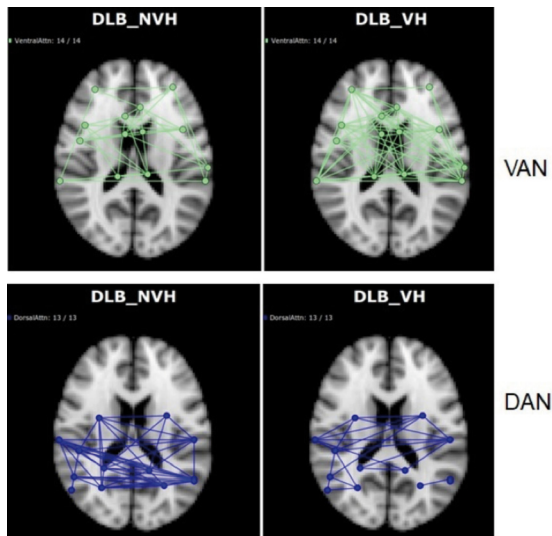
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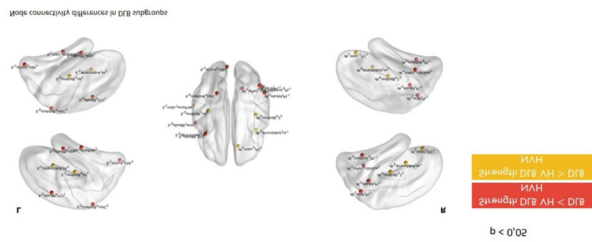
Background and aims: Recurrent-complex-visual-hallucinations-(VH) are common in dementia with Lewy-bodies-(DLB). Only 1 study investigated metabolic connectivity in DLB with VH using PET-FDG. We explore connectivity changes of PET-FDG data acquired with a hybrid-PET/MRI scanner in DLB-VH+ patients

Methods: 26-patients with a diagnosis of probable DLB (13VH+, 13VH-; mean age: 72.9 \pm 6.87yrs versus 70.2 \pm 7.96yrs) and 14-controls subjects (mean age: 65.5 \pm 7.94yrs) were enrolled. T1-MPRAGE-MRI and PET-FDG data were co-acquired for all subjects. T1-sequences were processed using Freesurfer standard-pipeline adapting Shaefer-Yeo-functional-atlas 7N for cortical parcellation. The standardized-uptake-values (SUV) for each ROI corrected for partial volume (Symmetric-Geometric-Transfer-Matrix-method), normalized to the cerebellum, were extracted. Graph analysis was performed using BrainGraph-package-R to extract clustering-coefficient, strength degree, and characteristic-path-length and hubs

Results: CTRL showed higher SUVr values for each network as compared to both DLB groups. SUVr values of the dorsal attention network were lower in the VH+ group compared to VH-. Graph analysis showed lower nodal strength globally in the dorsal attention, parietal and ventral attentive networks in VH+. VH+ patients showed lower strength degree in the inferior parietal lobe (default network) and post-central regions (dorsal attention) nodes; and higher strength degree in the orbitofrontal cortex and temporal-pole (limbic), and inferior frontal cortex (ventral attention) nodes. In VH+ many dorsal attention networks posterior hubs were lost, and anterior hubs in the default mode, fronto-parietal, ventral and limbic networks were



Connectivity of DAN and VAN between the two DLB subgroups
 Connectivity of DAN and VAN between the two DLB subgroups



Node strength connectivity differences between DLB subgroups

Conclusion: The presence of VHs are associated with metabolic decrements of connectivity in parieto-occipital-cortex, connectivity alteration of the dorsal and ventral attention networks, and relatively higher connectivity in the limbic system

Disclosure: Nothing to disclose

Cerebrovascular diseases 4

EPO2020

Mechanical thrombectomy in Albania

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Background and aims: Large vessel occlusion causes major cerebral lesions with a high mortality or recurrent disability (60-80%). Since 2014, with the publication of large studies of mechanical thrombectomy, the treatment of these patients has entered a new perspective where Albania has been involved too.

Methods: This prospective study includes results from the 1st 5 years of mechanical thrombectomy in Albania, in large vessel occlusion. It evaluated the association between NIHSS and mRS scores with the door-to-groin interval, localization, age, hospital stay and other variables on records of the "Mother Thereza" Hospital from January 2015 to October 2019. 43 patients were enrolled, subdivided in 3 groups according to door-to-groin interval, evaluating NIHSS upon discharge and the mRS upon discharge and after 90 days.

Results: Mean interval from symptoms onset to thrombectomy $M=5.4\pm 2.9$ hours, anterior localization (79.1%) and posterior (20.9%). Mean NIHSS improvement from admission to discharge was 5.6 (-2.8) points with a significant difference ($p<0.01$). Mean mRS improvement from admission to discharge was 1.4 (-0.4) points, with a significant difference ($p<0.01$). Mean thrombectomy interval was higher in posterior localization ($M=8.7\pm 4.8$ hours). At 90 days, symptomatic intracranial hemorrhage rate was 16.7%, death rate was 14% (95%CI). Mean mRS at the 90 days follow-up was $M=1.4 (\pm 1.9)$, with a significant difference with admission mRS ($p<0.01$).

Conclusion: Study confirms that early endovascular treatment was safe and effective in reducing disability score at 90 days and superior to intravenous thrombolysis in large-artery occlusion.

Disclosure: Nothing to disclose

EPO2021

Mechanical thrombectomy in Albania

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Background and aims: Occlusion of large cerebral vessels causes major lesions with a high mortality or disability. Noninvasive methods such as intravenous thrombolysis have a low success rate in recanalization of large vessels. Since 2014, with the publication of large studies of mechanical thrombectomy, the treatment has entered a new perspective where Albania has been involved quite rapidly.

Methods: We evaluated the association between the NIHSS and mRS scores with the door-to-groin interval, localization, sex, age, risk factors, hospital length of stay and other variables recorded from the medical charts of the UHC Mother Teresa from January 2015 to October 2019. The enrolled patients are subdivided in 3 groups according to door-to-groin interval, evaluating NIHSS upon discharge and the mRS upon discharge and after 90 days.

Results: 43 patients were enrolled, with a mean interval of time from symptoms onset to thrombectomy $M=5.4\pm 2.9$ hours. The mean NIHSS improvement from admission to discharge was 5.6 (-2.8) points ($p<0.01$). The mean mRS improvement from admission to discharge was 1.4 (-0.4) points ($p<0.01$). The mean interval of thrombectomy was higher in patients with posterior localization ($M=8.7\pm 4.8$ hours) ($p=0.04$). At 90 days, the rates of symptomatic intracranial hemorrhage were 16.7%, and rates of death were 14% (95%CI). The mean mRS at the 90 days follow-up was $M=1.4 (\pm 1.9)$, with a significant difference with the admission mRS ($p<0.01$).

Conclusion: The early treatment with mechanical thrombectomy is safe and effective in reducing the score of disability at 90 days in cases of large-artery occlusion.

Disclosure: Nothing to disclose

EPO2022

The woman who could not read the initial part of the words, but could otherwise see - an atypical stroke presentation as hemialexia

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Background and aims: Besides striated cortex, visual information is spread over a wide area of cortical and subcortical regions. The ventromedial occipital cortex and left angular gyrus are essential for color vision and reading, respectively.

Methods: A 57-year-old woman with diabetes mellitus and dyslipidemia presented with vision impairment with sudden onset 7 days before: she couldn't see the initial part of the words (but was able to write) and saw colorless and unfocused left hemifaces.

Neurological examination showed left hemialexia and hemiacromatopsia without visual field deficit nor visual neglect. No agraphia, digitagnosia, dyscalculia were noted. The remaining examination was normal.

Results: Brain magnetic resonance imaging revealed a right thalamocapsular lesion with extension to the ipsilateral cerebral peduncle (hyperintense on FLAIR and DWI, without clear restriction on the ADC nor contrast uptake) and also a FLAIR hyperintense left posterior occipital lesion.

The neurovascular and cardiac studies were normal. Blood workup was unremarkable (including immune study). Lumbar puncture was normal, with negative oligoclonal bands.

A small vessel stroke was assumed and the patient was discharged with statin and aspirin.

Conclusion: This case represents an hemialexic syndrome, a very unusual and challenging stroke presentation. This is usually due to splenic lesions of the corpus callosum.

The patient's left occipital lesion seems to affect the fibers originating from the right visual cortex, containing left visual field information (arising from cortical regions responsible for reading).

The thalamic lesion could explain the remaining visual deficits.

Disclosure: Nothing to disclose

EPO2023

Recurrence rate and hemorrhagic complications in patients with cardio-embolic transient ischemic attacks

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Background and aims: 20-30% of transient ischemic attacks (TIA) are due to cardio-embolic cause. Atrial fibrillation is frequently diagnosed after TIA. A prior detection is important to start anticoagulation. Therapy with direct-oral anticoagulants (DOACs) has shown no inferiority and less haemorrhagic risk in comparison with warfarin. Our aim is to describe clinical characteristics of patients who suffered an embolic or cryptogenic TIA as well as the recurrence and haemorrhagic complication rates due to anticoagulant treatment.

Methods: Retrospective cohort study of patients who were attended at Emergency room or admitted between 2014-2018.

Results: 49 patients with a median follow-up of 33±28 months. Most were men (61.2%), median age 75.5±16, hypertension 75.5%, dyslipidemia 53%, previous TIA/stroke 12.2%, diabetes 16.3%. 75.5% were cardio-embolic and 24.5% were cryptogenic. AF was newly diagnosed in 40.8% and was known in 42.9%. Most frequent clinical onset was aphasia 34.7%. An echocardiogram was performed to 59.2% showing moderate-severe left atrial dilatation in 40.9% and atrial septum aneurysm and/or patent foramen ovale (PFO) in 2 cases. MRI was performed in 34% and acute lesion was demonstrated in diffusion-weight imaging in 10.2%. The anticoagulation prescribed was warfarin 18.4%, apixaban 34.7% and dabigatran 18.4%. 53.1% was treated by usual dose. Recurrence rate was 12.2% or 0.37% cases per month. There was one haemorrhagic stroke and no deaths.

Conclusion: Accordingly to our data, the recurrence rate was lower in comparison to the data described in literature, possibly due to early implementation of an effective and safe treatment strategy.

Disclosure: Nothing to disclose

EPO2024

Understanding seasonal variability in cervical artery dissection in the Russian population

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Background and aims: Cervical artery dissection (CeAD) is the most frequent cause of ischemic stroke in young adults and some other manifestations. American, European and Australian authors showed seasonal CeAD variation with increased frequency in cold season.

Aim: To investigate the seasonal variation in incidence of CeAD in the Russian population.

Methods: We examined 270 patients (mean age 37.9 ± 8.7 ; 151 females, 56%) with CeAD, verified by MRI/MRA. We analyzed CeAD frequency during all months of the year and compared its frequency in the cold season (September 22–March 21) and warm season (March 22–September 21). Chi-square compliance criteria were used to test whether the difference was significant.

Results: CeAD frequency ranged from 11 to 26 over the months, being lowest in April (11), July (16) and November (19). The difference was not statistically significant ($p=0.2875$). CeAD had a tendency to occur more frequently in cold season compared to warm season (145 dissection, 54% vs 125 dissections, 46%; $p=0.22$). The frequency of infection, 1 of the precipitating factor of dissection did not differ in cold and warm seasons ($p>0.05$).

Conclusion: The absence of CeAD seasonal variability in Russia does not exclude the importance of environmental factors in its development. It is assumed the significance of atmospheric pressure fluctuation, which is typical for all seasons in Russia. Its decrease could cause vasodilatation, which in condition of arterial wall dysplasia could lead to an intimal tear and CeAD development. The cold season and associated infection and increased blood pressure do not play a role in CeAD provoking.

Disclosure: Nothing to disclose

EPO2025

Ischemic stroke due to calcium embolism

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Background and aims: Calcium embolism is an infrequent cause of ischemic stroke, with a prevalence around 2.7%. The most common causes of these emboli are calcified heart valves and calcified atheroma plaques.

Methods: A case of ischemic stroke due to calcium embolism is presented.

Results: A 34-year-old patient with a history of chronic renal disease secondary to extracapillary Glomerulonephritis type I (anti-Glomerular Basal membrane disease) in hemodialysis, secondary hyperparathyroidism and arterial hypertension in treatment with 5 drugs, who attended the emergency department with aphasia and left hemiparesis of unknown time of evolution. The patient had left-hand dominance. Advanced neuroimaging study was performed, which showed compatible images with 2 subocclusive calcium embolisms in segments M3 and M4 of the right middle cerebral artery and ischemic penumbra in the right parietal lobe and posterior frontal lobe.

The study was completed during his admission to the neurology ward. The analysis showed renal insufficiency and hyperparathyroidism (Hyperparathyroid hormone: 1558 picograms per milliliter -normal values: 10–25 picograms per milliliter-). Echocardiography was performed, showing severe calcification of the mitral ring.

Conclusion: Calcium cerebral embolism is a rare condition which can appear both spontaneously and after invasive procedure such as valve surgery. Because of the infrequency of this condition, there are not enough studies to establish a consensus on how to act in a patient with an ischemic stroke due to calcium embolism. Due to the nature of the embolus, it is considered that only thrombectomy could be useful, having already described some cases of good evolution after this procedure.

Disclosure: Nothing to disclose

EPO2026

Dual Mechanisms of Ischemic Stroke – Frequency and Outcomes in a University Hospital based Stroke Registry.

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Background and aims: Ischemic strokes (IS) are classified based on pathophysiologic mechanisms into large artery atherosclerosis (LAA), cardioembolism (CES), small-vessel disease (SVD) or others. Co-existence of dual stroke mechanisms in a patient is sometimes recognized.

This study examines the frequency and patterns of dual stroke mechanisms among patients with IS and its relation to stroke outcomes.

Methods: Case records of patients with IS entered into a University Hospital based stroke registry using TOAST classification were reviewed for reasonable evidence of an additional/coexisting stroke mechanism. Examples are significant extra/intracranial atherosclerotic stenosis with SVD or CES, or SVD with CES. Demographics, risk factors and stroke outcomes were compared between cohorts with single and dual stroke mechanisms. Univariate and multivariate analyses were used to explore factors influencing outcomes.

Results: Of a total of 772 patients with IS (mean age: 63±12 ys; M:F=1.7:1), 106 (13.7%) had an additional stroke mechanism. The most frequent additional stroke diagnoses were SVD (53%) and CES (33%). Patients with dual stroke diagnoses were older, had higher BP and lower GCS ($p<0.05$). Advanced age, a dual stroke diagnosis, presence of CES either as single or additional diagnosis, and anterior circulation stroke were associated with poor discharge outcome (MRS3-6). On logistic-regression analysis, age and GCS were independent predictors of outcome but not additional stroke mechanism.

Conclusion: Up to 1 in 8 patients with ischemic stroke may have an additional mechanism of stroke. Though SVD is more frequent as an additional stroke mechanism, cardioembolism may be associated with worse outcomes. Studies addressing long term management of such patients with dual stroke mechanisms are indicated.

Disclosure: Nothing to disclose

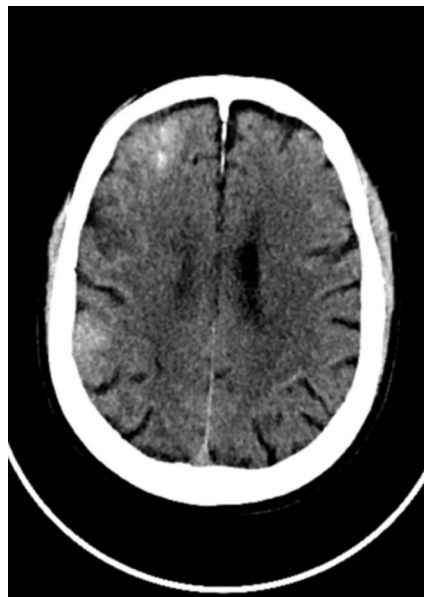
EPO2027

Am I still at CT room? A palinopsia case report secondary to acute stroke

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Valladolid, Spain

Background and aims: Palinopsia is an infrequent visual phenomenon defined as the persistence or recurrence of visual images once the stimulus disappeared. The hallucinatory palinopsias, long-lasting and of high resolution, represent a dysfunction in visual memory, and may present after cortical lesions. We aim to present a case of a palinopsia secondary to an acute stroke.

Methods: An 87-year-old man was admitted due to left faciobrachial weakness, being diagnosed of right hemisphere acute ischemic stroke, treated with primary mechanical thrombectomy. In a control computed tomography (CT), 12 hours after thrombectomy a right parietal as well as frontal hemorrhagic transformation was observed (Figure 1). After leaving the CT room, the patient began to perceive in the ceiling of the stroke unit (Figure 2), images of multiple voluminous green leaves, binocular and in all the visual field, either fixed or moving. They perseverated with some fluctuations during 48 hours.



CT with hemorrhagic transformation in parietal and frontal lobes.



The ceiling of the Stroke unit.

Results: Those images were really afterimages of the ceiling decoration of the CT room (Figure 3). This phenomenon did not cause negative emotional impact in the patient. However, as they were realistic, the patient tried many times to touch the leaves with his hands.



Picture in the roof of the TC room.

Conclusion: We describe a case of hallucinatory palinopsia, subtype formed image perseveration, due to a stroke complication affecting non-dominant parietal cortex. It is important to recognize this infrequent symptom of a stroke, in order to avoid unnecessary therapies. The patients must receive information about its benign nature and a probable spontaneous resolution.

Disclosure: Nothing to disclose

EPO2028

Post-partum Reversible Cerebral Vasoconstriction Syndrome: misdiagnosis of post-lumbar puncture headache and postpartum depression

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Introduction: Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by thunderclap headaches and focal neurological signs, although wide clinical heterogeneity has been described. Puerperium has been related to RCVS. Differential diagnosis in postpartum is challenging because this period is also associated with pathologies like venous thrombosis, preeclampsia, autoimmune encephalitis, posterior reversible encephalopathy syndrome, postpartum depression, post-lumbar puncture headache, and migraine relapse.

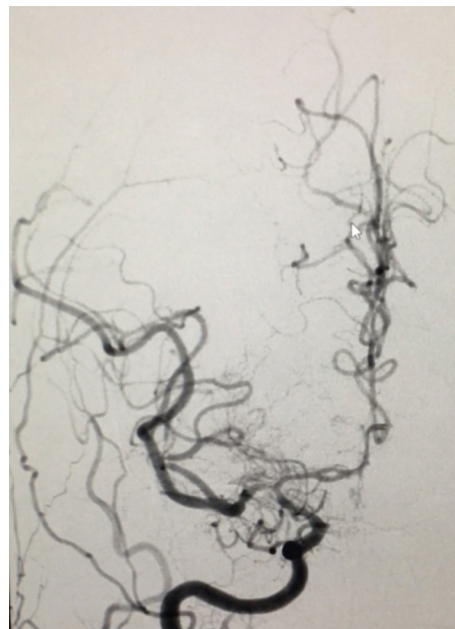


Figure 2. Arteriography shows moderate vasospasm of terminal intracranial segment of right internal carotid artery and proximal segment of media cerebral artery

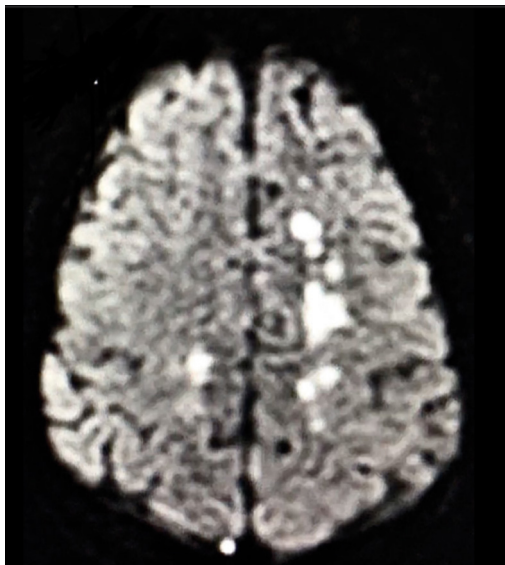


Figure 1. Bilateral hiperintense watershed lesions on diffusion-weighted magnetic resonance imaging with reduced apparent diffusion coefficient values (not shown), which confirm ischaemic etiology.

Methods: A 38-year-old 1st-time mother, immediately after delivery, developed post-lumbar puncture headache and computer tomography signs of intracranial hypotension attributed to epidural anaesthesia. With unimproved headache, she progressively started with severe depressive symptoms, refusing to eat and willing to die. 2 weeks postpartum, she was admitted to the neurology department because of a fluctuating incomplete left hemispheric syndrome. Lumbar puncture and electroencephalogram revealed no alterations. A magnetic resonance imaging study (Figure 1) showed bilateral watershed infarcts. A narrowing of M1 segments of both middle cerebral arteries was confirmed by angiography (Figure 2)

Outcomes: An extraordinarily fast and complete resolution of headache and psychiatric symptoms was observed with blood pressure management and the administration of intraarterial, intravenous and oral nimodipine. One week after diagnosis, left hemisphere focal signs had disappeared and the patient was discharged asymptomatic.

Conclusion: Retrospectively, non-improving headache credited to epidural anaesthesia and depression attributed to puerperium were the only RCVs symptoms for 2 weeks. Therefore, a high grade of suspicion is needed for an early diagnosis of RCVS. Differential diagnosis is wide and treatment for other conditions, such as glucocorticoids and serotonergic antidepressants, can be deleterious for RCVS.

Disclosure: Nothing to disclose

EPO2029

Inflating balloons uncovers patent foramen ovale

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Background and aims: 20-45% of young ischemic strokes is caused by cardiac embolism. Occult atrial fibrillation, cardiomyopathy, valvular disease and endocarditis are the main cardiac sources. Patent foramen ovale (PFO) is another cause, especially at young age. PFO can be detected by contrastechocardiography, or transcranial Doppler ultrasound (TCD) with bubble-contrast injection, detecting a right-to-leftshunt. Performing Valsalva maneuver increases the sensitivity. The RoPE-score (Risk of Paradoxical Embolism) assesses the likelihood that a PFO is related to the stroke. Young age, absence of classic vascular risk factors and cortical brain infarction lead to a higher probability.

Methods: We saw a 37-year-old man, without significant medical history or cardiovascular risk factors, who suffered a sudden numbness and weakness of the left arm during 5-7 minutes, occurring after blowing several balloons. Clinical assessment showed no abnormalities. Brain MR-imaging showed a FLAIR-hyperintensity in the right precentral gyrus with corresponding diffusion restriction which confirmed the diagnosis cortical brain infarction. Blood results were normal. Electrocardiogram and 24-h Holter rhythm detection showed sinus rhythm. MR-angiography showed no abnormalities, especially no carotid dissection.

Results: TCD of the middle cerebral artery with a 'bubble test' showed microembolic signals (MES). After performing Valsalva maneuver, a 'MES-curtain' was detected. This supports the diagnosis of PFO. The RoPe-score is 9, corresponding with a 85-90% likelihood that PFO is related to stroke.

Conclusion: Inflating balloons, resembling Valsalva maneuver, has created a right-to-left atrial shunt through a PFO in our patient, which led to paradoxical embolism and cortical brain infarction. The PFO and its functional impact could be diagnosed by TCD.

Disclosure: Nothing to disclose

EPO2030

Spontaneous intracranial hemorrhage due to rivaroxaban- associated thrombocytopenia- a case reportD. Iliev¹, M. Dimitrova², J. Samuel¹¹Sofia, Bulgaria, ²Neurology, UMHATEM "N.I.Pirogov", Sofia, Bulgaria

Background and aims: Rivaroxaban, a factor Xa inhibitor is a novel oral anticoagulant (NOAC) used to prevent ischemic strokes in patients with atrial fibrillation. Thrombocytopenia as a side effect has been reported immediately after treatment onset, but in rare cases, it can also present after long term therapy.

Methods: An 81-year-old woman with a history of hypertension and arrhythmia presented with acute right-sided weakness, drowsiness, unresponsiveness to verbal commands and with a high blood pressure of 190/90mmHg. The patient had been on oral anticoagulant therapy with Rivaroxaban (20mg/day), 20 months prior for atrial fibrillation (AF). The patient underwent physical and neurological examination (NE), laboratory tests with complete blood count and computer tomography(CT) of the brain.

Results: NE revealed right-sided hemiparesis, right upper motor neuron (UMN)- type Cranial nerve (CN) VII palsy, sensory-motor aphasia and impaired consciousness (NIHSS=18p., GLCS-13p.) Brain CT revealed intraparenchymal hemorrhage in the left hemisphere. Results from initial platelet counts were 44g/L with an INR of 1.06, 6 months previously her platelet levels had been normal. She was treated with vitamin K and Rivaroxaban was discontinued. The platelet count recovered rapidly soon after, and her secondary brain imaging showed cessation of bleeding. Possible etiologies for coagulation abnormalities and thrombocytopenia were excluded.

Conclusion: The incidence of thrombocytopenia due to NOACs is rare and can lead to life-threatening intracranial hemorrhages. Hence, careful and regular monitoring of patients during treatment is mandatory.

Disclosure: Nothing to disclose

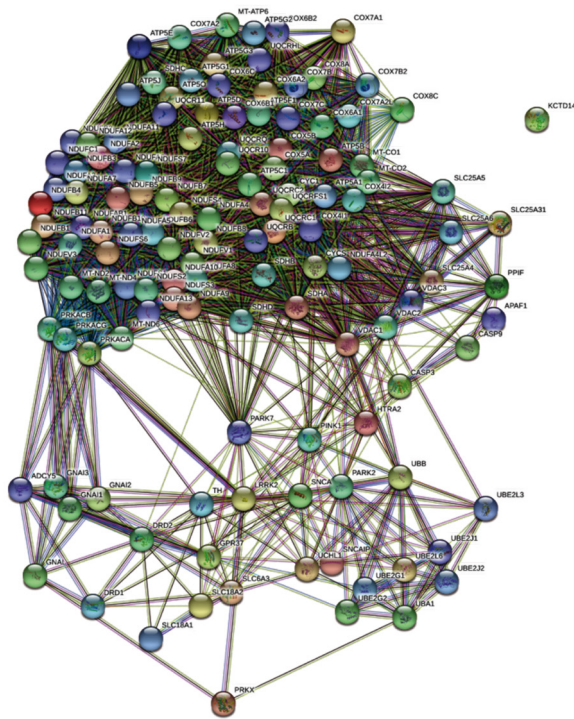
EPO2031

PARK7 as a peripheral blood biomarker in ischemic stroke: pathway analysis of its molecular function within peripheral blood mononuclear cellsG. Vavougios¹, M. Ioakeimidis², T. Doskas³¹Athens, Greece, ²2nd Department of Neurology, Athens University, Attikon University Hospital, Athens, Greece, ³Athens Naval Hospital, Athens, Greece

Background and aims: The PARK7 protein is a prospective biomarker for the early detection of stroke, regardless of etiology. Despite being considered brain specific, PARK7 is ubiquitously expressed, including in peripheral blood; Considering that stroke induces epigenetic changes in peripheral blood cells, and their potential contribution to measured PARK7 plasma levels, its functional and pathway associations should be further elucidated. The purpose of this study is to discover whether PARK7 is differentially expressed in peripheral blood donated by stroke patients, and further elucidate its functions and relevant pathways.

Methods: The Gene Expression Omnibus (GEO) database was inquired using a query containing the keywords "Stroke". Included studies involved ex vivo samples of peripheral blood mononuclear cells (PBMCs) following a case – control design. Differentially expressed genes and their functional correlates were detected via the GeneTrail2 software, employing a false discovery rate (FDR) cutoff of <0.05.

Results: Following the initial search, a single study fulfilled the predetermined criteria, GSE22255. PARK7 was differentially expressed, and included in several significantly enriched pathways involved primarily in mitochondrial and endoplasmic reticulum related stress response, cellular homeostasis and proteostasis (FDR<0.0001).



Conclusion: This is the 1st study to explore the functional correlates of PARK7 in ischemic stroke. Furthermore, its role as a regulator of PBMC stress during the acute phase of stroke may account for the noted fluctuations in measured protein levels. Despite the notion of PARK7 being a brain specific marker, this study provides indirect evidence that stroke induces a concurrent peripheral dysregulation of its expression.

Disclosure: Nothing to disclose

EPO2032

Therapeutic parent artery occlusion – a good treatment option for a giant unruptured saccular intracranial internal carotid aneurysm

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Background and aims: There is no actual consensus regarding the choice of treatment of intracerebral giant aneurysms (GA). Parent artery occlusion (PAO) is a percutaneous procedure that provides immediate thrombosis, improvement of compression symptoms and the prevention of recanalization.

Methods: We present the case of a 63-year-old female patient who gradually developed left inferior temporal quadransopia, limitation of vertical and horizontal left eye movements, partial left ptosis, stabbing paresthesia of the ophthalmic and maxillary divisions of the left trigeminal nerve and diminished left photomotor and corneal reflex 5 months prior to the hospital admission. The cerebral contrast MRI and the CT angiography scans showed a saccular unruptured GA (32/33/29mm) of the left ICA in its supraclinoid segment, with partial intraluminal thrombosis, wall enhancement and significant compression of the optic chiasm and cavernous sinus (PHASES score=10 points, 5 year rupture risk=5.3%). We performed therapeutic percutaneous PAO using 7 platinum coils, preceded by a balloon occlusion test.

Results: The therapeutic result was optimal, with immediate aneurysm thrombosis. After the procedure, due to a drop in blood pressure the patient developed transient right hemiparesis and aphasia, which resolved after fluid replacement.

Conclusion: We chose to present this case in order to highlight that in selected cases PAO might be the only choice of treatment for GAs with a high rupture risk, in which surgical procedure is not an option. It seems that maintaining a higher blood pressure after this procedure may lower the risk of immediate secondary ischemic events but further studies are needed.

Disclosure: Nothing to disclose

EPO2033

Diagnostic challenge of Adult onset Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like syndrome (MELAS)

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Background and aims: MELAS usually presents in childhood, with 65–76% of affected individuals presenting at/or before the age of 20 years. Adult onset of the disease and the wide neurological manifestation in MELAS can be misleading.

Methods: We report 2 cases of MELAS and we discuss clinical and radiological features.

Results: Case 1 is a 33-year-old female who presented with sudden right hemiplegia. The initial diagnosis was ischemic infarction. One year later, she presented with sudden left hemiplegia and epilepsy. Brain MRI showed stroke-like images with restricted diffusion in the right temporal, occipital and parietal lobes which did not correspond to a vascular territory. Spectroscopy revealed lactate accumulation. Muscle biopsy showed ragged red fibers.

Case 2 is a 26-year-old female. She presented with confusion, psychiatric disorders and seizures. Clinical features and radiological involvement of temporal lobe lead to the diagnosis of herpes simplex encephalitis (HSE). Antiviral treatment was initiated with full recovery. 1 year later, she relapsed. Brain MRI with spectroscopy revealed signal abnormalities with restricted diffusion in the right temporal and parietal lobes with lactate accumulation, not confined to a vascular territory. Muscle biopsy showed ragged red fibers. Genetic test revealed a A3243G mutation.

Conclusion: The clinical presentation of MELAS is markedly variable. Recurrent stroke-like episodes are the most common initial manifestation of MELAS and can easily be misdiagnosed as cerebrovascular diseases. MELAS presenting with the features of herpes simplex encephalitis is rare and can raise diagnostic challenges. Specific attention to imaging features can help suggest the diagnosis of MELAS.

Disclosure: Nothing to disclose

EPO2034

Unusual radiological features of posterior reversible encephalopathy syndrome (PRES) complicating a pheochromocytoma: a case report

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Background and aims: PRES is a clinico-radiographic diagnosis of transient cerebral vasogenic edema occurring preferentially in the posterior circulation that is frequently attributed to primary hypertension and drug. Secondary hypertension due to a pheochromocytoma and predominant involvement of the brainstem are less common causes of this syndrome.

Methods: We report and discuss a case of PRES with an unusual clinical and radiological features.

Results: A 47-year-old woman was admitted to our institution with subacute headache and sudden speech disorder. The patient had a history of confirmed pheochromocytoma. Clinical examination revealed conduction aphasia and high blood pressure. Brain computed tomography showed a non-specific cortico-subcortical parietal hypodensity. Brain magnetic resonance imaging (MRI) showed multiple supra-tentorial lacunar infarcts, watershed parietal infarct with hemorrhagic transformation. It also revealed bilateral and symmetrical T2/FLAIR hyperintensity of the brainstem, predominantly the pons with no enhancement nor diffusion restriction. The brainstem lesions were suspected to be in relation with a diagnosis of PRES. Clinically, the patient's symptoms resolved; speech improved and headaches disappeared following the normalization of blood pressure.

Conclusion: PRES may complicate the clinical course of a pheochromocytoma and should be considered after the onset of neurological signs. MRI is fundamental to allow an early diagnosis and obtain differential diagnosis. Our case highlights the importance of considering the diagnosis of PRES in brainstem involvement. The clinical and radiological features can resolve after stabilization of blood pressure.

Disclosure: Nothing to disclose

EPO2035

Changes in the quality of care in Polish stroke units - the role of RES-Q registry

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Background and aims: The Registry of Stroke Care Quality (RES-Q) was designed for quality monitoring and has been incorporated in Angels Initiative. Previous analyses showed that Polish centres participating in RES-Q perform significantly better than the national average. Our aim was to investigate whether they still manage to achieve improvement.

Methods: This analysis of Polish patients reported to RES-Q included only centres reporting ≥ 25 patients each consecutive year from January 2017 to December 2019.

Results: Of 175 Polish stroke units 68 participates in RES-Q. 20 centres reported patients from each year (2017, n=1873; 2018, n=3362 and 2019, n=3425). We found no differences in the proportion of ischaemic strokes (90%, 81%, 90%, respectively), age (median 72, 72, 73 years), gender (48% , 49%, 48% women). Baseline median NIHSS was 7 in each period. The length of hospital stay decreased from median 10 (year 2017) to 9 days (years 2018 and 2019). Proportion of ischaemic strokes treated with alteplase did not change (25%, 27%, 27%) but each year door-to-needle was shorter (median 50, 41, 35min) and early dysphagia screening more common (73%, 82%, 88%).

Although hospital mortality increased (from 12% in year 2017 to 13% in 2019), survivors were more often discharged home (from 67% to 70%).

Conclusion: Polish stroke units reporting cases to RES-Q in years 2017-2019 significantly improved their performance, including door-to-needle time and early dysphagia screening. It confirms that regular involvement in this quality oriented project may drive improvement, even in centres with high baseline standards of care.

Disclosure: Nothing to disclose

EPO2036

S 100 protein serum level as indicator of acute ischemic stroke severity

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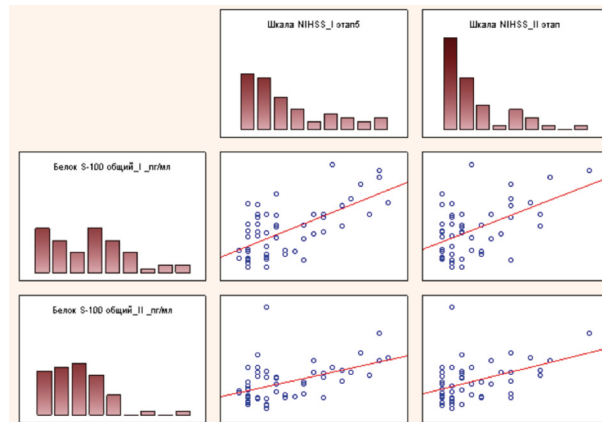
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Background and aims: S-100 is a calcium binding protein expressed mainly in human astroglial cells and is released in peripheral blood after hypoxic brain damage. Hence serum S-100 levels can be used as marker of severity in patients with acute ischemic stroke (AIS).

Aim: To investigate relationship between stroke severity with serum level of S-100 in patients with AIS.

Methods: The study was carried out in a total 120 patients with AIS in the middle cerebral artery (middle age 65 ± 6.3 years; NIHSS 1-18 points). Control group includes 40 healthy individuals. Patient's examination and blood sampling were performed on the 1st day and on 14th day from the stroke onset. Clinical neurological examination was completed with the National Institute of Health Stroke Scale (NIHSS). Patients were divided into low severity stroke (NIHSS 1-6, n=68) and moderate severity stroke (NIHSS 7-18, n=52) groups. Serum S-100 was determined by using DY1820-05 Human S100B DuoSet ELISA-kit (R&D Systems, USA.)

Results: Serum S-100 concentration was significantly elevated in patients with AIS $5.4 (+2.3)$ pg/ml compared to controls $2.6 (\pm 1.3)$ pg/ml ($p < 0.007$). Serum S-100 concentration was higher in low severity stroke group then in moderate severity stroke group at all time points: on 1 day $4.7 (\pm 1.6)$ vs $7.7 (\pm 1.8)$ pg/m ($p < 0.000.5$), on 14th day $4.0 (\pm 1.3)$ vs $6.2 (\pm 1.7)$ pg/m ($p < 0.000.9$).



Serum S-100 concentration was higher in low severity stroke group then in moderate severity stroke group at all time points

Conclusion: S-100 protein measurement can be used as a marker of acute ischemic stroke severity.

Disclosure: This study was supported by the Russian Science Foundation (RSF), grant No. 18-15-00082 “Laboratory for robotic rehabilitation”

EPO2037

The relationships between S-100 protein serum level on short-term functional outcome of patients with acute ischemic stroke

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Background and aims: S-100 proteins, identified as a plasmatic biomarker released in peripheral blood after hypoxic brain damage. S-100 protein may represent a useful neuro-biochemical marker of brain damage and functional outcome resulting from acute ischemic stroke.

Aim: To investigate relationships between S-100 protein serum level on short-term functional outcome of patients with acute ischemic stroke.

Methods: The study was carried out in a total 120 patients with acute ischemic stroke in the middle cerebral artery (middle age 65 ± 6.3 years; NIHSS 1-18 points). Control group includes 40 healthy individuals. Blood sampling were performed on 1st day from the stroke onset. Functional outcome was assessed by the modified Rankin Scale (mRS) on 90 day after discharge. Serum S-100 was determined by using DY1820-05 Human S100B DuoSet ELISA-kit (R&D Systems, USA).

Results: Serum S-100 concentration was significantly elevated in patients with acute ischemic stroke $5.4 (+2.3)$ pg/ml compared to controls $2.6 (\pm 1.3)$ pg/ml ($p < 0.007$). S-100 protein concentrations on 1st day from the stroke onset were associated with values on modified Rankin Scale on 90 day after discharge ($r = 0.701$, $p < 0.047$).

Conclusion: S-100 protein showed ability to predict short-term functional outcome of patients with ischemic stroke.

Disclosure: This study was supported by the Russian Science Foundation (RSF), grant No. 18-15-00082 “Laboratory for robotic rehabilitation”

Cerebrovascular diseases 5

EPO2038

Prevalence of chronic kidney disease among patients in the Stroke Unit with acute cerebrovascular disorder

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Background and aims: The cause of death in 50% of patients with stroke is extracerebral pathology, including impaired kidney function.

Purpose: To study the state of kidney function and the prevalence of chronic kidney disease (CKD) among the patients of the Acute Stroke Unit.

Methods: 142 patients with acute cerebrovascular events were examined in the Stroke Unit of Nizhny Novgorod Regional Hospital, Russia, in 2018-2019: 74 men (52%) and 68 women (48%). The average age of patients was 68±12 years. The diagnosis of stroke was carried out according to the World Health Organization Guidelines, the type of stroke (ischemic or hemorrhagic) was verified by CT. Renal function was investigated by determining GFR, evaluating proteinuria, microalbuminuria, and ultrasound of the kidneys. CKD was diagnosed and classified according to the KDIGO Guidelines (2012).

Results: CKD was detected in 69 patients (49%): 17.4%-CKDG2; 62.3%-CKDG3A; 17.4%-CKDG3B, and 2.9%-CKDG4. CKD was significantly more frequent ($p<0.05$) in patients with ischemic stroke (65 patients). The age of patients in the groups with CKD and without CKD did not differ significantly. History of IHD (RR1.3; 95% CI:0.9-1.9), atrial fibrillation (RR1.2; 95% CI:0.9-1.7), CHF (RR1.5; 95% CI:1.1-2.1), diabetes mellitus (RR1.4; 95% CI:1-1.9) and obesity (RR1; 95% CI: 0.3-4.2) in patients with stroke and CKD were diagnosed.

Conclusion: The prevalence of CKD among patients with acute cerebrovascular events in the Stroke Unit is very high (49%). This fact, apparently, is associated with negative renovascular interactions and an increase of cardiovascular risk in patients with CKD.

Disclosure: Nothing to disclose

EPO2039

Characteristics of antiphospholipid antibody in Korean ischemic strokeY. Kim¹, S.-H. Lee²

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Background and aims: Antiphospholipid syndrome (APS) is a multi-organ autoimmune disease, characterized by arterial and/or venous thrombosis, recurrent miscarriage, and circulating antiphospholipid antibodies (aPLs). Although prevalence of the aPLs in the general population is 1-5%, aPLs are positive in 13% of Ischemic stroke (IS) patients. However, the diagnostic criteria has not been clear, the distribution and significance of aPLs is not known well.

Methods: We collected ischemic stroke patients with aPLs. According to the latest APS diagnostic criteria, we evaluated 3 aPLs including lupus anticoagulant (LA), anticardiolipin antibodies (ACA IgM, IgG), and anti-Beta2 glycoprotein I (IgM, IgG). Since positive cut-off value was not defined clearly, we included patients with moderate or elevated levels.

Results: Among a total of 183 IS patients, mean age was 52.1±15.3 years. More than half of them showed embolic lesion patterns (52%). Although mono positivity was most common, double and triple positivity accounted for 12.3% and 2.8%, respectively. After adjusting multiple variables, LA was significantly associated with severe stroke (NIHSS≥4) (HR 2.391, 95% CI 1.079-5.296).

Conclusion: Although aPLs had been evaluated in only young patients with unknown stroke etiology, it might be more important risk factor for cryptogenic strokes. To evaluate the significance of aPLs in IS, further research should be needed.

Disclosure: This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (NRF-2018R1C1B5086320).

EPO2040

Delirium in Acute Stroke

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Background and aims: Delirium is frequently seen in intensive care units and acute stroke patients. Also delirium cause long-term hospitalizations, severe complications, high morbidity mortality of these patients.

Methods: The research included 115 patients who were hospitalized in Şişli Etfal Neurology Intensive Care Unit(ICU) with the diagnosis of acute stroke. Richmond-Agitation-Sedation-Scale(RASS) and Confusion Assessment Method for ICU(CAM-ICU) were applied to these patients for delirium diagnosis on the 1st-3rd-5th days of hospitalization. Delirium results were compared with sociodemographic data, comorbidities and cranial parenchymal&vascular radiological findings of these patients.

Results: The incidence of delirium in the research was 41.8%. Presence of grade 1 central and cortical atrophy, presence of grade 2-3 periventricular and deep white matter hyperintensities (Odds Ratio-OR, 4.86), presence of grade 2-3 perivascular space in white matter (OR, 3.86), presence of hemorrhage, microhemorrhage (OR, 5.73), hemorrhagic transformation (OR, 3.49), presence of <50% stenosis in left internal carotid arter, presence of intracranial occlusion (OR, 4.68), high NIHS(16.39±4.44) and mRS score (4.68±1.50), long-term ICU admission (12.36±8.96 day), GCS <15 (OR, 3.73), neglect (OR, 3.18), hemiparesis (OR, 2.77), metabolic disorder (OR, 4.09), aspiration pneumonia (OR, 5.8), presence of major risk factors in the outcome of transthoracic-echocardiogram were found to be significant risk factors for delirium.

Conclusion: Delirium was more frequent in patients with severe cranial parenchymal load and neurological deficit. Patients with these characteristics should be followed up closely for delirium. Therefore, we wanted to emphasize that early diagnosis and treatment can be possible and the complications that may occur will be prevented.

Disclosure: Nothing to disclose

EPO2041

Cerebrovascular disease and platelet reactivity in patients with diabetes mellitus.

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Background and aims: Cerebrovascular disease (CVD) is the main cause of death and disability in patients type 2 diabetes mellitus (T2DM). Platelet activation plays a key role in atherothrombosis in T2DM and increased platelet activation. Aspirin is essential antiplatelet therapy in patients with high risk of acute thrombotic events. Aspirin resistance can be defined as inability of the usual dose of aspirin to produce its antithrombotic effect.

Methods: Study included 60 patients, who were divided into 2 groups: the 1st group 30 with CVD and T2DM and 2nd group 30 patients with CVD without T2DM. All patients received 100mg of aspirin daily. Aggregation of platelets to agonists was estimated by light transmission aggregometry (LTA), fibrinogen, anti-thrombin III were measured. Its relationship with diabetes status, response to aspirin were investigated.

Results: With the usage of LTA, high platelet reactivity (HPR), was found in 23 (76%) patients with CVD and T2DM and in 14 (46%) patients with CVD without T2DM (p<0.05). HPR, level of fibrinogen found in patients with T2DM was significantly related to duration of diabetes (p<0.05). The level of anti-thrombin III was lower averagely in the first group, comparing to second group.

Conclusion: Our results showed that high-on-aspirin residual platelet reactivity was found more often in patients with CVD and T2DM. Blood coagulability investigation tests showed increased level of fibrinogen and subnormal level of anti-thrombin III in the 1st group, comparing to 2nd group. Monitoring of hemostasiological markers and active correction of antiagregant therapy are required for patients with CVD and T2DM.

Disclosure: Nothing to disclose

EPO2042

Influence of circulating CD34+ stem cells in the acute phase of ischemic stroke on patients' neurological status assessed according to the NIH scale.

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Background and aims: The analysis of the number of circulating CD34+ stem cells concerning all leukocytes examined in patients on the 1st day of ischemic stroke and investigation of changes in neurological status (according to NIHSS) assessed on the 1st and 8th day.

Methods: The study included 32 patients with stroke symptoms who were hospitalized in the Stroke Department and Early Post-stroke Rehabilitation Clinic of the Neurology Clinic of the Independent Public Clinical Hospital No. 4 in Lublin in 2015.

Peripheral blood was collected from patients, nuclear cells were isolated (erythrocytes were lysed), stem cells and leukocytes were labeled with fluorochrome-conjugated antibodies.

The patients were then divided into subjects whose neurological status had or did not improve (assessed using NIHSS, on the first and eighth day after stroke).

Then, the levels of CD34+ cells in all groups were evaluated for all leukocytes. The results were compared using the Mann-Whitney U test to obtain a statistically significant result ($p < 0.05$).

Results: In the group of patients with improved neurological status, there were more than 2.5 times more CD34+ cells (middle value: 0.2432% vs 0.0929%) concerning the total number of mononuclear cells.

Conclusion: In the group of patients with improved neurological status, there were more than 2.5 times more CD34+ cells (middle value: 0.2432% vs 0.0929%) concerning the total number of mononuclear cells.

Disclosure: Nothing to disclose

EPO2043

Diffusion tensor Magnetic resonance imaging (MRI) pattern of small vessel disease (SVD) and cognitive functions in elderly patients with atrial fibrillation (AFib)

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Background and aims: AFib is a complex cardiovascular risk factor that contributes to SVD and cognitive impairment by decreased brain perfusion due to altered cardiac cycle.

Methods: Elderly outpatients with AFib treated with one of the direct oral anticoagulants were enrolled in the study. Neuropsychological testing with Montreal cognitive assessment (MoCA), Free and Cued Selective Reminding Test (FCSRT), Trail making test part A (TMTA), and Digit coding test were performed. Patients with a major cognitive deficit were excluded. MRI was obtained in T1, T2, FLAIR, susceptibility-weighted imaging (SWI), diffusion tensor imaging (DTI) sequences along with non-contrast angiography. Fractional anisotropy (FA) data were obtained in the following white matter fascicles, tracts, and regions bilaterally: uncinate (UNC), corticospinal (CS), posterior thalamic radiation (PTR), inferior fronto-occipital (IFO), and corpus callosum with a region of interest of 0.09 sq.cm.

Results: 20 patients with a median age of 71.5 years (65-84) were enrolled. 11 patients had mild cognitive impairment with MoCA < 26. 13 patients had 1 of the FLAIR SVD signs, Table 1. Patients with signs of SVD had lower FA values in the right CS tract (U-test, $p = 0.02$). Executive functions showed a moderate correlation with FA values in several of the studied regions, Table 2.

Table 1: White matter hyperintensities on fluid-attenuated inversion recovery (FLAIR) sequence

	Microangiopathy	Fazekas 1	Fazekas 2	Fazekas 3
Number of patients	4	3	5	1

Table 2: Fractional anisotropy (Siemens MAGNETOM Skyra 3.0T) correlates with executive functions. Spearman correlation coefficient (r).

Region (median FA)	Right PTR 594 (447-705)	Left PTR 583 (436-677)	Left UNC 274 (226-406)	Left CS 639 (555-792)
Test				
TMTA, seconds	$r = -0.48, p = 0.031$	–	–	–
FCSRT Free recall, words	$r = -0.48, p = 0.028$	–	–	–
Verbal fluency, words	–	–	–	$r = -0.4, p = 0.07$
Digit coding, seconds	$r = -0.61, p = 0.005$	$r = -0.56, p = 0.011$	$r = -0.51, p = 0.025$	–

Conclusion: Vascular cognitive impairment and executive domain dysfunction are thought to emerge from frontal brain lesions. The study showed executive function to correlate with FA of posterior brain regions. It is of particular interest that primary hippocampal memory disorder (Free recall) correlates with white matter integrity in the PTR, which is a future studies aim.

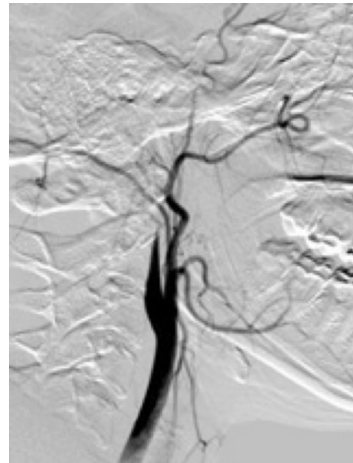
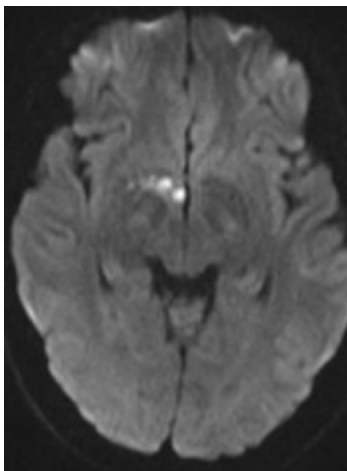
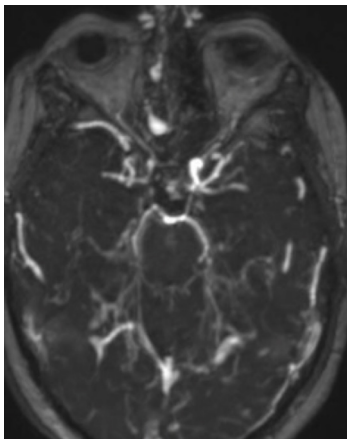
Disclosure: The reported study was funded by RFBR according to the research project 19-015-00383

EPO2044

Cavernous sinus and internal carotid thrombosis with hypothalamus infarction secondary to sinusitis.

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Background and aims: Cavernous sinus thrombosis (CST) is an entity which can be triggered by a local infection process as well as, by an infected region whose venous drainage goes through the cavernous sinus. We present a case of sphenoid-ethmoidal sinusitis (SES), complicated with meningitis, CST, internal carotid artery thrombosis (ICAT) and hypophysis insufficiency (HI) due to an acute hypothalamus infarction.



Methods: To present a case report.

Results: A 21-year-old woman who presented at the emergency department complaining about one week duration headache and diplopia followed by right eyelid drooping. She was smoker and was taking oral contraceptive pills. She had ptosis, arreactive mydriasis and complete ophthalmoplegia in her right eye and hypoesthesia in the 1st 2 right trigeminal branches. She underwent a brain CT with contrast which showed a SES along with a CST and right ICAT. In the lumbar puncture pleocytosis with neutrophilia was found starting with empiric antibiotherapy and corticosteroid treatment. After endonasal sinus surgery with sampling was performed, anticoagulation was initiated. Cerebral angiography confirmed ICAT and brain MRI showed, a recent hypothalamus infarction HI. Culture samples were positive to *Enterococcus Faecalis*. The patient evolved favourably, persisting a right 6th nerve palsy and a hypoesthesia in the 1st 2 right trigeminal branches at the 3-month follow-up.

Conclusion: SES is a well known etiology of CST, however ICAT is a rare complication. Our patient developed both CST and ICAT with an hypothalamus infarction. To exclude a HI, a hormonal study is advisable in these cases.

Disclosure: Nothing to disclose

EPO2045

Don't stop until you understand it - case series of Artery of Percheron infarction

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Background and aims: Early diagnosis of Percheron artery occlusion (AOP) is often missed due to its scarce occurrence and the inconsistency of its clinical picture. A high clinical suspicion is needed as it is difficult to detect the infarct on early brain imaging unless comprehensive evaluation is performed. AOP infarction represents only 0.1% to 2% of all ischemic strokes.

Methods: We present a series of 3 cases of AOP occlusion, each having different clinical presentation, physiopathological setting and outcome.

Initial brain CT scan was unremarkable for all of them and emergency MRI was unavailable. Neither was treated with intravenous alteplase.

Results: An 81-year-old patient presented to the emergency department with sudden behavioral changes. A diagnosis of stroke was made 24 hours later. The patient died subsequently due to the reactivation of her previously stable chronic lymphocytic leukemia. The 2nd patient was admitted with sudden alteration of consciousness following percutaneous coronary intervention. She was discharged to a rehabilitation center a few weeks later. A 70-year-old woman was admitted for sudden ocular movement abnormalities and aphasia. She eventually died 3 months later, after another infarction in the MCA territory, without an identified cause for her strokes. All the patients had bilateral thalamic and mesencephalon infarcts on their repeated brain scans.

Conclusion: Strokes in the AOP territory should be considered in patients with nonlaterizing neurological symptoms especially if MRI brain scan is not available and if the clinical features are not fully explained by the initial CT scan or the laboratory work-up.

Disclosure: Nothing to disclose

EPO2046

Basilar artery diameter and stroke risk in Chinese patients with Fabry disease

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Background and aims: Fabry disease is associated with end-organ involvement, and cerebrovascular events remain as one of the most debilitating conditions that occur with little warning. Vertebrobasilar dolichoectasia, a characteristic finding in Fabry disease, has been reported to be closely related with higher stroke risk. This study aims to evaluate the correlation between basilar artery (BA) diameter with stroke occurrence in Chinese patients with Fabry disease.

Methods: We retrospectively reviewed 22 patients who were diagnosed with Fabry disease and had neuroimaging (magnetic resonance imaging or computed tomography) done during the disease course. We assessed the association between stroke occurrence with neuroimaging markers (deep white matter hyperintensities, periventricular hyperintensities, and BA diameter) and other organ involvement (cardiomyopathy and nephropathy).

Results: 22 patients (aged 57.3±11.7years, 16 [72.7%] males) were evaluated. 5 patients (23%) developed ischaemic stroke, among which 2 patients demonstrated cortical infarcts. The mean basilar artery diameter was 3.74±0.81mm, and larger BA diameter was observed in patients who developed stroke than those who did not (4.74±0.64mm versus 3.44±0.58mm, p<0.001). BA diameter also showed moderate correlation with more extensive white matter changes (p=0.028, correlation coefficient 0.59). Cardiomyopathy and nephropathy, on the other hand, were not associated with higher stroke occurrence.

Conclusion: Larger BA diameter is associated with more extensive white matter changes and higher cerebrovascular event occurrence in patients diagnosed with Fabry disease. Baseline neuroimaging and regular monitoring is important in predicting stroke risk among this group of patients.

Disclosure: Nothing to disclose

EPO2047

Reasons and risk factors of cardioembolic stroke

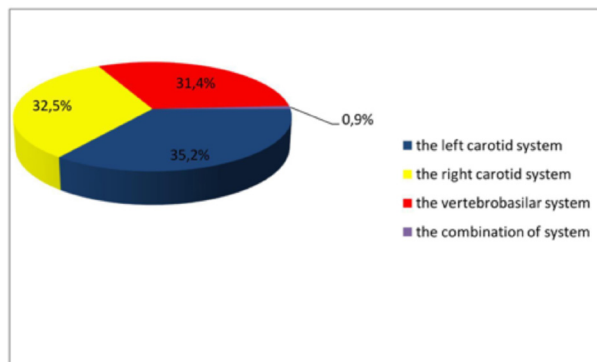
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Background and aims: Cardioembolic ischemic stroke (CIS) accounts 30-40% of all stroke cases, characterized by an unfavorable life and rehabilitation prognosis. The aim is analysis of risk factors for cardioembolic subtype of ischemic stroke.

Methods: 1294 case histories of patients who were hospitalized to the Regional vascular center in Ufa were studied, 440 (34%) of them with CIS. The diagnosis was established on the basis of clinical, instrumental, laboratory and neuroimaging examinations.

Results: The average age of patients was 71.3 ± 0.56 years, 258 (58.6%) women and 182 (41.4%) men. 380 (86.4%) patients suffered a stroke for the 1st time and 60 (13.6%) patients had recurrent stroke. The localization of the stroke is shown in picture 1. The CIS risk factors are presented in Table 1.

Thus, the main risk factor for CIS in our study was nonvalvular atrial fibrillation (AFib) with a predominance of a constant form of AFib in 246 (73.4%) patients. Coagulogram indices in 259 (58.9%) patients indicated hypercoagulation. The results of the risk assessment of stroke and thromboembolism according to the CHA2DS2-VASc scale in patients with nonvalvular AFib ranged from 3 to 6 points. All these patients needed antocoagulant therapy, however, adherence to anticoagulant therapy remains low. Most patients with AFib reserved ineffective antiplatelet therapy or did not regularly take anticoagulants. All patients were instructed to continue therapy with anticoagulants.



The localization of the stroke

Risk factor	Number of patients (%)
1. Atrial fibrillation (nonvalvular)	327 (74,3%)
2. Mitral insufficiency	173 (39,3%)
3. Global pathology of myocardial wall movements	97 (22%)
4. Calcification of the mitral ring	92 (20,9%)
5. Mechanical valve prostheses	34 (7,7%)
6. Mitral stenosis	19 (0,2%)
7. Sick sinus syndrome	15 (3,4%)
8. Infective endocarditis	8 (1,8%)
9. Dilated cardiomyopathy	4 (0,9%)
10. Myocardial infarction less than 4 weeks	4 (0,9%)
11. Myxoma	3 (0,7%)
12. Open oval window	2 (0,5%)

Risk factors of cardioembolic stroke

Conclusion: Thus, considering that nonvalvular AFib - based risk factor for CIS, the priority direction of its primary and secondary prevention is adequate systematic anticoagulant therapy.

Disclosure: Nothing to disclose

EPO2048

Primary Angiitis of the Central Nervous System involving Internal Carotid, Vertebral Arteries and their main branches.

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Background and aims: Primary angiitis (PA) of the central nervous system is one of the less-studied causes of ischemic stroke (IS). To study clinical manifestations of PA involving internal carotid (ICA), vertebral arteries (VA) and their main branches.

Methods: 45 patients (mean age 37.5 ± 11.5 years, men – 58%), with PA of ICA, VA and their main branches were prospectively studied. PA was verified by high-resolution vessel-wall MR imaging (by arterial-wall thickening and contrast enhancement). Atherosclerosis and dissection were excluded.

Results: Steno-occlusive process involved ICA in 25 patients (56%), in 8 of them with concomitant middle cerebral artery (MCA) damage; isolated MCA – in 9 (20%), VA – in 6 (13%), different combinations of anterior and posterior circulation in 5 (11%). The whole number of affected arteries was 76 (36% patients had bilateral damage). Clinical manifestations included IS (93%), transient ischemic attack (TIA) (2%), Tolosa-Hunt syndrome (2%). 1 patient was clinically asymptomatic. In 24 patients (57%) IS combined with TIA, which usually preceded IS by few weeks-months. In 48% of patients IS recurred over a period from 2 weeks to 2 years. Headache shortly before or concurrently with IS was presented in 36%. Before IS some patients (16%) noted unexplained fatigue for several weeks/months. Concomitant diseases and conditions included frequent herpetic rashes (27%), chickenpox at the age 18-28 years (4%), arthralgia (11%), psoriasis (4%).

Conclusion: Clinical manifestations of PA involving ICA, VA and their main branches have some peculiarities that, along with arterial-wall MR imaging, can be taken into account to recognize this pathology.

Disclosure: Nothing to disclose

EPO2049

A Case of Cadasil with Spinal Cord Involvement

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukodystrophy (CADASIL) is an hereditary disease presenting with recurrent strokes, migraine and cognitive impairment. While small arteries throughout the body are pathologically affected, these are not usually symptomatic. Spinal cord involvement has been previously described, albeit rarely, and is not typically considered as part of the disease phenotype.

Methods: A 32-year-old male presented with acute onset left hemiparesis. Brain MRI showed multiple periventricular and centrum semiovale white matter lesions. 2 years later, he again presented with acute onset dysphagia, dysarthria, dysphonia and right facial palsy. A lumbar puncture was performed and CSF was negative for oligoclonal bands. At this time, the patient was diagnosed with multiple sclerosis (MS) and started on interferon-beta therapy.

Results: At 41 years old he was admitted with an acute onset cerebellar syndrome. Brain MRI showed progression of white matter lesions, including bilateral involvement of the anterior temporal lobes. Cervical cord MRI revealed a central right paramedian cord lesion at the C3-4 level. On revision, family history was positive for early onset stroke. Both the patient and a symptomatic sibling tested positive for Notch-3 mutation, confirming the diagnosis.

Conclusion: Given the nature and initial transience of focal neurological impairment and white matter involvement on MRI, CADASIL is a frequent mimic of MS. Spinal cord involvement may further confound diagnosis. While coexistence of both diseases is possible, in this instance, the absence of documented inflammatory activity on CSF and the imagiological aspects of the cord lesion point toward a vascular etiology.

Disclosure: Nothing to disclose

EPO2050

Assessment of risk for cerebral ischemic recurrence in TIA patients with low-medium ABCD2 score

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Background and aims: The aim of our study was to identify clinical variables useful to provide prognostic information and help the management decisions in patients affected by transient ischemic attack (TIA) with low and medium ABCD2 score.

Methods: We analyzed data from patients discharged from the Emergency Department of Udine Hospital with diagnosis of TIA with ABCD2 score ≤ 5 . The duration and typology of clinical symptoms, cardiovascular risk factors, previous history of cerebral and cardiac ischemic events and etiological work-ups were recorded retrospectively from electronic medical records. Our aim was to assess the risk of stroke and TIA recurrence, new acute coronaric event and death from cardiovascular causes respectively at 90 days and 1 year follow up.

Results: In total 286 subjects fulfilled all our inclusion criteria. Mean age was 75.8 years. 90-day major vascular event occurred in 24 patients (8.3%), whereas 46 patients (16.1 %) had a 1 year cerebral ischemic recurrence (16.1%). Dyslipidemia, dementia, mRS ≥ 3 , age and prior TIA/Stroke history were associated with higher risk of recurrence in univariate analyses. In the multivariate analyses the prior transient ischemic attack remained as independent predictor of stroke recurrence at both 90-day and 1-year follow-up.

Conclusion: our present ability to identify patients at risk for early recurrence based only on clinical scales remains limited. Prior TIA history might help to identify a subgroup of patients at higher risk for early recurrence among TIA patients with low and medium ABCD2 score.

Disclosure: Nothing to disclose

EPO2051

Carotid dissection as the clinical presentation of Eagle syndrome: a case report

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Background and aims: Eagle syndrome is a clinical condition related to abnormally elongated styloid processes. Several patients present with unilateral facial pain, tinnitus and ophthalmalgia. The vascular form is a variant due to close contact between the styloid process and the extracranial tract of the internal carotid artery (ICA). We describe a patient diagnosed with Eagle syndrome after the development of carotid dissection and parietal ischemic stroke.

Methods: A 53-year-old woman presented to the emergency ward in a foreign hospital due to the sudden onset of right visual field impairment, confusion and decreased strength of the right arm. Cephalalgia was also reported. Brain computed tomography (CT) detected a left parietal ischemia, with a left ICA dissection. Heparin was started. Willing to seek another medical opinion, she was admitted to our Clinic.

Results: Both Magnetic resonance (MRI) and CT confirmed the ischemic stroke (figure 1) and the carotid dissection (figure 2). Neck scan detected elongated styloid processes, the left one being in close contact with the ICA (figure 3). After an otorhinolaryngologist and surgical evaluation, the diagnosis of Eagle syndrome was made. The woman was discharged with Aspirin and Clopidogrel. A follow-up CT detected increased canalization of the left ICA, with a reduction of the carotid diameter down to 7.1 mm.

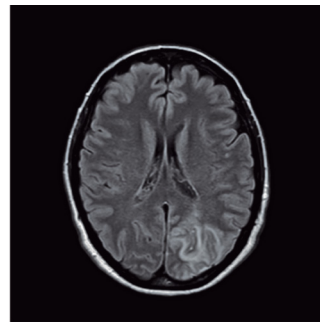


Figure 1: MRI - FLAIR sequence showing a left occipital ischemic lesion.

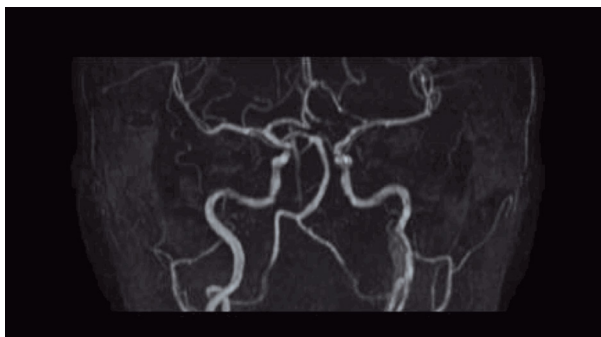


Figure 2: MRI showing the left carotid dissection

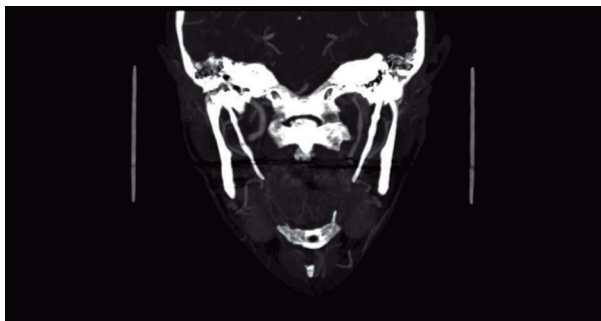


Figure 3: CT scan showing elongated styloid processes, the left one being in close contact with the dissected ICA.

Conclusion: Eagle syndrome is a rare condition, which can be slightly symptomatic or extremely disabling by triggering cerebrovascular damage. It must be considered in the presence of stroke in young population, in order to carefully evaluate the patient and start an adequate treatment.

Disclosure: Nothing to disclose

EPO2052

Neurological singularities of Posterior Circulation Stroke: functional outcome

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Background and aims: The NIHSS scale is used to assess functional disability after stroke. However, limitations to this scale are recognized. Namely, clinical features of posterior circulation ischemic strokes (PCIS) are usually not considered which might compromise prognostic stratification. We aimed to evaluate the correlation between neurological changes characteristic of PCIS at admission and the modified Rankin scale (mRS) at discharge

Methods: Retrospective study of a cohort of patients with PCIS admitted to a stroke unit between 2017-2018. We collected data regarding demographics, past medical history, neurological examination, mRS and NIHSS scores at admission and discharge. 2 groups were defined with $mRS \leq 1$ and $mRS \geq 2$ at discharge. We performed a multivariate analysis to determine which neurological findings were independent predictors of $mRS \geq 2$ at discharge.

Results: We included 98 patients, with a median age (standard deviation) of 62.6 (± 15.4) years and 66 (67.3%) were men. 52 had $mRS \geq 2$ at discharge. Diabetes (48.8% vs 25.7%, $p=0.058$), atrial fibrillation (32.3% vs 9.4%, $p=0.032$), altered state of consciousness (32.7% vs 6.5%, $p=0.002$), visual fields defects (28.8% vs 6.5%, $p=0.008$) and paresis (65.4% vs 43.5%, $p=0.042$) were significantly associated to $mRS \geq 2$ group in a bivariate analysis. Following multivariate analysis, independent predictors of $mRS \geq 2$ were visual fields defects (OR 0.08 IC95% [0.008-0.820], $p=0.033$) and altered state of consciousness (OR 0.110 IC95% [0.0018-0.669], $p=0.017$).

Conclusion: Neurological findings in PCIS which were independently associated with $mRS \geq 2$ were visual field defects and altered state of consciousness. Taking this into consideration, acute phase therapy should be considered in these patients despite $NIHSS \leq 4$.

Disclosure: Funding: Faculdade de Medicina da Universidade de Lisboa (Programa “Educação pela Ciência” GAPIC/FMUL) 20190021

EPO2053

Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL): neuromuscular characterization

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Background and aims: Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL) is a rare disease caused by HTRA1 gene mutations. In approximately 80% of cases, acute lumbago or spondylosis deformans occurs. While recent studies have focused on CARASIL small-vessel brain pathology, neuromuscular involvement is still unclear. Our aim was to investigate the peripheral nervous system involvement in CARASIL patients.

Methods: Patients who received a genetic diagnosis of CARASIL at a tertiary hospital were enrolled. Neurophysiologic evaluation included sensory (ulnar, median and sural nerves) and motor (ulnar, median and deep peroneal nerves) nerve conduction studies and electromyography. All patients underwent lumbar CT/MRI.

Results: Three male patients aged 30, 34 and 36 years were included. Median age at onset for ischaemic episodes was 31 years (range, 22-33). Initial symptoms were binocular diplopia in 2 patients and transient right hemiparesis in one. Median age at acute lumbago onset was 27 years (range, 16-33). In 2 patients, lumbago preceded initial ischaemic symptoms in 6 years. All patients had radiological evidence of spondylosis deformans. Median interval from lumbago onset to NCS was 7 years (range, 3-14). Neurophysiologic assessment was normal in all patients except in one, who showed chronic bilateral L5 radiculopathy and right carpal tunnel syndrome.

Conclusion: In line with recent evidence, all patients had early-onset acute lumbago, sometimes preceding ischaemic episodes in years. Surprisingly, although lumbago and spondylosis deformans were present in all patients, radiculopathy was only evident in one. These results indicate that peripheral neuropathy and myopathy may not be part of CARASIL phenotype.

Disclosure: Nothing to disclose

EPO2054

Eight-and-a-half-syndrome: neuro-ophthalmological manifestations

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Background and aims: Eight-and-a-half-syndrome is a rare neuro-ophthalmologic syndrome, 1st described by Eggenberger in 1998, characterized by conjugate horizontal gaze palsy, ipsilateral internuclear ophthalmoplegia and ipsilateral lower motor neuron-like facial palsy. It is most often caused by vascular etiology such as infarction or ischemia at the pontine level, but it may also be caused by demyelinating conditions at the level of the pons such as multiple sclerosis.

Methods: Data obtained through review of medical records, after evaluation and authorization of the patient and photographic record of the diagnostic methods to which the patient was submitted and literature review.

Results: A 50-year-old man attended our service complaining of dizziness, associated with diplopia and eye mobility weakness 9 hours before admission. He was referred to our neurology staff at the emergency room. The neurologic exam revealed conjugate horizontal gaze palsy to the left, ipsilateral internuclear ophthalmoplegia and central facial palsy. The cerebrospinal fluid analysis was normal. The brain magnetic resonance imaging showed signs of ischemia, at the periventricular and subcortical white matter around the cerebral hemispheres.

Conclusion: Conjugate horizontal gaze palsy, ipsilateral internuclear ophthalmoplegia, and ipsilateral peripheral facial nerve palsy features the eight-and-a-half-syndrome. Although it is most commonly caused by an infarction or demyelination, in rare cases, a space-occupying lesion, such as a cavernoma located at the level of the pons, can be the etiology. Recognizing the symptoms of the disease is paramount, so as to be able properly order the diagnostic exams, localize the lesion, and determine the proper treatment regimen catered to each patient.

Disclosure: Nothing to disclose

Cerebrovascular diseases 6

EPO2055

Non transitory global amnesia

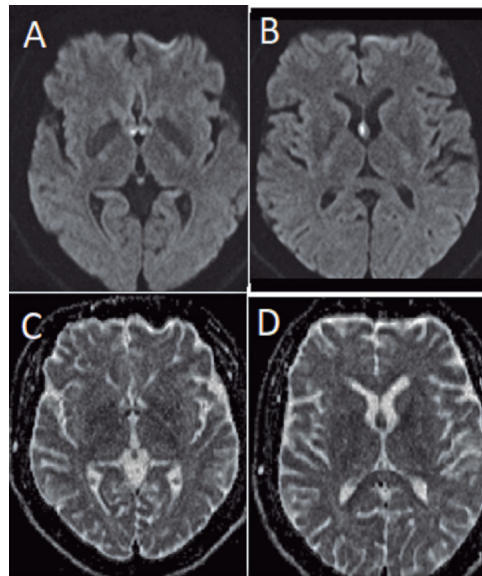
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Background and aims: Damage to the hippocampus, mammillary bodies, anterior thalamic nuclei, and cingulate gyrus can result in anterograde amnesia in patients. The mammillary bodies are considered to be relay nuclei, passing information from the hippocampal formation to the anterior thalamic nuclei, by way of the mamillothalamic tract. More than a half of the fibers of fornix continue forward to form the precommissural fornix and only one quarter participate in hippocampal-mammillary projections, being this part crucial in memory.

Methods: A 43-year-old male came to the emergency department due to repeated questions and the inability to remember previous 72-hour. He had a severe anterograde episodic amnesia with verbal predominance and slight reduction of verbal fluency with a phonetic key, mild retrograde episodic amnesia was also observed.

Results: Restricted and hypersensitive of both mammillary bodies and of the anterior column and anterior region of the body of the right fornix was observed in DWI-MRI. Within 2 months, this lesions turned into hypo-signal in ADC, congruent with ischemic injury. The patient was diagnosed of ischemic stroke in perforating territory of the anterior communicating artery. He had a fixed impairment of short term memory 6 months later so he lived like previous 4 years had not exist.



Brain MRI scan: DWI-MRI sequence reveals hyperintensity of mammillary bodies (A) and anterior region of the body of the right fornix (B). ADC-MRI, made 2 months after the stroke, shows hypointensity of the mammillary bodies (C) and anterior region of the body of the right fornix (D).

Conclusion: This is a peculiar case in which a minimal lesion located in the Papez Circuit causes great symptomatology and functional limitation of the patient's life. It should be remembered that in cases of apparent transient global amnesia whose duration exceeds 24 hours, screening of ischemic lesions must be performed.

Disclosure: Nothing to disclose

EPO2056

Middle cerebral artery occlusion presenting as hemichoreaP. Marques¹, E. Martins¹, C. Maia², F. Silva¹¹Neurology, Coimbra University Hospital Centre, Coimbra, Portugal, ²Neuroradiology, Coimbra University Hospital Centre, Coimbra, Portugal

Background and aims: Less than 1% of all strokes may present, as an hyperkinetic syndrome rather than the typical loss of function. In older patients with vascular risk factors, small lesions of basal ganglia or transient hypoperfusion by hypotension in the context of carotid stenosis may occasionally elicit these neurological presentations. We report the case of a patient with sudden hemichorea due to arterial embolization, resolved after thrombolysis.

Methods: Non applicable

Results: Case: An 81-year-old woman, with hypertension and dyslipidemia, fully autonomous for daily activities, presented to the emergency room after sudden onset of involuntary movements of her right members. Neurological evaluation revealed a slight right hemiparesis and choreic movements on the same side (NIHSS 3). No acute lesions were observed at initial brain computed tomography, but she had a thrombus at the M1 segment of her left middle cerebral artery. Prompt initiation of endovenous thrombolysis, about 3 hours after symptoms onset, was coincident with the cessation of the involuntary movements. Arterial reperfusion was angiographically documented. A few days after, brain magnetic resonance imaging revealed a ischemic vascular lesion affecting the left caudate nucleus. On follow-up, at 5 months, she didn't report new episodes of involuntary movements. Her 24 hour-Holter revealed atrial fibrillation and she is now on hypocoagulation therapy.

Conclusion: The presented case is notable because of the atypical presentation of a main cerebral artery occlusion that could, otherwise, be attributed to a less serious condition. Early diagnosis and treatment with thrombolysis were crucial for the patient's prognosis.

Disclosure: Nothing to disclose

EPO2057

Acute Bilateral Vocal Cord Paralysis After StrokeE. Martins Silva¹, J. Dentinho², F. Antunes¹, L. Pereira¹, M. Rodrigues¹¹Neurology, Hospital Garcia de Orta, Almada, Portugal, ²Otorhinolaryngology, Hospital Garcia de Orta, Almada, Portugal

Background and aims: Vocal cord paralysis (VCP) is uncommon in stroke and a bilateral presentation is even rarer. Clinical severity depends on glottic opening. VCP affects airway protection, respiration and phonation. We present 3 cases of bilateral VCP followed at a stroke unit in the previous year.

Results: 71-year-old female, with right deep parenchymal haemorrhage, was febrile and coughing purulent sputum at day 8, rapidly worsening with respiratory distress, stridor and hypoxemia. Laryngoscopy showed very small glottic aperture due to bilateral VCP and emergent surgical tracheostomy was performed. Tracheostoma closure was possible 6 months after stroke.

61-year-old male, with embolic ischemic stroke of the right middle cerebral artery (MCA), suddenly developed dyspnea and stridor at day 3. Laryngoscopy confirmed bilateral VCP requiring tracheostomy. The following day, pneumonia symptoms emerged. Tracheostoma closure was possible 3.5 months post-stroke.

57-year-old male, with malignant right MCA infarction requiring decompressive craniectomy. After prolonged mechanical ventilation, elective tracheostomy was conducted. Weeks later, recovering and breathing spontaneously, it wasn't possible to start the tracheostoma closure process due to bilateral VCP. He had marginal glottic space improvement at 7-month follow-up.

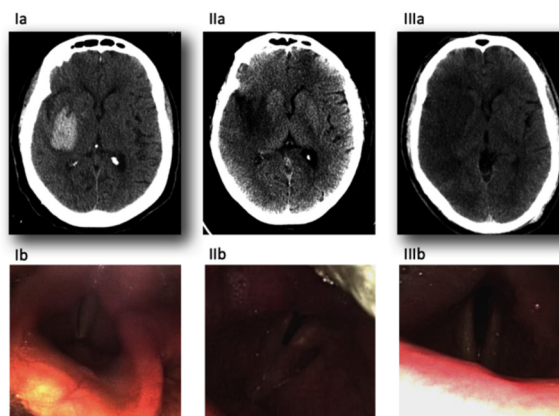


Image 1: CT scans showing lesions (Ia, IIa, IIIa) and laryngoscopy images with bilateral VCP (Ib, IIb, IIIb): Ia and Ib correspond to the 1st patient, IIa and IIb correspond to the 2nd patient and IIIa and IIIb correspond to the 3rd patient

Conclusion: VCP after a cortical event may be explained by dominant unilateral cortical projections to both ambiguous nuclei. Insular lesions and decreased vagus nerve activity have also been proposed as contributors. In the 1st 2 cases, there was sudden and severe upper airway obstruction and concomitant pneumonia. Why this event occurs late after stroke remains unclear.

Disclosure: Nothing to disclose

EPO2058

Mortality predictors in acute stroke

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Background and aims: Stroke is considered to be the main cause of death and disability after cancer throughout the world. Numerous studies have been conducted in recent years predicting factors for mortality in acute stroke.

The present study aims to analyse the most influential factors involved in mortality through acute stroke.

Methods: The study included 200 patients with bad outcome with acute stroke hospitalized in Neurology Department. Knowing vascular risk factors, analysing clinical, paraclinical evaluation and complications, a series of statistical correlations were made to identify the main predictors of mortality.

Results: The study included 200 patients with a mean age of 78 years, 128 females (64%) and 72 males (36%). Out of 200 patients, 147 (73.5%) presented ischemic stroke and the rest of 53 (26.5%) had haemorrhagic stroke.

The mean NIHSS disability score was 18.3.

86 (43%) patients had as cause of death aspiration pneumonia, 99 (49.5%) patients died because of intracranial hypertension, 12 (6%) patients had as causes of death a combination between aspiration pneumonia and intracranial hypertension, 2 (1%) patients associated acute myocardial infarction.

Conclusion: Stroke is a main cause of death throughout the world among elderly. The main predictors of mortality are considered to be advanced age, vascular risk factors such as arterial hypertension, diabetes mellitus and dyslipidaemia, association of cardiac rhythm disorders – atrial fibrillation, disability score NIHSS, size of the stroke, complications like intracranial hypertension and aspiration pneumonia, urinary tract infections and cardiac complications such as acute myocardial infarction.

Disclosure: Nothing to disclose

EPO2059

Artery of Percheron occlusion: Complex clinical course and acute diagnostic challenge

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Background and aims: Artery of Percheron occlusion (APO) classically produces bilateral thalamic infarctions, frequently involving the midbrain. Early diagnosis of APO can be difficult because it presents with a challenging clinical picture and early CT or MRI may be negative.

The aim of our study is to characterize the clinical features seen in these patients and their outcome.

Methods: We retrospectively identified all patients with brain imaging demonstrating a pattern compatible with an APO from 2017 to 2019. All patients had cerebral angiography (MRI or CT). Patients were excluded if a more likely etiology was suggested.

Results: 6 patients were included. There were 3 men and 3 women and the mean age (SD) was 79 (13). All patients had mental status changes ranging from delirium to stuporous. Ocular disturbances were present in 5 of them: 5 had vertical gaze palsy, 3 had partial horizontal gaze disturbances and 2 had ptosis. Motor disturbance was also present in 4 patients. None of the patients received tissue plasminogen activator (tPA) In addition to bilateral thalamic infarction, most patients (83%) also had unilateral deep midbrain lesions and the median time from initial symptoms to radiologic diagnosis was 26 hours.

There were 2 in-hospital deaths and 3 patients still presented significant morbidity, at 6 months follow up.

Conclusion: In our study, the prognosis seems to be not as good as some described. The most vital reason for timely recognition of APO infarct is intervention with tPA, which can improve the outcome of this patients.

Disclosure: Nothing to disclose

EPO2060

EMS triage of acute stroke optimized by use of the Los Angeles Motor Scale (LAMS)

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Background and aims: Transferring patients with large-vessel occlusion (LVO) or intracranial haemorrhage (ICH) to hospitals of the appropriate level of care. We aimed to determine how prehospital use of the Los Angeles Motor Scale (LAMS) allows accurately triaging stroke patients with LVO or ICH to target hospitals with (comprehensive stroke centre, CSC) or without (primary stroke centre, PSC) interventional treatment options.

Methods: In this stroke management pathway the LAMS was included in prehospital triage decision making by the emergency medical services. The proportion of patients accurately triaged to either CSCs (LVO and ICH) or PSCs (other types of strokes) was assessed.

Results: Of 53 patients, an accurate triage decision was reached for 37 (69.8%) patients. 7 of 17 (41.2%) patients with LVO or ICH required inter-hospital transfers from a PSC to a CSC. If selectively evaluating for the accuracy of the LAMS at a cut-point ≥ 4 , an accurate diagnosis of LVO or ICH for 42 of 53 patients (79.2%) and of LVO alone for 38 of 53 patients (71.7%) was reached.

Conclusion: Prehospital use of a simple stroke severity scale allows accurate triage decisions for approximately 70% of patients. This low-cost intervention may reduce the number of patients with LVO transferred to thrombectomy non-capable hospitals.

Disclosure: Nothing to disclose

EPO2061

Efficacy and prognostic factors of mechanical thrombectomy in acute basilar artery occlusion: a single centre study

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Background and aims: Stroke due to acute basilar artery occlusion (BAO) is rare but is potentially lethal. The benefit of endovascular treatment in acute ischemic stroke caused by BAO remains unestablished. Due to the severe neurological prognostic of BAO, thrombectomy is sometimes used as a rescue procedure, past this time window. Aims is to identify the prognostic factors of good functional outcome after thrombectomy for basilar artery occlusion in our centre.

Methods: Between January 2014 and December 2018, all patients referred to La Timone University Hospital of Marseille, France for thrombectomy of basilar artery were retrospectively included. Clinical data, radiological data and treatment procedure were collected. mTICI grades of 2b and 3 was defined as successful revascularization. Favourable outcome was defined as mRS (modified Rankin Score) between 0 and 2 at 90 days.

Results: 63 patients with a median age of 67 [56-74] were included. 25 patients were intubated on admission. Revascularization was achieved in 45 cases (71%). 19 of 63 had a favourable outcome. Absence of intubation (OR 4.19; IC 95% [1.05-20.3]; p=0.043) and revascularization with mTICI grades of 2b-3 (OR 6.40; IC 95% [1.32-48.5]; p=0.020) were both statistically significant predictors of favourable outcome. Intubated patients were younger (p=0.018) and had initially more extensive cerebral lesion on MRI.

Table 1 : Characteristics of the Study Population

characteristics	Total n=63	Favourable outcome (mRS 0-2) n=19	Poor outcome (mRS 3-6) n=44	p
Male gender n (%)	43 (68%)	12 (63%)	31 (70%)	0.57
Age years median [IQR]	67 [56-74]	65 [50-70]	68.5 [56-83.5]	0.19
Transfer prior to thrombectomy	19 (30%)	3 (16%)	16 (36%)	0.10
Risk factor				
Diabetes	6 (10%)	1 (5%)	5 (11%)	0.59
HBP	34 (54%)	8 (42%)	26 (59%)	0.32
Dyslipidaemia	18 (29%)	6 (32)	12 (27%)	0.77
Prior stroke	11 (17%)	3 (16%)	8 (18%)	0.51
Smoker	10 (16%)	4 (21%)	6 (14%)	0.73
OH consumption	5 (8%)	1 (5%)	4 (9%)	0.85
coronaryopathy	7 (11%)	0	7 (16%)	0.18
cervical atheroma	3 (5%)	0	3 (7%)	0.48
Atrial fibrillation	10 (16%)	2 (11%)	8 (18%)	0.58
Obesity	8 (13%)	4 (21%)	4 (9%)	0.35
Anticoagulant therapy	10 (16%)	1 (5%)	9 (20%)	0.13
Antiplatelet therapy	18 (29%)	5 (26%)	13 (30%)	0.79
Admission characteristics				
NIHSS	14 [7.5-19]	9 [5-17]	15 [11-21]	0.34
Intubation	25 (40%)	4 (21%)	21 (48%)	0.041
Glycaemia	1.32 [1.14-1.56]	1.32 [1.13-1.68]	1.32 [1.18-1.45]	0.42
INR	1.11 [1.03-1.20]	1.08 [0.99-1.17]	1.12 [1.04-1.22]	0.023
Radiological characteristics				
DWI-pc-ASPECTS	7 [5-8]	8 [5-8]	6 [5-8]	0.28
Basilar artery occlusion				0.56
Proximal	35 (58%)	13 (68%)	22 (54%)	
Middle	8 (13%)	2 (11%)	6 (15%)	
Distal	17 (28%)	4 (21%)	13 (32%)	
Treatment characteristics				
Thrombolysis	36 (57%)	14 (74%)	22 (50%)	0.081
Time from symptom onset to groin puncture min	268 [212-418]	230 [192-272]	332 [226-475]	0.032
Time from symptom onset to revascularization min	336 [257-507]	270 [239-336]	397 [283-547]	0.022
Thrombectomy duration min	62 [40-89]	43 [25-69]	65.5 [48-91]	0.034
mTICI grades 2b-3	45 (71%)	17 (89%)	28 (64%)	0.037
Per procedure adverse event	13 (21%)	4 (21%)	9 (21%)	0.96
Intracerebral haemorrhage	8 (15%)	3 (17%)	5 (15%)	0.85

Table 2 : Predictors of outcome: Multivariable Ordinal Logistic Regression Analysis

	OR	Confidence interval 95%	p
Thrombolysis	2.1	[0.49-10.2]	0.32
Absence of Intubation	4.19	[1.05-20.3]	0.043
Time from symptom onset to revascularization min	0.996	[0.990-1]	0.066
mTICI grades 2b-3	6.40	[1.32-48.5]	0.020

Table 3 : Predictors of outcome: Subgroup analysis on intubated patient

characteristics	Intubated n=25	Non-intubated n=38	p
Age years	57 [44-72]	70 [58.75-78]	0.018
Time from symptom onset to groin puncture min	270 [247.5-402.5]	241 [186.5-377.2]	0.16
Time from symptom onset to revascularization min	367 [266-448.5]	322 [251.5-520.5]	0.17
Thrombectomy duration min	54 [39.5-70.5]	65 [41-104.25]	0.078
DWI-pc-ASPECTS	6 [4-7]	7.5 [6-8]	0.011
mTICI grades 2b-3	21 (84%)	24 (63%)	0.073
Thrombolysis	14 (56%)	22 (58%)	0.88
Good outcome	4 (21%)	15 (39%)	0.041
Dead	16 (53%)	14 (36%)	0.034

Conclusion: In stroke due to BAO, successful thrombectomy revascularization is associated with a better outcome. Intubation upon admission was a clinical predictor of poor outcome. Identifying predictive factors could lead to personalised medical care for these patients.

Disclosure: Nothing to disclose

EPO2062

Three-year follow-up of elderly patients with “silent” infarctions

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Background and aims: The prevalence of “silent” infarction (SI) in the total population ranges from 5.5% to 48.0% and is much higher in patients with cardiovascular diseases. Dynamics of the SI course is poorly researched. The aim was to perform dynamic monitoring of patients with arterial hypertension, atherosclerosis and SI during 3 years.

Methods: 72 patients with average age of 66.5±1.9 years were observed. Clinical-neurological, psychodiagnostic, MRI, and EEG methods were used.

Results: Analysis of vascular risk factors showed increasing the number of patients with hypertension ($\phi=2.025$), dyslipidemia ($\phi=1.690$), sleep apnea ($\phi=1.709$) during the observation, as well as with amyostatic ($\phi=1.676$), pseudobulbar ($\phi=1.697$) and asthenic ($\phi=1.770$) syndromes. The average Tinetti score decreased by 1.3±0.2 points, indicating the progression of movement disorders in these patients. Dynamics of cognitive functions, according to the MoCA scale, showed that the mean score significantly decreased from 25.6±1.4 to 23.1±0.9 points due to impairments in memory, abstract thinking, visual-spatial capabilities, constructive praxis. The number of patients with single SI is decreased from 27.8% to 13.9%. New lacunae were localized mainly in the basal ganglia, subcortically. The number of patients with leukoaroosis was increased by 25%, sometimes there was a progression of its severity and cerebral atrophy. EEG studies demonstrated a lower spectral power and density of alpha-rhythm indices over time.

Conclusion: SI as a particular form of cerebrovascular pathology is progressive in nature and can lead to stroke development and impaired cognitive function.

Disclosure: Nothing to disclose

EPO2063

Reactivity features of cytokines and vasoendothelial growth factor in patients with chronic cerebral ischemia and metabolic syndrome

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Background and aims: Metabolic syndrome (MetS) is a risk factor for cerebral stroke. Along with this, there is a need to research a pathogenesis of chronic cerebral ischemia (CCI) in MetS more profoundly. The purpose of the study is to determine the relations of cytokines, vasoendothelial growth factor (VEGF), biochemical and anthropometric indicators in patients with CCI on the background of MetS

Methods: 77 patients with CCI were examined. They were divided to 2 groups: the main 1 with MetS and the comparison group without MetS. Average age of patients was 58.29±0.92 years old. Clinical and neurological, anthropometric, neuroimaging, biochemical (level of interleukin-6 (IL-6), interleukin-10 (IL-10), VEGF in blood serum) methods were used.

Results: In the patients, neurological syndromes, mild cognitive impairments, psycho-emotional disorders, structural brain changes (“silent” infarcts, leukoaroosis, atrophy, dilatation of perivascular spaces) were identified. It was found out that patients with CCI and MetS had significantly higher levels of IL-6 and VEGF as compared with the group without MetS (see table). In the examined patients with CCI it was found a direct correlation between IL-6 and glucose concentration, weight, waist size (WS) and between VEGF and WS, whereas in the group with MetS the direct correlation was found between IL-6 and IL-10.

Table - Concentration of biomarkers of IL-6, IL-10, VEGF in patients with and without CCI and MS.

Group	Main group (n=41)	Comparison group (n=36)	Normal
IL-6, pg/ml (min, max)	2,11 (1,23; 3,32) ¹	1,45 (0,94; 2,02)	< 10,00
IL-10, pg/ml (min, max)	6,05 (5,00; 7,81)	5,75 (5,00; 8,67)	< 31,00
VEGF, pg/ml (min, max)	230,82 (84,65; 359,49) ¹	64,21 (20,41;202,13)	< 691,00
Note: 1 - p < 0,01 as compared with the comparison group			

Concentration of biomarkers of IL-6, IL-10, VEGF in patients with and without CCI and MS.

Conclusion: Inflammation and endothelial dysfunction plays an important role in the pathogenesis of the CCI development in patients with MetS.

Disclosure: Nothing to disclose

EPO2064

Neurovascular coupling impairment: a useful biomarker for cerebral small vessel disease in hypertensive subjects?

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Background and aims: The mechanistic link between hypertension and cerebral small vessel disease (CSVD) is still poorly understood. We hypothesized that hypertension could impair cerebrovascular regulation prior to established cerebrovascular disease.

Methods: 59 hypertensive patients [56% males; age 64±10 years; 58% with comorbid diabetes mellitus (DM)] without irreversible symptomatic cerebrovascular disease, underwent transcranial Doppler (TCD) monitoring in the middle (MCA) and posterior (PCA) cerebral arteries, to assess dynamic cerebral autoregulation (dCA), vasoreactivity to carbon dioxide (VR) and neurovascular coupling (NVC), as well as brain MRI. TCD data from 20 healthy controls was obtained for comparison (24% males; age 59±16 years).

Results: Hypertensive patients showed significant impairment of neurovascular coupling in the PCA, with smaller increases in cerebral blood flow (CBF) velocity during visual stimulation ($p=0.037$), as well as disturbed NVC time-varying properties, with lower natural frequency ($p<0.001$) and lower rate time ($p=0.010$), when compared to controls. dCA and VR remained relatively preserved in MCA and PCA. NVC dysfunction was more pronounced in those with coexisting DM resulting in lower natural frequency ($p=0.025$) and smaller increase in CBFV during visual stimulation ($p=0.052$). TCD measures did not relate to white matter burden on MRI in the monitored vascular territories.

Conclusion: These findings suggest that hypertension and DM particularly affect NVC in PCA territory, irrespective of established white matter lesions. Neurovascular coupling could be useful as an early, non-invasive surrogate marker for CSVD to guide therapies and prevent future clinically relevant impairment.

Disclosure: Nothing to disclose

EPO2065

Posterior Reversible Encephalopathy Syndrome with an unusual trigger.

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Background and aims: Posterior Reversible Encephalopathy Syndrome (PRES), caused by endothelial dysfunction, is related to many diseases (hypertension, autoimmune disorders, immunosuppressive drugs, renal failure...). It usually presents with confusion, headache, seizures, parieto-occipital symptoms and brain MRI lesions that are hyperintense in T2 and FLAIR sequences without significant restricted diffusion (vasogenic edema) and predominantly parieto-occipital. The trigger must be solved and the hypertension and seizures must be controlled. It has good prognosis, not always reversible.

Methods: Male, 43 years, no background. In September, he presented rapidly progressive glomerulonephritis and hemoptysis, positive for anti-glomerular basement membrane antibodies. Goodpasture syndrome was diagnosed and hemodialysis and treatment with corticosteroids, cyclophosphamide and plasmapheresis were initiated until antibodies negativization. Cyclophosphamide was stopped due to leukopenia, switching to Rituximab in November. In December, he suffered pneumonia due Enterococcus, being Meropenem prescribed. During admission he had hypertension, and after 3 days of non-disabling headache, he presented 2 seizures. He had chronic infarction in the right caudate nucleus and subtle occipital hypodensity in cranial CT and normal cerebrospinal fluid.

Results: Due to the fact that PRES was suspected, blood pressure control was intensified and antiepileptic drugs were prescribed. In brain MRI typical frontal-parieto-occipital lesions were identified. He had a good progress with thunderclap headache episodes, and nimodipine was added due to possible associated reversible cerebral vasoconstriction syndrome (RCVS). No brain MRI lesions after one month.

Conclusion: PRES has been associated with various autoimmune diseases, with few cases related to Goodpasture syndrome. In our case, hypertension and renal failure could participate in the etiopathogenesis.

Disclosure: Nothing to disclose

EPO2066

Superficial siderosis of central nervous system. Report of four cases and review of literature

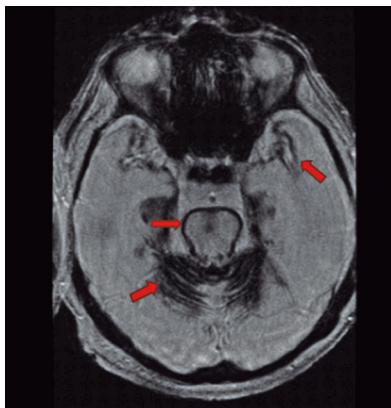
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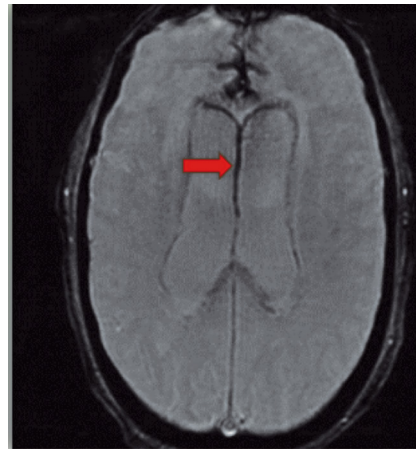
Background and aims: Superficial siderosis is a rare entity produced by hemosiderin deposits in subpial layers of the brain, cerebellum and spinal cord due to chronic bleeding into the subarachnoid or intraventricular space. It produces a characteristic clinical Picture with neurosensorial hearing loss, cerebellar ataxia and pyramidal signs. dural injuries, tumors, traumas and vascular malformations are among the most common causes. Magnetic resonance is the diagnostic test, where the characteristics hypointense lines are seen in areas of pigment deposit. The objective of this study is to emphasize the peculiarities of this disease by describing four cases diagnosed in hospitals in our region.

Methods: Review of the medical histories of our patients and literature search about the disease.

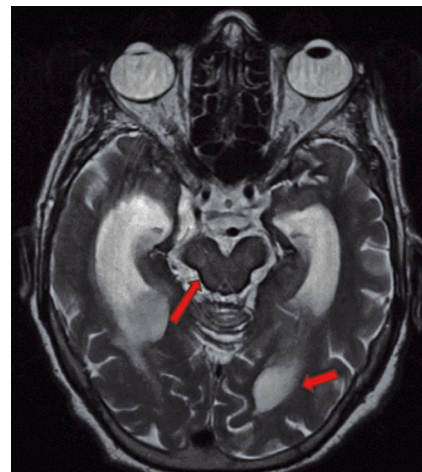
Results: 3 of the patients have the typical clinical triad. In 2 of these, rare signs such as hydrocephalus and impaired deep sensitivity were found. The etiology of the chronic bleeding was found in 3 of our cases: post-radiotherapy telangiectasias in case 1, pseudomeningocele in case 2 and arterial aneurysm in the case 4. In case 3 no cause was found. 2 of the patients were anticoagulated, so we thought it might be a risk factor for this disease. The management of patients consisted in the administration of iron chelators in cases 1 and 2, surgery in case 4 and symptomatic treatment in case 3.



Gradient-echo T2 MRI. Case 2. Linear hypointensities surrounding pons, cerebellum and temporal lobes.



Gradient-echo T2 MRI. Case 1. Subependymal hypointense lines.



Gradient-echo T2 MRI. Linear hyperintensity surrounding midbrain and ventriculomegaly.

Conclusion: Superficial siderosis is a rare entity to be considered in the differential diagnosis of patients with progressive neurological symptoms, mainly when hearing loss and ataxia are present.

Disclosure: Nothing to disclose

EPO2067

Eye tracking as a potential tool to evaluate treatment efficacy in acute ischemic stroke clinical trials

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Background and aims: N-PEP-12 is peptide-based dietary supplement with neuroprotective and pro-cognitive effects, as described by several experimental studies. We used eye movement tracking latency, an evidence-based indicator for cognitive status, to explore the efficacy of N-PEP-12 supplementation for 90 days in patients with acute ischemic stroke.

Methods: Eye movements of patients with supratentorial, radiologically confirmed ischemic stroke were measured using a standardized vertical saccades test captured with a Tobii Pro TX300 eye tracking device at 30, and 101 days after patient recruitment (n=121). After artifact and outlier removal, valid saccades were aggregated by individual examination to explore group differences in baseline change vertical saccadic eye movement latency (VSEML) between N-PEP-12 and placebo populations, using a mean difference parametric hypothesis (independent samples t-test), in accordance with sample distributions and other assumptions.

Results: A statistically significant difference in baseline change VSEML between N-PEP-12 and control groups were observed at day 101 ($F=4.719$, $p=0.038$).

Conclusion: N-PEP-12 may have a favorable effect on patients after acute ischemic stroke eye tracking parameters. Vertical latency should be assessed in conjunction with other eye tracking indicators such as velocity and gain to provide a multidimensional snapshot of the intervention's potential to improve acute ischemic stroke outcomes.

Disclosure: Nothing to disclose

EPO2068

Evaluation of cognitive impairment with P300 evoked potential method in patients with cerebrovascular impairment and type 2 diabetes

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Background and aims: Type 2 diabetes mellitus (T2DM) is an established risk factor for cognitive deficit. There are several studies indicating that cognitive impairment in T2DM patients with cerebrovascular diseases can be developed on the earlier stages of the disease. P300 evoked potential is one of the most promising methods of assessing cognitive dysfunction.

Methods: In a non-randomized controlled study we investigated 52 patients with chronic cerebrovascular diseases being main criterion for inclusion. The baseline characteristics of the patients were balanced. In the main group were 23 patients with T2DM and in the control group were 29 without T2DM. 12 patients from the main group and 16 from the control group were with mild cognitive impairment (MCI). We confirmed MCI with neuropsychological assessment tests. All patients were examined with P300 evoked potentials. The amplitude and latency of P300 waves were the main target of this study.

Results: Of the all patients enrolled latency in patients form both groups with MCI was statistically longer (372ms average versus 389ms average) while the amplitude was lower (8.7 average versus 10.6 average). In the main group six patients with T2DM without confirmed MCI were noted; they had lowered amplitude and longer latency compared to the patients from the control group.

Conclusion: In the patients with T2DM P300 evokes potential method can be used to easily and safely detect cognitive dysfunction on the onset of the clinical course. Further studies required to determine reliability of this method.

Disclosure: Nothing to disclose

EPO2069

Concomitance of subdural thoracic spinal hematoma and diffuse subarachnoid hemorrhage in the neuroaxis simulating acute myocardial infarction: a Case Report

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Background and aims: Spinal subdural hemorrhages (SDHs) are rare, accounting for 4.1% of all spinal hematomas. Simultaneous SDH and subarachnoid hemorrhage (SAH) have been reported in only a few cases. We present a case of this instance, simulating an acute myocardial infarction (AMI).

Methods: 67-year-old male, hypertensive, dyslipidemic, with mild chronic renal impairment (CRI), in use of apixaban for atrial fibrillation, was admitted for retrosternal pain. ECG demonstrated an increase of the ST segment and slight elevation of serum troponin. Later, he showed lacunar amnesia, lasting for about 4 hours, which later improved. Brain MRI showed hypersignal in DWI in the parahippocampal regions. Serial test of myocardial necrosis markers did not displayed a typical behaviour of AMI, being the increase of troponin attributed to CRI. 2 days later, patient presented paraplegia and areflexia of the lower limbs, with sensory loss below T6 level. MRI showed a subdural hematoma at T6, with spinal compression, as well as a diffuse subarachnoid hemorrhage in the neuroaxis, reaching the encephalon, of presumed origin at the same site of the SDH. The hematoma was drained by the neurosurgical team and the patient underwent corticotherapy, with partial improvement. Angiography revealed a paravertebral venous ingurgitation, which could be caused either by extensive hemangioma or paravertebral arteriovenous fistula. The patient remained restricted to bed, in need of intermittent vesical relief probing.

Results: Intramedullary bleeding in concomitance with subdural and subarachnoid hemorrhage simulated an AMI.

Conclusion: Intramedullary bleedings in concomitance with subdural and subarachnoid hemorrhage should be considered as differential diagnosis of thoracic pain.

Disclosure: Nothing to disclose

EPO2070

Clinical and neuroimaging differences in lacunar ischemic stroke patients with cerebral amyloid angiopathy and hypertensive cerebral microangiopathy

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Background and aims: Lacunar ischemic stroke (LS) may be associated not only with hypertensive cerebral microangiopathy (hCMA) but sometimes with cerebral amyloid angiopathy (CAA). The secondary stroke prevention for patients with combination of hCMA and CAA (hCMA+CAA) differs from that in isolated hCMA, thus the intravital diagnosis of probable CAA is extremely important.

The aim of the study was to compare clinical and neuroimaging features in LS patients with hCMA+CAA and hCMA.

Methods: 47 patients (aged 65.6±6.3 years) with 1st-ever acute LS were examined by the Montreal Cognitive Assessment scale, Frontal Assessment Battery and Fazekas scale. The diagnosis of CAA was based on the Boston criteria, hCMA was diagnosed according to the Standards for Reporting Vascular changes on neuroimaging. In all cases CAA was associated with hCMA.

Results: The patients were divided into 2 groups: 1) with hCMA+CAA (12 patients); 2) with isolated hCMA (35 patients). There was no difference between the groups by age, sex, comorbidities, lesion site and severity of acute LS. Fazekas grade 3 was significantly more often in group 1 (83.3%) than in group 2 (11.2%, p<0.001). Cognitive dysfunction including executive disorders in group 1 were significantly more pronounced than in group 2 (Mann-Whitney U Test = 69.0, p<0.001 and U = 14.5, p<0.001).

Conclusion: Stroke patients with combination of probable CAA and hCMA have more severe cognitive impairment and white matter lesion than patients with isolated hCMA. CAA has its own negative effect on the deep white matter of brain.

Disclosure: Nothing to disclose

EPO2071

Long-term outcome of mechanical thrombectomy for acute ischemic stroke patients on therapeutic anticoagulation

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Background and aims: We analyzed long-term outcome as measured as mRS on day 90. in acute ischemic stroke (AIS) patients on therapeutic anticoagulation treated by mechanical thrombectomy (MT). There are limited data on long-term outcome of anticoagulated patients treated by MT.

Methods: The study was conducted in 291 AIS patients (49% women, mean age 66±15 years) who underwent MT in Comprehensive Stroke Center in Krakow, Poland. The following data were collected: demographics, stroke risk factors, NIHSS on admission, TICI score after the procedure, hemorrhagic transformation (ECASS-2) on CT 24 hours after stroke, and time lapse between stroke onset and groin puncture (SO-GP). Outcome measure was mRS on the day 90. after stroke onset. Good outcome was defined as mRS≤2.

Results: 37 patients (13%) were on therapeutic anticoagulation during procedure: warfin: 14 (37,8%); full dose heparin:5 (13,5%); dabigatran:5 (13,5%) or rivaroxaban:13 (35,0%). Univariate analysis showed that anticoagulated patients were older, had more often ischemic heart disease or atrial fibrillation (p<0,05). They didn't differ in respect to clot location, TICI score after procedure, hemorrhagic transformation on CT or mRS profile on the day 90.

Multivariate analysis showed that older age (OR=0.94;95%CI=0.91-0.97), hemorrhagic transformation (OR= 0.36;0.95%CI=0.20-0.67), SO-GP (OR=0.72;95%CI=0.60-0.87), poor recanalization (OR=0.14;95%CI=0.07-0.29), diabetes mellitus (OR= 0.32;95%CI=0.16-0.64), hypertension (OR=2.35;95%CI=1.11-4.95) affected recovery as measured by mRS 0-2 at day 90.; however therapeutic anticoagulation didn't (OR=0.92;95%CI=0.38-2.21).

Conclusion: MT in anticoagulated patients doesn't affect long-term outcome.

Disclosure: Nothing to disclose

Child neurology/developmental neurology; Neuroepidemiology

EPO2072

Mortality rates of hospitalized patients in Neurology: a tertiary hospital experience

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Background and aims: Cerebrovascular disease is the 1st cause of death in Spanish women and the 3rd in general population. Alzheimer and Parkinson's disease are the only causes of death which currently keep increasing in frequency. We aim to study mortality causes of Neurology inpatients.

Methods: Descriptive analysis of deceased inpatients in the neurology department of a tertiary hospital from January 2014 to December 2018 including demographic and clinical variables, specifically treatment with anticoagulant drugs.

Results: 408 deaths out of 7145 admissions (5.7%) were included, 58.8% women with mean age of 82.3 years (SD 10.4). The most common cause of death was ischemic stroke (56.1%, 27.5% under treatment with acenocumarol and 4.8% with direct oral anticoagulants), followed by haemorrhagic stroke (32.4%, 38.7% under treatment with acenocumarol and 5.3% with direct oral anticoagulants) and status epilepticus (4.2%). Other causes of death (7.4%) were meningoencephalitis (5), amyotrophic lateral sclerosis (4) and Parkinson's disease (3) among others. There was an increase in the age at death (80.1 (SD 9.7) in 2014 vs. 85.2 (SD 8.9) in 2018, as well as in mortality rates (5.7% in 2014, 5% in 2015 and 2016, 5.5% in 2017 to 7.2% in 2018).

Conclusion: Ischemic stroke was the most frequent cause of death in our study, in agreement with previous epidemiological studies. The progressive increase of mortality in our study may be related with the parallel increase in age, but more comprehensive prospective studies are warranted.

Disclosure: Nothing to disclose

EPO2073

Alzheimer's disease and vascular dementia as main cause of death in a rural southern Italian population: data from the Zabùt Aging Project

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Background and aims: To identify the contribution of AD and VA in determining the exitus using population-based data from a cohort study conducted in a rural village in Italy.

Methods: This study was carried out using data of the Zabùt Aging Project (ZAP), a comprehensive survey on neuropsychiatric disorders carried out on all subjects aged ≥ 50 years living in a rural village in south Italy (n=2,028). Information about deaths in the cohort was obtained from the Sicilian Regional Statistical Office using death certificates. Death causes were coded using the International Classification of Diseases (ICD-9). The risk of dying (mortality risk ratio) was calculated using multivariate Cox (proportional hazards) regression models.

Results: 1,957 subjects aged 50 or more years were analyzed in the present study. Of these 613 (31.3%) deceased during the follow-up period (2001-2014), whereas 1,344 (68.7%) withdrew alive. Death was more frequent among men (33.9% vs 29.1%), in patients aged more than 70 years old and in those with less than 10 years of education, and in subjects with dementia. Factors associated with the highest hazard risk of death after multivariate analysis were age (adj-HR=2.49; 95% CI 2.28-2.72), AD (adj-HR= 2.13; 95% CI 1.56-2.89) and VD (adj-HR= 3.55; 95% CI 2.58-4.87).

Conclusion: In conclusion, AD and VD significantly increase the risk of mortality at a given age than subjects without dementia; however, death certificate - due to underreporting - can be not considered an accurate public health tools for detecting subjects suffering from dementia.

Disclosure: Nothing to disclose

EPO2074

Exploring the association between *Helicobacter pylori* and Parkinson's diseaseL. Eisenberg¹, N. Giladi², C. Peretz¹¹Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, ²Tel Aviv Medical Center, Tel Aviv, Israel

Background and aims: Epidemiological studies provided controversial results on the association between *H. pylori* infection and the risk for Parkinson's disease (PD). However, some of these studies included only a small number of participants.

Methods: In this work we explored this association by a retrospective large-scale cohort of subjects (n=118,531), who underwent 179,060 *H. pylori* breath tests. 3 stratified Cox proportion hazard models were applied to evaluate HR and 95%CI for PD risk associated with *H. pylori* breath test results by sex, socioeconomic status and age groups. A logistic regression was applied to evaluate OR and 95%CI for positive *H. pylori* breath test results among PD patients.

Results: The proportion of PD patients who performed breath tests before PD diagnosis was almost 2-fold higher than those who performed the test after PD diagnosis, therefore suggesting an association between *H. pylori* testing and PD. However, men with positive *H. pylori* breath test results were found to be at a significantly lower risk for PD [HR= 0.65 (95% CI 0.48-0.88)]. Furthermore, the risk for a positive *H. pylori* breath test result was significantly lower for PD patients who performed the test either before or after PD diagnosis, as compared to non-PD patients [OR= 0.62 (95% CI 0.46-0.83), OR= 0.46 (95% CI 0.30-0.71) respectively].

Conclusion: Our results suggest that *H. pylori*-like symptoms, rather than the *H. pylori* infection itself, are a risk factor for PD. Therefore, we propose that *H. pylori* negative patients, that experience *H. pylori*-like clinical symptoms, should be monitored for early signs of PD development.

Disclosure: Nothing to disclose

EPO2075

Analysis of interconsultations to a secondary-level hospital neurology service

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Background and aims: Intrahospital consultations (IC) are a very important part on the daily care activity of a hospital medical service. The objective of this study is to know the characteristics of the IC made to a secondary-level hospital Neurology Service (NS), such as who are the services that are most consultant ones and for what reasons.

Methods: Retrospective descriptive study of the IC performed to the Reina Sofía General University Hospital Neurology Service during a 5 month period (August-December, 2018).

Results: 73 patients were included (mean age 65.99, men 54.8%, women 45.2%). There was an average of 17.6 days of admission. Most demanding services: Internal Medicine 35.6%, Cardiology 17.8%, Traumatology 9.6% and General and Digestive Surgery 8.2%. IC reasons: cognitive disorders 23.3%, neurological focus on limbs (excluding hemiparesis or hemihypoesthesias) 13.7% and movement disorders 12.3%. IC objective: diagnosis 65.3% and treatment 34.2%. 12.3% of the patients died during admission or in less than a month after discharge.

Conclusion: Comparing with other hospitals that count on with a neurologist on call, most ICs do not perform urgent neurological pathology, probably due to this reason (the urgent pathology is solved by other doctors on call). Taking into account this fact, we see the most interconsultant service was Internal Medicine (IM), probably because it is the service with more beds available, being the most frequent reason for admission in IM the infectious pathology, motivating the interconsultation for cognitive disorders in a greater number of cases.

Disclosure: Nothing to disclose

EPO2076

Hospitalizations for acute confusional syndrome: from emergencies to the neurology service

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Background and aims: Acute confusional syndrome (ACS) is the presentation of serious pathologies, requiring an etiological diagnosis with high resource consumption. The objective of this study is to know the characteristics, studies and imaging tests and final diagnosis of patients admitted by ACS in Neurology.

Methods: Descriptive retrospective study of hospitalizations due to SCA from the Emergencies Service (ES) to the Neurology Service of the General University Hospital Reina Sofia during a 5 years period (2014-2018).

Results: 44 patients were included (Age: Median 77.5 years, Men: 63.6%; Women 36.4%) whose diagnosis at hospitalization was ACS. The prevalence of cardiovascular risk factors 61.4%, toxic consumption 13.6%, cerebrovascular disease 27.3%, cognitive impairment 25%, psychiatric pathology 22.7%, chronic treatment associated with ACS 34.1% and infectious focus 20.5% was collected. 86.4% of the patients presented disorientation, and 45.5% psychomotor agitation. 90.7% of CT performed on ES were not pathological. 56.8% of ACS were due to primary neurological disease; infectious (non-CNS) 25%; Others: 38.6%, and 11.4% unknown. Multifactorial origin: 25%.

Conclusion: Our sample is aged and pluripathological, so the etiological diagnosis is complex. However, in 55.6% of patients with an infectious focus identified on ES (not CNS), ACS was attributed to this infection, as in 23.5% of toxic-metabolic pathology already identified in ES, so some hospitalizations could have been redirected. A factor that explains this fact is the absence of a neurologist on call, making it difficult to identify neurological pathology on the ES.

Disclosure: Nothing to disclose

EPO2077

The role of vascular risk factors and determination of vascular remodeling parameters in patients with acute lymphoblastic leukemia

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Background and aims: The aim of this study was to assess if there is an impact of vascular risk factors (VRFs) in patients with acute lymphoblastic leukemia (ALL) on vascular remodeling parameters before and after 1 month of chemotherapy treatment measuring the Intima-Media-Thickness (IMT) using Extracranial-Doppler (ECD), ankle-brachial index (ABI), arterial stiffness aortic pulse wave velocity (PVW) and arterial age.

Methods: We enrolled 52 patients with ALL aged between 19-82 scheduled for 1 cycle of chemotherapy treatment. The ECD and evaluation of systolic blood pressure(SBP), diastolic blood pressure(DBP), heart rate(HR), vascular remodeling parameters were performed prior and 1 month after the treatment and correlated with VRFs.

Results: Out of the 52 study patients, 22 (42.51%) were with VRFs: 5 (9.61%) patients had hypertension and diabetes mellitus, 12 (23.07%) had hypertension and smokers. HR (b/min) significantly increased from 79.09±16.82 to 85.71±14.48.29 (p<0.001). IMT (mm) significantly increased from 0.78±0.20 to 0.83±0.18 (p<0.001) in the left carotid artery. ABI (%) significantly decreased from 1.11±0.15 to 1.10±0.10 (p<0.05) on the left side. PVW(m/s) and the arterial age significantly increased (p<0.001) after chemotherapy treatment with slightly worse values in hypertensive and dyslipidemia patients.

Conclusion: It is recommended to identify the VRFs, to evaluate the carotid artery with ECD and to calculate the vascular remodeling parameters for patients with ALL before, during and after the chemotherapy treatment. Where it is possible, in order to prevent the occurrence of vascular complications, it is very important the correction of the VRFs for the strategy of adherence to cytostatic treatment.

Disclosure: Nothing to disclose

EPO2078

Recovery of consciousness in pediatric disorders of consciousness: long-term outcomes and predictors

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Background and aims: 1st, to determine the long-term outcome of a pediatric sample with disorders of consciousness due to a severe acquired brain injury with the Coma Recovery Scale-Revised (CRS-R); and second, to describe the most frequent items of this scale that determine recovery of consciousness.

Methods: 21 children from 2 to 16 years old who were admitted to the Neurorehabilitation Unit of Vithas Hospitals participated in the study. Participants had a mean age of 9.4±4.7 years old. 7 of them had suffered a traumatic brain injury and 14 a non-traumatic brain injury. All subjects were included in a personalized multidisciplinary rehabilitation program. Participants were assessed using the CRS-R at admission and weekly during the 1st year after the injury or until recovery of consciousness.

Results: At admission, 8 children (42.9%) were in an Unresponsive Wakefulness Syndrome (UWS) state, nine children (38.1%) in a Minimally Conscious State minus (MCS-), and four children (19%) in a Minimally Conscious State plus (MCS+). One participant diagnosed as UWS, and ten participants diagnosed as either MCS+ or MCS- at admission, regained consciousness. The most frequent feature of recovery of consciousness was functional communication, alone (n=5) or associated with functional object use (n=4). Most participants (72.7%) regained consciousness during the 1st 6 months after the injury. Time since injury and initial CRS-R scores were found to be predictors of outcome.

Conclusion: Most frequent feature of recovery of consciousness was functional communication. Best predictors of recovery included time since injury and CRS-R score at baseline.

Disclosure: This study was funded by Conselleria de Educació, Cultura y Deporte of Generalitat Valenciana of Spain (Project SEJI/2019/017) and Universitat Politècnica de València (Grant PAID-10-18).

Table 1: Correlation between risk factors, ASPECTS and stroke outcome after 3 months

Variable	All patients	MRS 0-2 favorable outcomes	MRS 3-6 poor outcomes	P Value
Number	150	95 (63.3%)	55 (33.7%)	0.05
Age (years)	64.0 ±11.5	59.11 ±7.45	68.7 ±6.98	0.001
Male	79 (52.7%)	49 (51.5%)	30(54.5%)	0.725
Hypertension	102 (68%)	54(56.8%)	48(87.3%)	0.005
DM	39 (26%)	23(24.2%)	16(29.1%)	0.511
Smoking	60 (40%)	37(38.9%)	23(41.8%)	0.729
Hyperlipidemia	22 (14.6%)	13(13.7%)	9(16.4%)	0.654
AF	28 (18.6%)	17(17.9%)	11(20%)	0.749
IHD	15 (10%)	10 (10.5%)	5 (9.1%)	0.778
NIHSS on admission	12.9 ± 7	10.97 ± 4.64	18.92 ± 6.32	0.001
ASPECTS	8.23 ± 1.87	8.23 ± 1.87	4.96 ± 2.56	0.001

EPO2079

Long-term effects of prenatal stress on synaptic proteins and motor coordination in the rat cerebellumJ. Pascual¹, M. Valencia²¹Valparaíso, Chile, ²Kinesiology, Pontificia Universidad Católica de Valparaíso, Valparaíso, Chile

Background and aims: Prenatal stress and/or in utero exposure to elevated levels of glucocorticoids (GCs) can adversely affect

the cerebellar maturation and motor development in animal models. However, the precise mechanism by which GCs exposure impairs synaptic protein expression is unknown. Therefore, the purpose of this study was to investigate the effect of prenatal exposure to a clinical dose of synthetic GCs on the cerebellar pre- and postsynaptic structural proteins, whose synchronized synaptic activity is crucial for motor coordination.

Methods: 8 pregnant rats were randomly classified into 2 experimental groups: control (CON) and betamethasone (BET). Mothers in the BET group were subcutaneously administered 2 injections of BET (0.17mg/kg, separated by an 8h interval at gestational day 20, G20). The CON mothers were given an equal volume (1ml) of saline. Progeny of CON and BET mothers were evaluated for motor coordination and cerebellar content of synaptic proteins synaptophysin (SYN) and postsynaptic density-95 (PSD-95).

Results: Rats prenatally treated with BET exhibited underexpression of synaptophysin accompanied by motor coordination impairments. However, the PSD-95 remains unchanged.

Conclusion: In conclusion, the current data confirm and extend our previous histological observations that prenatal stress induced by exogenous GCs alters the expression of structural proteins (mainly synaptophysin) associated with mild motor coordination impairments.

Disclosure: Nothing to disclose

EPO2080

Metabolic ataxia linked to new mutation in L2HGDH geneA. Potic¹, E. Salsano², C. Gellera², B. Castellotti², F. Taroni²¹Belgrade, Serbia, ²Milan, Italy

Background and aims: L-2-hydroxyglutaric aciduria (L2HGA) is a rare neurometabolic disorder caused by homozygous or compound heterozygous mutations in L2HGDH gene. The resultant abnormal metabolism of L-2-hydroxyglutaric acid leads to the accumulation of L-2-hydroxy-glutarate which has a toxic effect on central nervous system. Clinical presentation varies and may include: psychomotor delay, cerebellar, pyramidal and extrapyramidal signs, macrocrania, seizures. Brain magnetic resonance imaging (MRI) inevitably points to a leukoencephalopathy. We report a novel mutation in L2HGDH gene and the phenotype in this second genetically proven patient with L2HGA from Serbia.

Methods: A 6-year-old boy was referred to neurologists with a history of slowly progressive cerebellar ataxia which was firstly observed at 2 years of age. No other complaints existed upon admission. The key investigations undertaken were brain MRI and metabolic screening. Genetic analysis followed afterwards.

Results: Apart from the predominant cerebellar signs, neurologic exams detected also mild bilateral pyramidal signs and a minor intellectual disability. Brain MRI showed diffuse supratentorial white matter T2-hyperintensity along with altered signal of nuclei dentati and putamina. Metabolic study showed increased urinary L-2-hydroxyglutaric acid values which led to the diagnosis of L-2-hydroxyglutaric aciduria. Genetic analysis confirmed the diagnosis and revealed that the patient was a compound heterozygote for a known (c.530_533delinsATT) and a novel (c.404G>A) pathogenic mutation in L2HGDH gene. The patient was put on high-dose riboflavin with a good response.

Conclusion: L-2-hydroxyglutaric aciduria should be timely recognised for the proper treatment, genetic counseling, and the possibility of accompanied brain malignancies in this disorder.

Disclosure: Nothing to disclose

EPO2081

Comparison of comorbidities in adult patients with epilepsy versus general population of Moscow

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Background and aims: The high prevalence of comorbid conditions in people with epilepsy (PWE) is well known. In population based study, we compared prevalence of somatic comorbidities in adult PWE in Moscow to age and gender matched controls.

Methods: Case-control study (1:3 match) of 1317 (671 female, 646 male) adult PWE and age- and gender-matched controls seen in the same outpatient clinics and diagnosed with an acute upper respiratory infection (ICD 10J00-J06) in 2018. Data source was from the “Unified medical information analytical system” of Moscow. Frequency of specific comorbid groups was compared between PWE and controls. Pearson’s chi-squared test was used.

Results: The mean number of comorbidities was significantly higher in PWE versus controls in most age groups ($p < 0.05$). Cerebrovascular disease was more prevalent in PWE 51 years and older ($p < 0.05$), ulcers and liver diseases – in PWE over 41 years old ($p < 0.05$). Differences in heart disease prevalence, especially the prevalence of arterial hypertension were significant only in limited age groups. Allergies were more common in PWE in most age groups ($p < 0.05$). The prevalence of official disability status was higher in PWE ($p = 0.0000$).

Conclusion: The mean number of comorbidities was higher in adult PWE versus controls in Moscow. The prevalence of cerebrovascular disease, allergies, and ulcers and liver diseases, were higher in PWE, especially in older age groups. The higher prevalence of official disability status in PWE could be explained by frequent seizures and comorbidities, but social reasons as well. The high number of comorbidities should be taken into consideration in the management of PWE.

Disclosure: Nothing to disclose

EPO2082

Arachnoid cyst management in child neurology

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Purpose: To develop the concept of the personalized neurological diagnostics and neurosurgery of the intracranial arachnoid cysts (IAC) in children

Methods: Results of diagnostic and treatment of 804 children aged 1-17y.o. were analyzed in 2 groups: with 1gr.-hydrocephaly, 2gr.- intracranial arachnoid cysts. The most part (57.5%) were in the age up to 3 years, the most frequent - till 1 year. The clinic, disease dynamics, outcome of treatment IAC and monitoring of the amplitude-frequency characteristics of liquid pressure fluctuation, the reserved subdural volume, deformations of a brain and ventricles, researches of biomechanical properties, pressure were carried out

Results: There were 116 children with IAC in 2gr. Hypertension syndrome (47.4%), focal symptoms of damage of the nervous system (52.5%) and remitting type (86.2%) were typical for children with IAC. The structure and expressiveness of manifestations IAC depended from the volume of local congestion of liquid, craniocerebral disproportion. The main directions of preoperative diagnostics were: the assessment of expressiveness and clinical manifestations, morphometry and biomechanical properties. Unsatisfactory results were caused by permanent resorption frustration in 19.8 %. Informative criteria of an outcome were: the age, anatomic-topographical features, dissociation level, cavities deformation expressiveness and forecast of probable postoperative complications.

Conclusion: Priority methods directed to elimination of the prime cause of liquor current violation and deformations of the brain should be used in the management of the intracranial arachnoid cysts in children.

Disclosure: Nothing to disclose

EPO2083

Evaluation of Parent Support Program on Attention-Deficit/Hyperactivity Disorder Symptoms in Young Children: a randomized controlled trial

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Background and aims: Attention Deficit Hyperactivity Disorder (ADHD) is a chronic condition affecting millions of children worldwide. There has been no cure but with medication and behavioural management, symptoms can be managed with great effect. Previous studies explored the effect of parent training intervention in children aged 5 and 8 years old and found beneficial effects in children and parents.

Methods: Present study evaluated parent support program (L.E.A.D) in ADHD-risk children. 75 children aged between 8 to 12 years old were having ADHD symptoms were recruited from community clinic. Parents were enrolled in support groups where they were skilled to manage their children's challenging behaviour. Intervention consisted of 60mins group session followed by parenting one to one support. Children were assessed before and after the 3 months of intervention. Outcome measures were parent ratings of ADHD symptoms, behavior, mood, attitude and understanding toward peers.

Results: Post data included seventy parents. AT the end of intervention, parents reported significant decrease in ADHD symptoms: $p < 0.001$; oppositional symptoms: $p < 0.001$; mood symptoms; $p < 0.01$. Parents reported better behavior towards peers but that did not reach significance levels.

Conclusion: To our knowledge, this is the 1st randomized trial to address parent support intervention for an ADHD-risk sample. This study provides significant evidence on the beneficial effect of parent support program on at-risk ADHD Children.

Disclosure: Nothing to disclose

EPO2084

Seroprevalence of Tick-Borne Encephalitis Virus in Agricultural Population on Jeju Island, South Korea

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Background and aims: Tick-borne encephalitis virus (TBEV), which is endemic in Europe and Northeast Asia, causes tick-borne encephalitis (TBE). Although there are some reports for TBE from China and Japan, it has not yet been reported in South Korea. We investigated seroprevalence of TBEV among the agricultural population on Jeju Island, South Korea, where tick-borne disease is common.

Methods: A Serosurvey was conducted for the agricultural population living in rural areas between January 2015 and December 2018. 10 rural villages were chosen based on the type of farming practiced and the distance from urban areas. Of the 500 participants, 423 agreed to participate in the research, 321 of which were enrolled in the study. Serum samples were tested for TBEV IgM and IgG using a enzyme-linked immunosorbent assay.

Results: Of the 313 participants, 4 (1.3%) were positive for anti-TBEV IgG, while 2 (0.63%) were positive for anti-TBEV IgM. None of the seropositive participants reported having typical manifestations of TBE or a history of travel to a TBEV-endemic area, within the 3 years before sample collection. Neither of the IgM positive participants had fever in the 2 weeks preceding serum sampling. There was no particular pattern in residential areas of seropositive participants.

Conclusion: This is the 1st study of TBEV infection in South Korea. Even though the seroprevalence in the study population was lower than that reported in countries in Far-East Asia, the results confirm the possibility of TBE among people in South Korea who have contact with ticks.

Disclosure: Nothing to disclose

EPO2085

Early parent-child interaction and child temperament features as predictors of self-direction skills formation at the age of 24 months

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Background and aims: The system of regulation of activity is a temporary functional structure providing selective, coordinated and purposeful flow of sensory-perceptual, intellectual, mnemonic, motor, and speech processes to achieve arbitrarily selected individual specific tasks. The research aim was to assess the degree of influence of temperament and features of early parent-child interaction on the regulatory functions in children at the 24-month stage.

Methods: 13 dyads of healthy, typically developed full-term infants (6 boys) were assessed at 5, 10, 14, 24 months age - longitudinal study design. Adaptive Behavior Scale (from Bayley-III, certified specialist) was used for self-direction skills assessment. The Revised Infants Behavior Questionnaire (IBQ-r) was filled by parents for evaluate the child temperament. Parent-child interaction Scale (PCI) was evaluated through video analysis (certified specialists). All parents signed informed consent form. One-tailed Pearson correlation was measured (SPSS Statistics).

Results: Self-direction (the Bayley-III) in children at 24 months age didn't significantly correlate with either 5-month age super-factor on IBQ-r or parent features of interaction (PCI). There was significant correlation with parent Indirectivity (PCI) at the 10-month age ($r_{xy}=0.45$; $p=0.05$) and significant negative correlation with super-factor on IBQ-r "Negative emotionality" at the 14-month babies ($r_{xy}=-0.5$; $p=0.04$).

Conclusion: Self-regulation is a systematic integrative skill which includes cognitive (speed of information processing, goal setting, working memory, executive control, switching) and emotional (self-checking) components, which develops from birth and hard to be but must be assessed through the early stage of life with the help of complex approach.

Disclosure: The research was supported by the grant of the Russian Science Foundation 20-18-00343

EPO2086

Rare neurological diseases in a tertiary referral center in northern Greece

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Background and aims: Rare diseases affect a small number of people compared to the general population and can manifest symptoms in multiple organs, including the central and peripheral nervous system. In Europe, a disease is considered to be rare when it affects 1 person per 2000. The aim of this study is to present the 5 year experience acquired in the neurological department of a tertiary referral hospital in northern Greece.

Methods: Data from consecutive patients hospitalized in the 2nd Neurology Department of AHEPA University Hospital from January 2015 to December 2019 were assessed in order to study demographic features of patients with rare neurological diseases in northern Greece.

Results: From the total of 7842 admissions in the 2nd Neurology Department of AHEPA University Hospital during the study period (2015-2019), 263 patients were diagnosed with a rare neurological disease, with a ratio of almost 1:1 between male and female patients (m:133/f:130). 35/263 (13.3%) were diagnosed with Neuromuscular diseases, 13/263 (4.9%) were diagnosed with Cerebrovascular diseases, 3/263 (1.2%) were diagnosed with Metabolic disorders, 28/263 (10.7%) were diagnosed with Neuroimmune diseases, 4/263 (1.5%) were diagnosed with Neurocutaneous diseases, 166/263 (63.1%) were diagnosed with Neurodegenerative diseases and 14/263 (5.3%) were diagnosed with other rare clinical entities, including several congenital syndromes.

Conclusion: Rare diseases represent a global public health problem due to multiple hospitalizations during a long diagnostic journey and little chance of specific treatment options. We suggest that rare disease registries could play a crucial role towards the early diagnosis and appropriate management of these clinical entities.

Disclosure: Nothing to disclose

EPO2087

The prevalence of psychiatric symptoms before the diagnosis of Parkinson's disease

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Background and aims: Psychiatric symptoms (PS) can be non-motor features in Parkinson's disease (PD). Our objective was to explore retrospectively the prevalence of PS before the first diagnosis of PD.

Methods: In the framework of the Hungarian Brain Research Program we created a database from medical and medication reports submitted for reimbursement purposes to the National Health Insurance Fund in Hungary, a country with 10 million inhabitants and a single payer health insurance system. We used record linkage to evaluate the prevalence of PS before the diagnosis of PD and compared that with patients with ischemic cerebrovascular lesion (ICL) in the period between 2004-2016 using ICD-10 codes of G20 for PD, I63-64 for ICL and F00-F99 for PS. We included only those PD patients who got their G20 diagnosis in at least 2 different calendar years.

Results: There were 75,723 patients with PD and 783,843 patients with ICL. Of the PD patients 36.6% whereas of those with ICL 29.7% had a psychiatric diagnosis before the first appearance of PD or ICL ($p < 0.001$). The higher rate of PS in PD compared to ICL remained significant after controlling for age and gender in logistic regression analysis. The difference between PD and ICL was significant for Mood disorders (F30-F39), Organic, including symptomatic, mental disorders (F00-F09), Neurotic, stress-related and somatoform disorders (F40-F48) and Schizophrenia, schizotypal and delusional disorders (F20-F29) diagnosis categories.

Conclusion: The higher rate of psychiatric morbidity in the premotor phase of PD may reflect neurotransmitter changes in the early phase of PD.

Disclosure: Nothing to disclose

Clinical neurophysiology

EPO2088

Estimation Of Attention Deficit And Hyperactivity Disorder (ADHD) With Artificial Neural Networks Using EEG Signals

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Background and aims: Attention deficit and hyperactivity disorder (ADHD) is one of the most common diseases in the world. Several studies have been conducted on the use of electroencephalogram (EEG) signals in the diagnosis of this disease. Although a certain classification success has been achieved with the different methods applied in these studies, new studies are needed to achieve higher classification success.

Methods: In this study, retrospective records of 9 individuals diagnosed with ADHD and 10 healthy individuals were used. 4 of the patients with ADHD were female and 5 were male. 6 of the healthy individuals were female and 4 were male. EEG signals were recorded from individuals at 500Hz sampling frequency with 16 channel EEG device according to 17 different recording conditions. EEG data from 16 channels were divided into 5 and 10 second sections.

Results: Power spectral density (PSD) values of 1-49Hz frequencies were calculated by applying Welch method to the average EEG segments. These calculated features were applied to the Feed Forward Back Propagated Artificial Neural Network (FFBPNN) and Self Organizing Maps (SOM) network.

Conclusion: The accuracy and classification success of the classifiers were analyzed. According to the results of the analysis, the success rate of SOM network was calculated as 70% and the success rate of FFBPNN model was 89%. Accuracy from the FFBPNN model can support specialists in the diagnosis of ADHD disease.

Disclosure: Nothing to disclose

EPO2089

The relay race of the brain: characteristics of changing electroencephalographic peak alpha frequency in normal infants

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Background and aims: Alpha peak frequency is defined as the maximum power value in the EEG alpha/mu frequency spectrum (5-9Hz in infants). It has been previously reported that alpha peak frequency is characterized by significant interindividual differences and shift with age. Several studies identified mu (5-9Hz) peaks frequency during the first year of life: 5.4±0.8Hz at 6 months (Nyström P. et al., 2008), 7.03±0.47Hz at 8 months and 7.42±0.46Hz at 11 months (Stroganova T.A. et al., 1999); 7.5Hz at 12 months (Thorpe S.J. et al., 2016).

This study is attempt to confirm hypothesis that alpha peaks are not disappear with age, but become less prominent (subdominant). Moreover, apparently, alpha peaks are pre-existing (i.e. can be identified before become maximal).

Methods: Cross-sectional study. The EEG was recorded with a 128-channel EGI system referenced to vertex in 2 groups: 16 normal infants (mean chronological age (ma)=5.7±0.17 months), 15 other normal infants (ma=10.67±0.33 months). Power spectral density was estimated over the sensorimotor area (electrodes: 35, 41, 36, 30, 37, 7, 31, 55, 106, 80, 105, 87, 104, 103, 110) for each recording by Welch's method (Hanning window, size – 8s, overlap 50%) in 10-second fragment of resting EEG.

Results: The identified maximal peaks in younger age group had a mean frequency of 5.6±0.44Hz and 7.3±0.55Hz in the elder group. Subdominant peaks were identified at 7.43±0.23Hz at 5 months, 5.5±0.21Hz at 10 months.

Conclusion: To a first approximation, the achieved results have demonstrated validity of hypotheses mentioned above.

Disclosure: The reported study was funded by RFBR, project number 18-313-00180

EPO2090

Hippocampal sclerosis is not always accompanied by generation of epileptiform activity

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Background: The surgery of structural pharmacoresistant epilepsy is aimed at removing the epileptogenic zone, however, currently there are no methods to determine its reliable localization. There is not always a concordance between all diagnostic methods, in particular, when there are structural changes in hippocampus. Therefore, it is important to determine the epileptogenic zone regardless of etiological factor.

Aim: Determine the concordance of epileptiform activity according to electro subcorticography (ESubCoG), and signs of hippocampal sclerosis according to MRI.

Methods: 28 patients with structural pharmacoresistant temporal lobe epilepsy were examined. The age of the patients was from 20 to 50 years (mean 35±15). The disease duration ranged from 4 to 38 years (mean 21±17). The standardised examination algorithm included clinical analysis of seizure pattern; intraoperative neurophysiological monitoring, brain MRI according to the epileptological protocol. Various tactics of surgical intervention were used.

Results: The patients were divided into 4 groups, according to ESubCoG and MRI results. 1) Patients with both hippocampal sclerosis and epileptiform activity in mesiobasal structures. 2) Patients with hippocampal sclerosis and without epileptiform activity. 3) Patients without MR-signs of hippocampal sclerosis and with epileptiform activity. 4) Patients without both structural changes in hippocampus and epileptiform activity. This retrospective study revealed no correlation between structural changes in hippocampus and epileptiform activity according to electro subcorticography (Chi square=0.016).

Conclusion: The hippocampal sclerosis is not always associated with generation of epileptiform activity.

Disclosure: Nothing to disclose

EPO2091

Electrophysiological characteristics and anatomical differentiation of epileptic and non-epileptic myoclonus.

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Background and aims: This study was conducted on a series of patients with myoclonus to identify the electrophysiological characteristics and the anatomical classification of myoclonus of different causes.

Methods: The current study included 50 patients with different types of myoclonus in comparison to 30 control subjects. Electrophysiological study was done for all patients by Somatosensory Evoked Potential (SSEP) and Electroencephalography (EEG) while the control group underwent SSEP. SSEP was studied in the patients and control group by stimulation of right and left median nerves

Results: This study included 50 patients with myoclonus of different etiologies with average age 39.30±15.73 and consisted of 23 male and 27 female patients. 29 (58%) of the patients were epileptics, while 21 (42%) were non-epileptics. Patients were classified anatomically into 31 patients with cortical myoclonus (62%), 8 patients with subcortical myoclonus (16%) and 11 patients with cortical-subcortical myoclonus (22%). There were significant statistical differences regarding P24 amplitude, N33 amplitude, P24-N33 peak to peak complex amplitude, with no significant difference in N20 amplitude, N20, P24, N33 latencies regarding all types of myoclonus. PME showed marked giant response, JME showed no enhancement in comparison to controls, secondary myoclonus showed giant response but of less values than PME in comparison to controls.

Conclusion: We concluded that myoclonus is a symptom of different origins. Electrophysiological testing is an important tool in the diagnosis and anatomical classification of myoclonus may help in decision-making regarding therapeutic management.

Disclosure: Nothing to disclose

EPO2092

An examination of EEG findings and associated demographic, radiological, and clinical variables among patients following a first clinical seizure

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Background: Epilepsy has a national prevalence rate of 10 per 1,000 people In Ireland, EEG is an essential tool used to diagnose seizure activity.

Aim: To examine the outcomes of EEG analyses following the 1st clinical seizure and the effects of time to the study, together with clinical, demographic and radiological variables.

Methods: This study examined EEG outcomes among 51 patients presenting to the neurophysiology department at Cork University Hospital following a 1st clinical seizure between January and May 2019 and investigated the effect of time-to follow-up and other demographic, clinical and radiological variables on the presence or absence of abnormal EEG findings in these patients.

Results: 29.4% of these patients were found to have an abnormal study. There was a mean of 7.45 days from seizure onset to EEG analysis. 55% of patients who underwent EEG recordings within 36 hours of seizure onset were found to have an abnormal EEG versus 13% of those who had their EEG between 4 and 10 days of seizure onset and 12.5% of those whose EEG was completed over 10 days later. This relationship between time to EEG completion and outcome was statistically significant ($p=0.006$). Females were also significantly more likely than males to have an abnormal EEG ($p=0.03$; $p=0.033$) at univariate and multivariate analysis.

Conclusion: This data suggests that early EEG recording following a 1st seizure may significantly improve its diagnostic yield, enables early intervention and reduces the risk of seizure recurrence.

Disclosure: Nothing to disclose

EPO2093

Carpal tunnel syndrome (CTS) symptoms correlate with strength duration time constant (SDTC)

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Background and aims: CTS is the most common entrapment neuropathy of the upper extremities, causing pain, paresthesia, numbness, and weakness in the territory corresponding to the median nerve. Although nerve conduction studies have been proposed for the diagnosis, the electrodiagnostic severity of CTS may not be associated with its clinical severity. The Boston Carpal Tunnel Questionnaire (BCTQ) is an easy, brief self-administered tool for assessing symptom severity and functional status in CTS and recently Greek version has been validated. The aim of our study was to correlate BCTQ with electrodiagnostic measurements including nerve axonal excitability.

Methods: BCTQ was administered to 29 consecutive patients referred to our laboratory with symptoms consistent with CTS. All the patients and 19 age matched control subjects underwent motor conduction study and excitability measurements using QTRAC software

Results: Only SDTC, a property of the nodal membrane which increases with demyelination, was found to be strongly correlated with the BCTQ score whereas the latency and amplitude of compound muscle action potential (CMAP) were not. The amplitude of CMAP correlated only with the functional status scale of BCTQ.

Conclusion: The measurement of SDTC may shed light on axonal properties in CTS patients and could constitute a useful, relatively simple technique in clinical practice.

Disclosure: Nothing to disclose

EPO2094

Emotional and personality characteristics of patients in the late recovery period of ischemic stroke

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Background and aims: The aim of the research work was to study the emotional and personal characteristics of patients with ischemic stroke.

Methods: The work was based on the analysis of the results of examination of 120 working patients with ischemic stroke in the middle cerebral artery. The psychological study included the following tests: subjective asthenia rating scale (MFI-20); Toronto Alexithymic Scale (TAS -26).

Results: The dominant types of asthenia (in decreasing order) are physical asthenia, decreased activity, general asthenia, decreased motivation, mental asthenia. It was found that all the examined patients had alexithymic features. It is noteworthy that in patients with speech impairment, the TAS score is significantly higher than in patients with pyramidal symptoms -80.3 ± 4.0 (severe alexithymia) and 68.25 ± 7.13 points (borderline level), respectively. Moreover, in men with speech disorders, this indicator is 81.8 ± 1.92 points (pronounced alexithymia), while in women it is 65.5 ± 6.4 points (borderline level). A direct strong correlation was also found between the level of anxiety, depression and the level of alexithymia ($r=1.0$).

Conclusion: For cerebral infarction of both left- and right-hemisphere localization, the occurrence of not only focal neurological, emotional-volitional disorders, but also an increase in the level of alexithymia, which in turn depends on neurological deficit, is characteristic (higher in patients with speech disorders) and the patient's gender (higher in men). The presence of severe alexithymia in patients with cerebral infarction leads to impaired adequate self-assessment of the physical and mental state, which may complicate the rehabilitation of these patients.

Disclosure: Nothing to disclose

EPO2095

Electrophysiological correlates of pyramidal signs and clinical motor status: a "real world" TMS study

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Background and aims: Few non-recent evidences on the transcranial magnetic stimulation (TMS) correlates of pyramidal signs and clinical motor status were reported. We assessed motor evoked potentials (MEPs) in patients with pyramidal signs and motor deficit compared to those with pyramidal signs without clinical weakness.

Methods: 43 patients with cervical spondylotic myelopathy were dichotomized in 21 with pyramidal signs and mild motor deficit (Group 1) and 22 with pyramidal signs and normal strength (Group 2), both compared with 33 healthy controls (Group 0). MEPs were recorded through a circular coil on the "hot spot" of the 1st Dorsal Interosseous and Tibialis Anterior (TA) muscle, bilaterally. Central motor conduction time (CMCT) was estimated as the difference between MEP cortical latency and peripheral motor latency by magnetic stimulation. Peak-to-peak MEP amplitude and right-to-left differences were also measured.

Results: The 3 groups were matched for age, sex, and height. MEP latency at 4 limbs and CMCT at lower limbs were significantly prolonged in Group 1 with respect to the other 2. Compared to the same groups, MEP amplitude from TA bilaterally was significantly decreased in Group 1 (Table 1 and 2). Unlike motor deficit, pyramidal signs were not significantly and independently associated with any TMS measure, also when age, sex, and height were considered as confounding factors (Table 3).

Table 1. Demographic features and TMS variables of the three groups.

Variable, unit	Group 0 (n = 33)	Group 1 (n = 21)	Group 2 (n = 22)	p value	Post hoc analysis
					Difference p value
Age, years	54.00 (32.50)	57.00 (14.00)	49.50 (21.80)	0.250*	NS NS
Sex, male (%)	18.00 (54.50)	14.00 (66.70)	8.00 (36.40)	0.130†	NS NS
female (%)	15.00 (45.50)	7.00 (33.30)	14.00 (63.60)		
Height, cm	163.00 (7.80)	165.00 (10.50)	163.00 (7.80)	0.260*	NS NS
Right FDI Amplitude, mV	7.80 (4.10)	7.80 (6.80)	7.75 (5.90)	0.860*	NS NS
Right FDI Latency, ms	20.10 (1.90)	21.20 (2.60)	18.75 (2.60)	<0.001*	2 vs 1 0.024 0 vs 1 0.001
Right FDI CMCT, ms	6.40 (1.80)	6.70 (3.10)	5.90 (1.80)	0.180*	NS NS
Left FDI Amplitude, mV	7.50 (3.80)	6.80 (5.10)	8.25 (4.70)	0.170*	NS NS
Left FDI Latency, ms	19.80 (1.70)	21.60 (2.10)	18.50 (1.70)	0.010*	2 vs 1 <0.001
Left FDI CMCT, ms	6.20 (0.90)	6.80 (2.80)	6.05 (1.20)	0.390*	NS NS
Right TA Amplitude, mV	5.20 (3.40)	3.00 (2.60)	5.15 (3.30)	0.004*	1 vs 2 0.029 1 vs 0 0.004 2 vs 1 0.001
Right TA Latency, ms	27.20 (2.70)	34.50 (13.60)	25.65 (3.00)	<0.001*	2 vs 1 0.001 0 vs 1 <0.001
Right TA CMCT, ms	14.40 (2.00)	20.50 (10.20)	13.95 (3.20)	<0.001*	2 vs 1 0.001 0 vs 1 0.001
Left TA Amplitude, mV	4.60 (2.70)	2.90 (3.20)	5.00 (3.60)	0.005*	1 vs 2 0.023 1 vs 0 0.006 2 vs 1 0.001
Left TA Latency, ms	27.40 (3.40)	34.00 (13.00)	25.45 (2.40)	<0.001*	2 vs 1 0.001 0 vs 1 <0.001
Left TA CMCT, ms	14.00 (2.50)	20.70 (12.60)	13.70 (2.60)	<0.001*	2 vs 1 0.001 0 vs 1 <0.001

Legend: values are expressed as median and interquartile range; n = number of subjects; FDI = First Dorsal Interosseous muscle; TA = Tibialis Anterior muscle; CMCT = central motor conduction time; NS = not significant; * = Kruskal-Wallis test; † = Chi-Square test; numbers in bold = statistically significant p values.

Table 1

Table 2. Intra-group analysis of TMS variables (right vs. left) of the three groups (Mann-Whitney test).

Variable, unit	Group 0 (n = 33), p	Group 1 (n = 21), p	Group 2 (n = 22), p
FDI Amplitude, mV	0.91	0.20	0.75
FDI Latency, ms	0.67	0.73	0.78
FDI CMCT, ms	0.39	0.96	0.95
TA Amplitude, mV	0.56	0.75	0.83
TA Latency, ms	0.95	1.00	0.69
TA CMCT, ms	0.81	0.74	0.73

Legend: n = number of subjects; FDI = First Dorsal Interosseous muscle; TA = Tibialis Anterior muscle; CMCT = central motor conduction time.

Table 2

Table 3. Predictors of TMS parameters: (A) Linear regression analysis; (B) Multiple linear regression analysis.

(A) Dependent variable	Predictor	Std beta	p	Adjusted R2
Right FDI MEP Amplitude	Pyramidal signs	-0.04	0.770	0.02
	Motor deficit	-0.05	0.690	
Right FDI MEP Latency	Pyramidal signs	-0.18	0.130	0.21
	Motor deficit	0.56	<0.001	
Right FDI CMCT	Pyramidal signs	-0.07	0.550	0.10
	Motor deficit	0.39	0.003	
Left FDI MEP Amplitude	Pyramidal signs	-0.06	0.630	0.32
	Motor deficit	-0.19	0.146	
Left FDI MEP Latency	Pyramidal signs	-0.16	0.199	0.18
	Motor deficit	0.51	<0.001	
Left FDI CMCT	Pyramidal signs	0.56	0.741	0.10
	Motor deficit	0.62	0.005	
Right TA MEP Amplitude	Pyramidal signs	-0.06	0.610	0.10
	Motor deficit	-0.32	0.015	
Right TA MEP Latency	Pyramidal signs	-0.06	0.530	0.37
	Motor deficit	0.65	<0.001	
Right TA CMCT	Pyramidal signs	0.02	0.850	0.30
	Motor deficit	0.58	<0.001	
Left TA MEP Amplitude	Pyramidal signs	0.35	0.790	0.09
	Motor deficit	-0.38	0.006	
Left TA MEP Latency	Pyramidal signs	-0.04	0.670	0.34
	Motor deficit	0.63	<0.001	
Left TA CMCT	Pyramidal signs	0.006	0.959	0.30
	Motor deficit	0.56	<0.001	

(B) Dependent variable	Predictor	Std beta	p	Adjusted R2
Right FDI MEP Amplitude	Age	-0.26	0.040	0.07
Right FDI MEP Latency	Motor deficit	0.50	<0.001	0.22
Right FDI CMCT	Motor deficit	0.41	0.003	0.07
Left FDI MEP Amplitude	Motor deficit	-0.23	0.090	0.10
	Age	-0.23	0.050	
Left FDI MEP Latency	Motor deficit	0.43	0.001	0.21
Left FDI CMCT	Motor deficit	0.40	0.004	0.08
Right TA MEP Amplitude	Sex	-0.32	0.017	0.18
	Motor deficit	-0.37	0.005	
Right TA MEP Latency	Motor deficit	0.66	<0.001	0.39
	Sex	0.23	0.042	
Right TA CMCT	Motor deficit	0.61	<0.001	0.31
Left TA MEP Amplitude	Motor deficit	-0.38	0.006	0.12
Left TA MEP Latency	Motor deficit	0.63	<0.001	0.36
Left TA CMCT	Motor deficit	0.58	<0.001	0.30

Legend: FDI = First Dorsal Interosseous muscle; TA = Tibialis Anterior muscle; MEP = motor evoked potential; CMCT = central motor conduction time; numbers in bold = statistically significant p values.

Table 3

Conclusion: in a “real world” clinical environment, routine MEPs represent an accurate diagnostic test in cervical spondylotic myelopathy patients with even mild motor deficit, whereas clinically isolated pyramidal signs may not be associated, at this stage, with gross TMS changes.

Disclosure: Nothing to disclose

EPO2097

Connectivity features of the epileptic systems for multi-focal pharmaco-resistant epilepsy

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Background and aims: connectivity features of the epileptic systems for multi-focal pharmaco-resistant epilepsy in surgical treatment

Methods: Analysis of the results of examinations and surgical treatments of 117 patients between 2015 and 2018. All patients underwent video-EEG monitoring to determine the epileptogenic zone. 2 or more synchronous and asynchronous foci of epileptiform activity were recorded in 39 patients, in 2 cases with a clinically pharmaco-resistant form of epilepsy, but no reliable data on epileptiform activity was received. For the localization of the epileptogenic zone it was decided to carry out a 2-stage surgical treatment.

Results: 5 patients were diagnosed with multi-focal epilepsy. 5 other patients had recorded activity generation in the deep structures of the temporal lobe, as a result of which a decision was made regarding the stereotactic destruction of the amygdalo-hippocampal complex. The remaining patients underwent surgical treatment with resection of the epileptogenic zone. The outcomes of surgical treatment 2 years after surgery: out of the 5 patients who underwent stereotactic destruction of the amygdalo-hippocampal complex in 2 cases diagnosed En (Engel) 1. Out of the 31 patients En 1 and En 2 were diagnosed in 12 patients, 3 patients had no data stated, 1 patient died, 2 patients cannot provide reliable information about availability of seizures, in 13 patients - En 3 and En 4.

Conclusion: With surgical treatment of pharmaco-resistant epilepsy in the presence of several foci of epileptiform activity, the removal of the leading foci does not always lead to the elimination of seizures.

Disclosure: Nothing to disclose

EPO2098

Correlation of pattern reversal and flash visual evoked potentials with optical coherence tomography in patients with optic neuropathy and patients with multiple sclerosis without optic neuropathy.

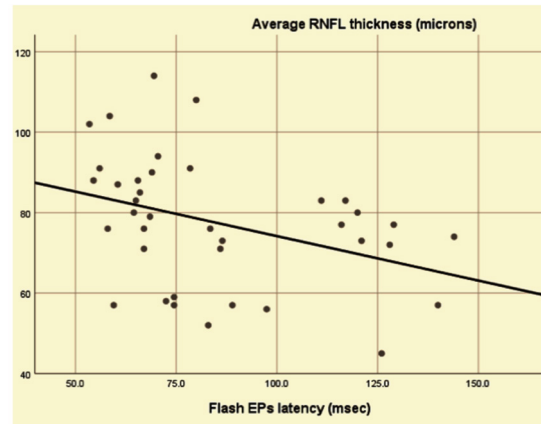
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Background and aims: This study aims at correlating the physiological and structural variables between the visual evoked potential latencies and retinal layer thickness in eyes with optic neuropathy and multiple sclerosis.

Methods: We studied the pattern reversal VEP (PRVEP), flash VEP (fVEP), and optical coherence tomography (OCT) in 42 eyes with optic neuropathy (ON), 28 eyes of patients with multiple sclerosis without ON (MS-nonON), and 34 normal eyes. We correlated the P100 latency of PRVEP, P1 of fVEP, and the peripapillary nerve fiber layer thickness (pRNFL) and ganglion cell inner plexiform layer thickness (GCIPL) of OCT in all subjects.

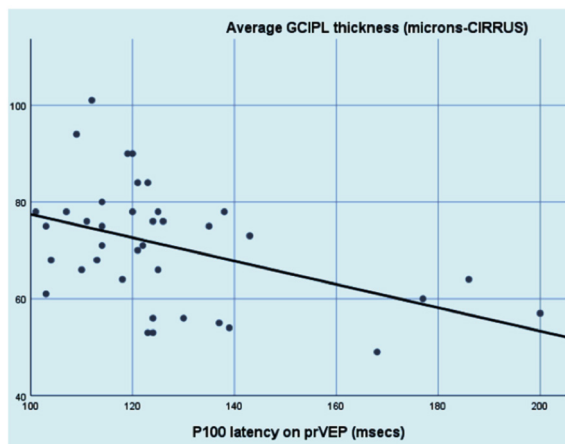
Results: The mean P100 PRVEP latency is delayed in patients with ON compared to controls and patients with MS-nonON ($p < 0.0001$). The mean fVEP latency is delayed in patients with ON compared to controls ($p < 0.0001$), but not compared to patients with MS-nonON ($p = 0.998$). The mean pRNFL and mean GCIPL thickness are thinner in patients with ON compared to controls and patients with MS-nonON ($p = 0.036$ and $p = 0.001$). fVEP correlated negatively with pRNFL thickness ($p = 0.023$), but not with GCIPL thickness in ON. Conversely, PRVEP didn't correlate with pRNFL thickness, but correlated negatively with GCIPL thickness in ON ($p = 0.006$). fVEP and PRVEP did not correlate with pRNFL or GCIPL in MS-nonON or controls.



Correlation of RNFL thickness with flash VEP latencies in optic neuropathy

Conclusion: In eyes with ON, VEPs are delayed and OCT measures are decreased in comparison to MS-nonON eyes. fVEP correlated with pRNFL thinning, while PRVEP correlated with GCIPL thinning. Thus, delayed PRVEP indicates pathology in the ganglion cell layer while delayed fVEP reflects pathology in the retinal fiber layer.

Disclosure: Nothing to disclose



Correlation of GCIPL thickness with PRVEP latencies in optic neuropathy.

EPO2099

Median SEP in acute internal carotid occlusion as predictor of clinical outcome after surgical recanalization.

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Background and aims: Emergent internal carotid artery (ICA) desobiteration is a feasible procedure, after unsuccessful endovascular treatment (EVT) after acute ischaemic stroke (AIS).

We aimed to evaluate the direct neuronal activity of rolandic cortex as a predictor of clinical outcome.

Methods: Prospective enrollment from 05/2013 to 8/2019. Including criteria: AIS<24 hours from onset, extracranial ICA occlusion not feasible for EVT. Excluding: any contraindication to surgical treatment, pre-stroke disability (mRS>2). Median somatosensory evoked potentials (SEP) were obtained bilaterally before surgery. Absolute N20/P25 amplitude (SEP-amp) and side-to-side ratio (SEP-ratio) were evaluated. Abnormal cutoff values for SEP-amp and SEP-ratio were <0.8uV and <0.5 respectively. Clinical performance mRS was evaluated 3 months after stroke.

Results: Cohort consisted of 27 patients (25 males (92.6%)) aged from 52 to 88 years, mean 71.3±8.3, median NIHSS 5, interquartile range (4-14). After 3 months functionally independent (mRS 0-2) were 23 (85.2%), remaining 4 were mRS 5-6. Abnormal SEP-amp and SEP ratio were in 5 (18.5%) and 4 (14.8%) cases respectively. Abnormal SEP values were statistically significant SEP-amp: p=0.004, SEP-ratio: p=0.002. None with favourable outcome had abnormal SEP-ratio and vice versa.

Conclusion: Direct evidence of neuronal survival in the rolandic cortex in the median SEP seems to be a highly reliable predictor of clinical outcome.

Disclosure: Nothing to disclose

EPO2100

Diagnostic Criteria of Nonconvulsive Status Epilepticus depend on the duration of the patient's unconscious state

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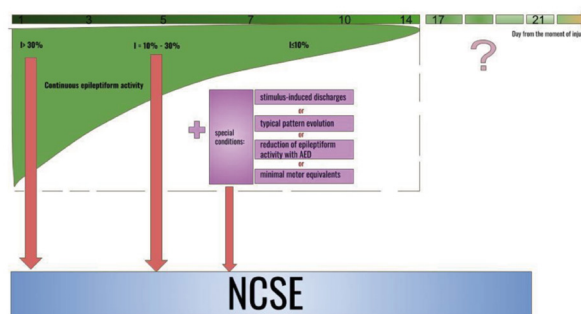
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Background and aims: Non-Convulsive Status Epilepticus (NCSE) is 1 of the variants of a prolonged unconscious state, associated with continuous epileptiform activity on EEG, but without major motor signs. The NCSE complicates the course of severe brain injury and worsens the prognosis for the patient. The existing "Salzburg criteria" are considering clinical and electrophysiological indicators apart from the duration of unconsciousness.

Methods: A total of 31 patients with NCSE in severe traumatic brain injury aged 20 to 65 years were examined. EEG registration was carried out on the "Mitsar-EEG-202" complex (LTD "Mitsar", Russian Federation). EEG was performed dynamically at different times from the moment of injury.

Results: In those patients who were examined upon 1-4 days from the moment of brain injury, the index of epileptiform activity ranged from 30 to 60%.

For those to whom EEG was performed after 5-10 days, epileptiform activity was registered with an index from 10% to 30%. On EEG performed on days 11-15, epileptiform activity was present with an index of at least 10%.



Modified diagnostic criteria of Non-convulsive status epilepticus

Conclusion: The criteria for diagnosing of non-convulsive status epilepticus depend on the duration of the patient's unconscious state since the restoration of brain stem functioning, and also depend on the time elapsed since the moment of brain injury.

Disclosure: Nothing to disclose

EPO2101

Dropped Head Syndrome: a clinical and electrophysiological study in six patients

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Background and aims: Dropped head syndrome (DHS) is a rare neurological condition that can be caused by several neuromuscular disorders. The aim of our study is to describe the clinical and electrophysiological characteristics and the underlying etiology in a series of consecutive patients with DHS.

Methods: From 2016 to 2019, patients presenting to our neurophysiology unit with DHS were included. Medical history, neurological examination, and electrophysiological investigation and the neostigmine test results were described. The etiological diagnosis of DHS was also specified.

Results: 6 patients were included (mean age=68years, sex ratio=2). The mean diagnostic delay was 4.8 months. All the patients reported symptoms fluctuation in time. Neurological examination showed a motor deficit of neck extensor muscles in all cases and half of them presented with proximal weakness of the upper limbs and/or bulbar muscle deficit. Nerve conduction studies were normal in all patients and needle EMG showed a neurogenic pattern in 4 patients and pseudo-myogenic patterns in 1 patient. Repetitive stimulation revealed a decremental response in all patients. The neostigmine test was positive in 3 patients. Final diagnoses were myasthenia gravis (3 patients, 2 with anti-acetylcholine receptors antibodies and 1 with anti-Musk antibodies), amyotrophic lateral sclerosis (2 patients) and type 4 Spinal muscular atrophy (one patient).

Conclusion: Accurate etiological diagnosis of DHS requires a thorough clinical and electrophysiological assessment and use of neostigmine test. Our series helped us advancing a diagnostic algorithm of DHS.

Disclosure: Nothing to disclose

EPO2102

Nerve conduction and Vitamin B12 alteration in Type 2 diabetics on metformin

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Introduction: Metformin, an oral hypoglycemic agent is the 1st line treatment in patients with T2DM, as approved by US Food and Drug Administration (FDA) in 1994. However, the use of metformin is associated with malabsorption of vitamin B12, which may lead to detrimental effects on peripheral nerves. Our study aimed to compare the peripheral nerve conduction study (NCS) parameters with serum vitamin B12 levels in T2DM (on metformin and non- metformin therapy) and control.

Methods: This comparative cross-sectional study enrolled type 2 diabetic patients on metformin therapy for more than 6 months (Group A, n=30), type 2 diabetics on non-metformin therapy (Group B, n=11) and healthy controls (Group C, n=30). NCS parameters of median, tibial, common peroneal & sural nerves, serum glucose and serum vitamin B12 levels were measured. One way ANOVA (post hoc: Tukey) test was used to compare the variables using SPSS. 22.0.

Results: Group A had reduced vitamin B12 levels as compared to Group B [194.03 (164.86-223.53) vs. 297.82 (258.99-363.00), p=0.001] and Group C [194.03 (164.86-223.53) vs. 287.50 (204.25-351.50), p=0.001]. NCS parameters of median, tibial and sural nerves showed more demyelinating type effects in Group A. Motor and sensory nerve latencies as well as amplitudes were significantly longer and lower respectively in Group A.

Conclusion: Long term metformin therapy in diabetic is associated with significant vitamin B12 depletion, leading to alteration in motor and sensory NCS parameters. Thus we recommend regular vitamin B12 screening and oral or parenteral vitamin B12 supplementation to the diabetic on metformin therapy.

Disclosure: Nothing to disclose

EPO2103

Surface Electromyography as a Tool for Evaluation of the Association Between m.Masseter and m.Temporalis Activity and the Variables of Craniofacial Morphology

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Background and aims: The function of the masticatory muscle has a considerable influence on craniofacial morphology. And craniofacial morphology is related with biting force and resting activity of the masticatory muscles. The knowledge of surface electromyography (sEMG) and the rapid growth of the numbers of applications underlines the high potential of this technique. The aim of the study was to evaluate the correlation between vertical facial patterns, cephalometric indices and EMG activity of the masticatory muscles.

Methods: 3 groups of patients were included in the study. Group 1e (N=15) consisted of hypodivergent type patients; group 2 (N=22) consisted of normodivergent type and group 3 (N=24) - hyperdivergent type patients. The age of the patients is between 14 to 23 years old. All the patients have lateral cephalometry, study models and EMG evaluation of the anterior m. temporalis and m. masseter at rest and during maximal voluntary clench. Statistical analysis was performed by SPSS 10.0

Results: The study found statistically significant differences between the 3 groups in the activity of m.Masseter dex. (p<0.05). The significant difference between the 1st and 2nd group was detected in the absolute value average of m.Temporalis activity.

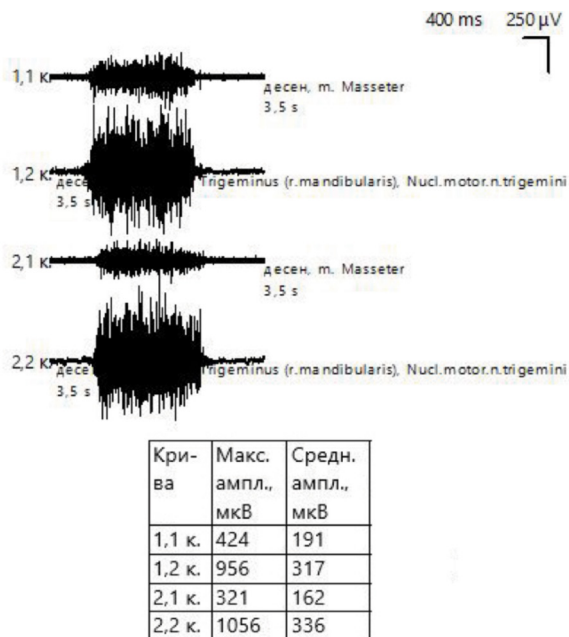


Fig.1: EMG activity during maximal dental clenching from Masseter and Temporalis muscle.

Conclusion: This study underlines the high potential of sEMG as a useful, non-invasive tool for the assessment of the activity of the masticatory muscles and to evaluate the effect of therapeutic resources in neurologic and orthodontic practice. Further studies on a larger group of patients will better clarify the interrelations between the cephalometric variables and EMG activity.

Disclosure: Nothing to disclose

EPO2104

The correlation between EEG and prognosis in patients treated with ECMO

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Background and aims: Early prediction of prognosis in the patients receiving treatment using extracorporeal membrane oxygenation (ECMO) is difficult. Electroencephalography (EEG) is widely used to evaluate neurological outcomes. The purpose of this study is to identify the reliable factors for predicting the neurological prognosis using a single routine EEG performed within 48 hours after ECMO initiation.

Methods: Routine EEG was performed within 48 hours after ECMO initiation in patients treated with ECMO and was interpreted according to the standardized EEG-terminology proposed by the American Clinical Neurophysiology Society. EEGs were classified into highly malignant (suppression, suppression with periodic discharges, burst-suppression), malignant (periodic or rhythmic patterns, pathological or nonreactive background), and benign EEG (absence of malignant features). Poor outcome was defined as best Cerebral Performance Category score 3–5.

Results: A total 18 patients were included. The median time from ECMO initiation to EEG was 1189.5 minutes. Five patients had a highly malignant EEG and all had a poor outcome (specificity 100%, sensitivity 50%). Any malignant EEG pattern had a low sensitivity (40%) and low specificity (37.5%) to predict poor prognosis. 4 patients had a benign pattern, 3 of whom had good prognosis.

Conclusion: Highly malignant EEG which conducted ECMO initiation reliably predicted poor outcome in half of patients without false predictions. This is significant because the specificity is very high even though the EEG was performed within 48 hours. The results of this study may help predict poor prognosis early in the course of treatment in patients treated with ECMO.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 1

EPO2105

Cambridge Automated Neuropsychological Test Battery (CANTAB) in midlife adults: Cognitive Performance and Neuroimaging

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Background and aims: The aim of the study is to investigate the cognitive performance of middle-aged adults that have some MRI or Doppler sonography findings.

Methods: We examined 98 healthy adults (38 men and 60 women) with normal daily functioning between the ages of 45-55 years (mean age 50.37 ± 3.24). The subjects were selected according to the authors' inclusion criteria. After testing with the computer neuropsychological system CANTAB Eclipse participants went through MRI and Doppler sonography examination. A comparison between groups with and without findings from MRI or Doppler Sonography was conducted according to results from the CANTAB (statistical product SPSS 17).

Results: Our study found that participants without Doppler Sonography pathological findings show better result than those with Doppler Sonography findings in relation to the CANTAB subtest outcome measure SOC (Stockings of Cambridge) - mean initial thinking time 5 moves ($p < 0.05$). There was no statistically significant difference between groups with and without findings from MRI.

Conclusion: Established results demonstrate that the CANTAB outcome measure of subtest SOC suppose the presence of "asymptomatic" neuroimaging findings. Our study underlines the importance of computerized neuropsychological methods for screening cognitive impairment due to subclinical cerebrovascular disease in the middle adulthood.

Disclosure: This study was supported by the University Grant Project NO 13/2014, Medical University, Plovdiv, Bulgaria.

EPO2106

The Brief Evaluation of Receptive Aphasia test for the detection of language impairment in severely brain-injured patients

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Background and aims: The presence of language deficits may lead to an underestimation of consciousness level in brain-injured patients. At the same time, the assessment of language in patients with disorders of consciousness (DoC) is prevented by their limited behavioral responses. We present a new language comprehension assessment tool based on visual fixation of images for DoC patients.

Methods: The Brief Evaluation of Receptive Aphasia (BERA) assesses receptive phonological, semantic and morphosyntactic abilities. The BERA as well as the Language Screening Test (LAST) were 1st administered to 52 aphasic conscious (AC) patients on 2 consecutive days in order to determine its validity and reliability. Next, this new tool was administered to 4 post-comatose patients, who were also examined by means of the Coma Recovery Scale-Revised (CRS-R), positron emission tomography and structural magnetic resonance imaging.

Results: In AC patients, the BERA showed satisfactory intra- and inter-rater reliability, internal and concurrent validity with the LAST. In DoC patients, the BERA scores suggested the presence of selective receptive difficulties for phonological, semantic and particularly morphosyntactic abilities. These results were in line with their functional and structural neuroimaging data.

Conclusion: The BERA may complement the widely used CRS-R when assessing and diagnosing DoC patients by providing a more systematic and detailed characterization of language abilities in these severely brain-injured patients.

Disclosure: Nothing to disclose

EPO2107

Autoimmune encephalitis associated with anti adenylate kinase 5 (Anti-AK5) antibodies manifesting as subacute semantic and episodic memory loss : a case report

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Background and aims: To present a patient with anti-AK5 autoimmune encephalitis admitted for subacute memory disorders associating episodic and semantic involvements and to compare this case with others in literature

Methods: We report the case of a 64-year-old man admitted for a few weeks progressing memory disorder associated with asthenia and anorexia. There were no history of seizure, abnormal behavior or psychiatric signs. Brain magnetic resonance image (MRI, figure 1) showed bilateral temporal lobe FLAIR (Fluid Attenuated Inversion Recovery) hypersignal. Cerebrospinal fluid (CSF) showed a moderate pleocytosis (15 cells per mm³) with high protein level (0.67g/L). Electroencephalography (EEG) was normal. Neuropsychological tests found memory disorders with episodic disorders depicted as very low score at free recalls with no normalization of cued recalls and semantic disorders, depicted with semantic paraphasia on oral naming test, low score on word definitions, reversal scores on phonemic and semantic verbal fluences (Table 1). Anti-AK5 were found in the CSF. Despite intensive treatment regimen associating RITUXIMAB and CYCLOPHOSPHAMIDE, clinical prognosis remained poor and MRI evolved towards hippocampal atrophy.

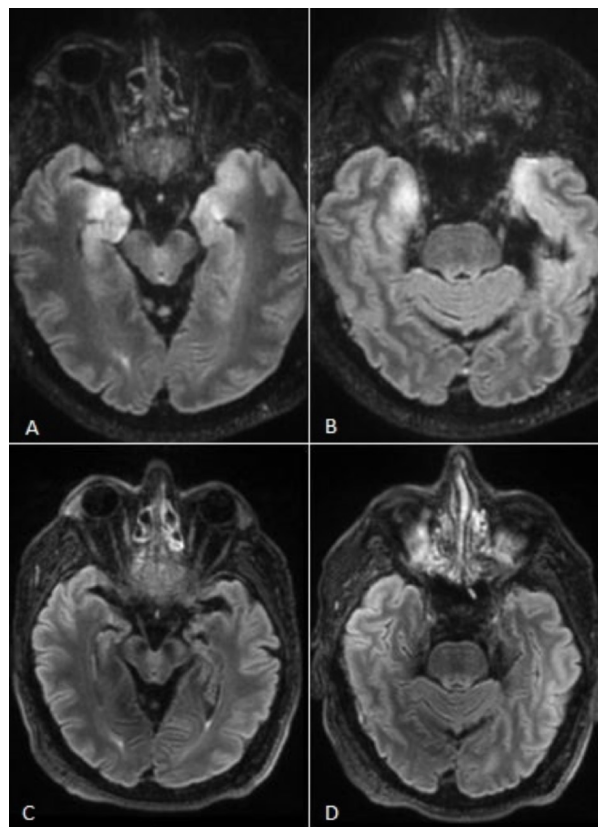


Figure 1 : Axial FLAIR MRI Sequences. At the diagnosis, bilateral temporal hypersignal (A,B). After one year of immunotherapy, bilateral temporal atrophy but no abnormal signal (C,D)

Results: We describe here a clear semantic involvement in limbic encephalitis associated with anti-AK5 antibodies. As previously reported, episodic memory loss, MRI and CSF abnormalities, poor prognosis were also found.

Conclusion: We present a case of autoimmune encephalitis associated with anti-AK5 antibodies with unexpected semantic involvement. This rare diagnosis should not be ignored in patients with subacute memory disorders, MRI abnormalities in temporal lobes especially if there is not history of seizure.

Disclosure: Nothing to disclose

		At the diagnosis	At 6 months
Global cognitive test	Mini Mental State Examination	26/30	24/30
Attention/Working Memory	Spatial span forward	6	-
	Digit span forward	7	-
Executive function	Verbal Fluency Test	Animals	15
		Phonemic Fluency (« P »)	18
	Trail Making Test	A (seconds)	25
		B (seconds)	54
	B (errors)	0	
	B-A (seconds)	29	
Verbal episodic memory Free and cued recall test 16-items	Immediate cued recall		13/16
		Free recall 1	1
		Free recall 2	0
		Free recall 3	NA
		Total free recall	1
		Total recall 1	1
	Total recall 2	1	
	Total recall 3	NA	
	Total recall	2	
Rey Complex Figure Test	Copy (36)	36	36 (Rey/Taylor)
	Delayed recall (36)	4	-
a	BECS-GRECO Semantic Battery	Oral Naming test (40)	39
		Semantic paraphasia	5
		Phonemic paraphasia	0
		Word definition (4)	3
		Denomination 80 : 77/80	-

Table 1 : Neuropsychological test at the diagnosis and after 6 months of treatment (NA : Not Answered)

EPO2108

TMA-93 (Binding by images): Normative data from elderly spanish people

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Background and aims: The Memory Associative Test of the district of Seine-Saint-Denis (TMA-93), a new test of episodic memory, examines binding (associative learning) by images, an advantage for the less-educated. The aim was to extend the Spanish normative study for the test to people aged 75 and over.

Methods: A cross-sectional normative study. Partners of patients who attended the Outpatient Clinic were systematically recruited if they are eligible: age \geq 75, no memory complaints, and a total score \geq 10th percentile on Phototest. Age (4 ranges: 75-77, 78-80, 81-83, \geq 84 years), gender, and educational attainment (incomplete primary studies, only primary studies completed, and higher than primary studies) were considered as sociodemographic variables. TMA-93 was administered and the total score was registered. A stratified analysis by sociodemographic variables with significant influence on total TMA-93 score was undertaken.

Results: 354 participants were included (age=78.7 \pm 3.4 years, range=75-93; 44.6 % females; 39%, incomplete primary studies). Total score on TMA-93 showed a non-normal, left asymmetric, and leptokurtic distribution (median=28, IQR=24-30, range=5-30). There were significant differences on TMA-93 total scores only by educational attainment (p<0,001). Scores for 10th percentile varied from 19 out of 30 in the less-educated group to 24 out of 30 in the more-educated group.

Conclusion: This extension of the Spanish normative study for the TMA-93 shows that binding in Spanish elders mainly depends on the educational attainment.

Disclosure: This work was supported by Hoffmann-La Roche.

EPO2109

The assessment of cognitive disorders post stroke at Romanian elderly - pilot study

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Background and aims: The incidence of stroke varies from country to country. In Romania, there are approximately 300 new cases/100,000 inhabitants, compared to a European average of almost 200 strokes/100,000 inhabitants. 20% of those who survive have a continuous cognitive deterioration. Prevalence of dementia highest in months following stroke (3%/year) being bigger than without stroke. Age, education or cardiovascular factors can be risk post-stroke cognitive impairment

Methods: 1 year retrospective study in 220 in-patients after 6 months from stroke; 64% men; mean age 70.58y \pm 10.504, from Sf. Luca Geriatrics Hospital, Bucharest. We assessed: incidence of stroke by age, education; incidence of vascular factors (hypertension, atrial fibrillation, previous stroke, diabetes mellitus, dyslipidemia); functional capacity using the standardized daily instrumental activity (IADL) scale; cognitive disorder using standardized Mini-Mental State Examination (MMSE) and Geriatric Depression (GDS) Scales. Descriptive analysis by SPSS 12 statistical tools.

Results: 90.90% had high degree of disability by IADLscale; 82% have moderate cognitive dysfunction by MMSE (10-20 points); 84% have depressive disorder by GDS (7-15 points). Relationship of risk post-stroke cognitive impairment by age: 74.54% patients were in old age group (76-85y) (p<0.003), from which 61% are men; education: 59% of patients had elementary studies (p<0.005); vascular factors: recurrent stroke (31.81%) (p<0.001), hypertension and dyslipidemia (22.72%) (p<0.006), atrial fibrillation (15.90%) (p<0.001), diabetes mellitus (9.09%) (p<0.124).

Conclusion: The most vulnerable patients for dementia post stroke are elderly more 75 years old, men prevalent, with low level of education and with several vascular risk factors. A management of cognitive disorders post stroke is focused on prevention: cognitive training and monitoring risk factors. Brain reserve can protect against cognitive deterioration by leisure activities, social interactions and education, before early 60th ages.

Disclosure: Nothing to disclose

EPO2110

Memory self-appraisal and cognitive outcomes in a memory clinic sample

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Background and aims: Subjective cognitive decline (SCD) and mild cognitive impairment (MCI) are early indicators of neurodegeneration. The feeling of worse performance than others correlates with amyloid deposition. We evaluated if SCD and MCI patients referring worse performance than others (SCD+ and MCI+) had more conversion to dementia.

Methods: Retrospective study including patients with memory complaints without impaired activities of daily living and with follow-up >6 months. Objective cognitive impairment was defined as a score <1.5SD for age and education in Addenbrooke Cognitive Examination (ACE)/MMSE (patients ≤ 1 year of education) and a SCD and MCI group were created. Memory self-appraisal was assessed by the Geriatric Depression Scale (GDS-15) question: “Do you feel you have more memory problems than most?” and, removing this question, a modified GDS cut-off >4 was established.

Results: Of 174 patients, 83 were included. 29 patients (34.9%) had SCD and 54 (65.1%) MCI. SCD+ and MCI+ groups had comparable demographics and cognitive performance at baseline to SCD and MCI, respectively, but were more frequently depressed (71.4% vs 20.0%; 52.6% vs 0). SCD+, but not MCI+, showed higher dementia conversion rate (64.3% vs 26.7%). MCI+ patients had less vascular risk factors (median 2 vs 3). Tables 1 and 2 display further data on SCD+ vs SCD and MCI+ vs MCD groups.

	SCD (n=15)	SCD+ (n=14)	p
Age in years, mean ± SD	76.00±6.98	75.92±7.35	0.832
Male/female gender, n (%)	9/6 (60.0/40.0)	5/9 (35.7/64.3)	0.191
Additional SCD+ features, median (range) ¹	2 (0 – 2)	2 (1 – 2)	1.000
Education in years, median (range)	4 (0 – 16)	4 (4 – 9)	0.780
Number of vascular risk factors, median (range)	3 (0 – 5)	3 (0 – 4)	0.451
ACE-R total score (0-100), mean ± SD	66.93 ± 11.59	70.79 ± 6.86	0.290
ACE-R memory subscore (0-26), mean ± SD	14.50 ± 3.25	13.93 ± 2.52	0.603
MMSE score, mean ± SD	23.86 ± 3.16	23.53 ± 3.60	0.799
Conversion to dementia, n (%)	4 (26.7)	9 (64.3)	0.042*
Time to conversion in months, median (range)	31 (8 - 55)	30.5 (4- 84)	0.940
GDS total score (0-14), median (range)	3 (0 – 11)	6 (2 – 11)	0.014*
GDS>4, n (%)	3 (20.0)	10 (71.4)	0.005*
FBI total score (0-72), median (range)	6 (0 – 35)	8 (0 - 19)	0.224

Table 1. Demographic, clinical and neuropsychological characteristics of patients with SCD and SCD+. Patients were defined as SCD+ if they reported worse memory than most and as SCD otherwise. 1 - Additional features include: age at SCD onset >60 years and cognitive complaints for <5 years. * p< 0.05

	MCI (n=16)	MCI+ (n=38)	p
Age in years, mean ± SD	73.12 ± 6.08	74.15 ± 4.93	0.515
Male/female gender, n (%)	8/8 (50.0/50.0)	15/23 (39.5/60.0)	0.475
Additional SCD+ features, median (range) ¹	2 (0 – 2)	2 (0 – 2)	0.768
Education in years, median (range)	4 (0 – 10)	4 (0 – 16)	0.585
Number of vascular risk factors, median (range)	3 (1 – 4)	2 (1 – 5)	0.038*
ACE-R total score (0-100), mean ± SD	53.20 ± 13.22	52.89 ± 12.11	0.936
ACE-R memory subscore (0-26), mean ± SD	11.93 ± 3.10	10.24 ± 3.55	0.114
MMSE score, mean ± SD	19.06 ± 4.96	19.37 ± 3.69	0.803
Conversion to dementia, n (%)	11 (68.8)	18 (47.4)	0.150
Time to conversion in months, median (range)	19 (18 - 43)	20 (7 - 69)	0.796
GDS total score (0-14), median (range)	1 (0 – 4)	5 (0 – 11)	<0,001*
GDS>4, n (%)	0	20 (52.6%)	<0,001*
FBI total score (0-72), median (range)	9.5 (1 – 25)	7 (0 - 37)	0.181

Table 2. Demographic, clinical and neuropsychological characteristics of patients with MCI and MCI+. Patients were defined as MCI+ if they reported worse memory than most and as MCI otherwise. 1 - Additional features include: age at SCD onset > 60 years and cognitive complaints for <5 years. * p<0.05

Conclusion: Worse memory self-appraisal showed higher dementia conversion in SCD but not MCI, where an opposite trend exists. In both groups, depression was more common in patients with worse self-appraisal, highlighting the complex interplay of mood, subjective and objective cognition.

Disclosure: Nothing to disclose

EPO2111

The Time-Traveler: Post-Surgical Charles Bonnet Syndrome

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Background and aims: Visual hallucinations may arise from various brain disorders, such as migraine, epilepsy, neurodegenerative diseases or cerebrovascular disease. In the vast majority of cases, if visual hallucinations are complex in nature, the parieto-occipital or the temporo-occipital cortical transitions are involved. However, lesions at any point of the optic pathways, causing a partial or complete loss of vision, can induce Charles Bonnet Syndrome (CBS).

Methods: Clinical case study.

Results: A 62-year-old man was admitted to a Neurosurgery Center for elective removal of a right occipital metastasis. After surgery, the patient had complex visual hallucinations limited to the left visual hemifield. When looking at the street he saw old green colored cars, such as Citroën DS, Volkswagen Beetle or Renault 4L, where he knew modern cars of different colors were. In the place of the normal buildings, he saw old brick walled buildings, also green colored. He also saw puddles of water on the floor. The patient had self-criticism, recognizing the unrealistic nature of the hallucinations. Neurological examination showed no visual field defects and partial achromatopsia for blue and green in the left visual hemifield. One month after the surgery, the patient's hallucinations were only of puddles of water on the floor.

Conclusion: CBS exists when complex visual hallucinations arise from visual deficits, and it is characterized by self-criticism of the situation. In this case, the authors assume that given the location of the lesion in the association visual cortex, the patient hallucinates only objects he cannot interpret and colors he cannot see.

Disclosure: Nothing to disclose

EPO2112

Impact of different neuropsychological definitions for cognitive impairment after stroke

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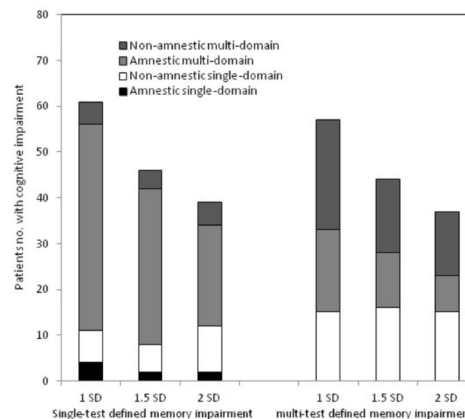
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Background and aims: Based on different neuropsychological definitions, the rate of cognitive impairment after stroke was analyzed, and the cut-offs for cognitive screening scales were investigated.

Methods: Hospital-based stroke patients underwent a comprehensive neuropsychological assessment. The rate of cognitive impairment was estimated using thresholds of 1, 1.5, or 2 standard deviations below the normal control, and impairment of a certain cognitive domain defined by a single or multiple tests. Meanwhile, the effectiveness of cognitive screening through face-to-face assessment using the Mini Mental State Examination (MMSE) and the Montreal Cognitive Assessment Scale (MoCA), and telephone assessment using a 5-min NINDS-Canadian Stroke Network (NINDS-CSN) scale and a 6-item screener (SIS), were both tested under different definitions, with the optimal cut-off selected based on the highest Youden index.

Results: In stroke patients, the rate of cognitive impairment ranged from 46.3% to 76.3% upon different definitions. The face-to-face MoCA was more consistent with comprehensive cognitive assessment compared to MMSE. The optimal cut-off of cognitive impairment was MMSE \leq 27 and MoCA \leq 19. For the telephone tests, the 5-min NINDS-CSN assessment was more reliable, and the optimal cut-off was \leq 23, while for SIS \leq 4.



Number of patients with cognitive impairment according to different neuropsychological definitions

Conclusion: The rate of cognitive impairment in stroke patients can vary by 1.6 times for different neuropsychological definitions. The face-to-face MMSE and MoCA, together with the telephone assessment of NINDS-CSN 5-min protocol and SIS, were simple and effective cognitive screening tools. The corresponding threshold values for cognitive impairment were 27 points, 19 points, 23 points and 4 points.

Disclosure: Nothing to disclose

EPO2113

Perceived cognitive deficits in Wilson’s disease and different types of multiple sclerosis course

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Background and aims: The quality of self-evaluation of cognitive conditions by patients with multiple sclerosis (MS) depends on the disease course and the presence of comorbid conditions, such as depression, fatigue, pain, sleep problems. A determination of the role of these factors in a subjective evaluation of cognitive deficits by patients with MS is still relevant.

Methods: Cognitive functions, levels of fatigue, depression, pain, sleep/wake disturbances, and perceived cognitive deficits were assessed (Figure 1) in 14 patients with relapsing-remitting MS (RRMS), 6 patients with secondary progressive MS (SPMS) and 8 patients with Wilson’s disease (WD).

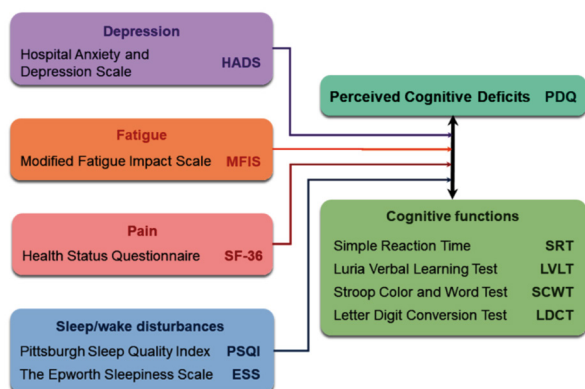


Figure 1. Methods of assessment

Results: Relationships between PDQ score and results of the cognitive tests were not found in patients with RRMS (Figure 2). Patients with WD underestimated their speed of test performance and overestimates their efficiency of performance of these tests. Only patients with SPMS had a subjective evaluation of cognitive functions, which corresponded to an objective one. These patients also showed differences on a level of association of PDQ scores with scores of other scales, beside HADS, which was similar to such in patients with RRRS. Along with this, patients with RRRS and WD, on the contrary, differed only on a level of connection between PDQ and HADS scores.

	MFIS	HADS	PSQI	ESS	SF-36 BP	SRT	LDCT 90	LDCT ES	SCWT IC	LVL
WD	0,62	0,15	0,37	0,73	-0,82	-0,34	-0,02	-0,47	0,65	0,42
RRMS	0,78	0,58	0,41	0,80	-0,40	0,12	0,13	-0,08	0,43	-0,16
SPMS	-0,59	0,55	0,82	0,12	0,14	0,58	-0,87	0,85	-0,44	-0,52

WD – Wilson’s disease; RRMS – relapsing-remitting MS; SPMS – secondary progressive MS; MFIS – Modified Fatigue Impact Scale; HADS – Hospital Anxiety and Depression Scale; PSQI – Pittsburgh Sleep Quality Index; ESS – The Epworth Sleepiness Scale; SF-36 BP – Health Status Questionnaire Bodily Pain Scale; SRT – Simple Reaction Time; LDCT 90 – Letter Digit Conversion Test encoded symbols per 90 seconds; LDCT ES – Letter Digit Conversion Test encoding speed; SCWT IC – Stroop Color and Word Test interference coefficient; LVL – Luria Verbal Learning Test

Figure 2. Heatmap of relationships between Perceived Deficits Questionnaire (PDQ) score and cognitive functions, levels of fatigue, depression, pain and sleep/wake disturbances in WD and different types of MS course

Conclusion: A stability of clinical symptoms progression enabled patients to identify fatigue within a subjective evaluation of their cognitive abilities. In patients with RRMS, the main contributor to discrepancy between subjective and objective evaluation of cognitive functions was a perceived fatigue; daytime sleepiness and the pain level also played their roles.

Disclosure: Nothing to disclose

EPO2114

Proper names anomia after thalamic ischemic lesion

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Background and aims: Proper names anomia is a specific naming impairment and may involve different categories, including people or places. Although the role of thalamus in naming remains poorly understood, it is thought to modulate cortical regions involved in naming.

Methods: We report a case of proper names anomia.

Results: A 51-year-old man, right-handed, was admitted to the emergency department due to sudden loss of consciousness and left hemiparesis 2 hours before. Neurological examination disclosed drowsiness, left central facial palsy, dysarthria, and left hemiplegia (NIHSS 14). CT showed no acute ischemic lesions and angioCT was normal. He was treated with IV-rtPA and neurological improvement was observed (NIHSS 3). Brain-MRI showed bilateral anterior thalamic ischemic lesions and aetiological investigation revealed a patent foramen ovale. During hospitalization, he had cognitive complaints of difficulty in remember recent events. Neuropsychological assessment documented an amnesic syndrome, typically associated with lesions in this topography, but also revealed a severe impairment in retrieving names of famous people. This deficit was present both with visual (photo) and oral (description) presentations. He had no impairment in face recognition, being able to provide information about the people he could not name. Naming was partially facilitated by phonological and semantic cues. The capacity to name other semantic categories, including places, was intact. He had a good clinical improvement, with partial recovery at discharge.

Conclusion: This is a case of specific proper name anomia following an anterior thalamic lesion. Naming deficits improved with phonological and semantic clues, suggesting a putative facilitation of abnormal cortical activation after thalamic lesion.

Disclosure: Nothing to disclose

EPO2115

Rapidly progressive posterior cortical atrophy: a case report

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Background and aims: Posterior cortical atrophy (PCA) is a rare neurodegenerative disorder characterised by progressive impairment of cortical visual function. In most cases, the underlying pathology is Alzheimer's disease. However, other aetiologies are possible, such as prion disease (PCA-prion). We describe a patient with rapidly progressive PCA, with a diagnosis of probable PCA-prion.

Methods: Case report

Results: A 69-year-old female patient presented with a 2-month progressive visuospatial impairment, without significant memory decline. Neuropsychological assessment showed Balint syndrome, visual perception errors (macropsia), visual and tactile agnosia, visual perseveration and dressing apraxia. She later developed asymmetrical left-sided negative myoclonus and an alien limb phenomenon. Brain MRI, performed early in the course of the disease, was normal. Cerebrospinal fluid biomarkers revealed increased tau-protein levels (3180pg/mL) with normal phosphorylated tau and beta-amyloid values. Protein 14.3.3 had a weak positive result. The electroencephalographic pattern evolved from occipitoparietal slowing with right fronto-central epileptic discharges to focal status epilepticus, and later to generalized periodic triphasic sharp-wave pattern. 18F-FDG PET revealed a right frontal, parietal and occipital hypometabolism. 11C-PiB PET was normal. The patient had a rapid functional decline, achieving an akinetic mutism state and died within 3 months from symptom onset. According to Kropp's adapted criteria, a diagnosis of probable Heidenhain variant of Creutzfeldt-Jakob disease was made. We await brain pathological studies for a definite diagnosis.

Conclusion: PCA identification and diagnostic work-up are complex and require significant clinical training. We presented a case of a rare aetiology for an uncommon clinical entity.

Disclosure: Nothing to disclose

EPO2116

Timely detection of Neurocognitive disorders in primary care thanks to General Practitioner and Nurse Cooperation

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Background and aims: In Europe, there is a lack of detection of Neurocognitive disorders (NCD) by General Practitioners (GP), due to time constraints and unawareness of current assessment guidelines and tools. Collaboration between GPs and nurses may improve management of NCD in clinical practice.

Methods: During the “Act on Dementia” European Joint Action, GP-Nurse collaborations were implemented in France (Lyon), Italy (Modena) and Bulgaria (Sofia). Common detection tools were used in Bulgaria and France (DLA, DLA-I, MMSE, Mini-GDS and NPI); GP-COG was also used in Italy and France. In Bulgaria, 19 subjects were assessed by GPs alone and 12 subjects by a GP-nurse team. In Italy, 16 subjects were assessed by nurses and 9 were also assessed independently by GPs. In France, 1 nurse assessed 15 subjects referred by 14 GPs.

Results: Assessed patients did not differ in age. Cognitive complaint occurred since less than 2 years (n= 6) or 2-5 years (n=24). Reduced daily-life activities occurred in 40 patients. Evaluation showed significant differences of DLA (p=0.03), Mini-GDS (p=0.015) and NPI (p=0.001). There were no significant differences in GP-COG scores between France and Italy, nor in GP-COG scores collected by nurses and by GPs. Half of patients assessed were referred for additional testing. The patients were satisfied with this management model.

Conclusion: This pilot showed the feasibility of the GP/nurse cooperation to detect and manage cognitive impairment in daily clinical practice. All primary care health professionals should be involved to provide early/timely NCD management.

Disclosure: Nothing to disclose

EPO2117

Cerebellar cognitive affective syndrome (CCAS), Schmahmann’s syndrome, as the only sequel of an infarction in the territory of the superior cerebellar artery (ASC)

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Background and aims: For years the cerebellum has been regarded as engaged only in motor control. Current evidences support that posterior lobe lesions result in the CCAS. We describe a patient with cognitive impairment and affective component, secondary to ischemic infarction in the territory of the ASC.

Methods: A 45-year-old patient suffered a stroke in the ASC territory, without motor or sensory sequelae. In the following months, he presents progressive cognitive deterioration with psycho-behavioural alterations with irritability, agitation, aggressiveness and affective symptoms.

Results: Cerebral CT scan and MRI showed chronic infarction with a malacic area in the left ASC territory. The psychometric assessment evidenced a multidomain cognitive impairment with mnemonic predominance, with alterations in working memory, as well as in the speed of processing, selective and alternating attention, visuo-constructive and executive functions.

Conclusion: The cerebellar posterior lobe is linked to association areas of the cerebral cortex concerned with higher order behaviour. The CCAS is postulated as a symptomatic complex produced by the alteration in association networks between the cerebellum and mainly frontoparietal and limbic systems. The CCAS hallmark features include personality change and deficits in executive function, visual spatial processing, linguistic skills, social cognition and regulation of affect. We must be attentive to the appearance of cognitive clinic in patients with cerebellar damage, especially that involving posterior lobes. The current understanding of the cerebellum leads to the recognition of motor, vestibular and cognitive-affective syndromes. Knowledge of the so-called cognitive or limbic cerebellum has a direct impact on patient care and provides opportunities for new therapies.

Disclosure: Nothing to disclose

EPO2118

Cognitive impairment in very early stage of multiple sclerosis: reason for early aggressive therapy?

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Background and aims: Cognitive impairment (CI) is a frequent symptom of multiple sclerosis (MS), which is a significant factor in reducing the quality of life of patients from the very early period of disease. Aim was to assess frequency and severity of CI in early diagnosis group (McDonald, 2010), the relationship between CI, demographic factors and features of disease.

Methods: 67 MS patients (44 females), relapsing-remitting, remission, age – 38.4 [Q1:Q3=24.5:41.2], disease duration – 70.2 months [56.2:84.3]. Methods - Beck Scale, SDMT, PASAT, MoCA. Inclusion: 1) Diagnosis according McDonald 2010 criteria; 2) duration of disease <8 years; 3) EDSS<5.0. Exclusion: 1) inability to complete test; 2) taking medications that affect mental functions, 3) severe depression; 4) severe comorbidity. Statistical analysis – R Spearman, Chi-square, ROC.

Results: In 71% of cases CI was determined: 18.2% - severe CI, 12.1% - moderate CI, 40.6% - mild CI. Frequency and severity of CI significantly increase by the age ($R=0.40$, $p=0.001$). CI for women was more common than men (74% vs 65%). SDMT strongly correlate with EDSS score ($R=-0.47$, $p<0.001$), but not with duration of disease ($R=-0.14$, n/s). SDMT (sensitivity 78% and specificity 82%) was more sensible to detect mild and moderate CI than PASAT and MoCA.

Conclusion: High prevalence of mild and moderate CI on early stage of the disease with most sensible diagnostic criteria in patient with young age was detected. Decline the cognitive function could influence the quality of life and reflect the reducing functional reserve of the brain. Thus, it may be reason of early high aggressive therapy of main disease.

Disclosure: Nothing to disclose

EPO2119

Features of indicators of serum immunoreactive antibodies to neuromediator receptors and their influence on the development of cognitive disorders in neurospid

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Background and aims: To examine AAT indicators for NF200, GFAP, S100 and their effect on the cognitive functions of HIV-infected patients.

Methods: Level of autoantibodies to neurotropic proteins was determined in the blood serum of 90 patients with HIV infection. The average age of patients was 38.9 ± 1.2 years, of which 44.4% (44) were women, 55.6% (55) were men. Patients were divided into 2 groups: 25 patients without and 74 patients with certain disorders in the NS. We used ELI-N-Test solid-phase enzyme-linked immunosorbent assay among 70 HIV patients and 16 clinically healthy individuals (control group).

Results: In patients with NS disorders due to HIV, this indicator of AAT to S100 exceeded the standard values by an average of 1.9 times ($p<0.01$), and in patients without NS disorders - 1.6 times ($p<0.05$). Analysis of the AAT level for NF200 protein also showed a significant increase in HIV patients (on average 1.7 times with disorders of NS and 1.3 times without, $p<0.05$). In HIV patients with and without disorders, a significant increase in GFAP was found in groups with NS disorders by an average of 1.8 times, and without NS disorders by 1.6 times ($p<0.05$).

Conclusion: The data obtained as a result of the study indicate circulating AAT to neurotropic proteins and neurotransmitter receptors in the blood serum of HIV-infected patients can be used as additional prognostic “immuno-biochemical” criteria for the disease and the effectiveness of treatment.

Disclosure: Nothing to disclose

Critical care; Neurotraumatology

EPO2120

CAPTAIN-PH: A multicenter, single-blind, multicomponent intervention in TBI in the Philippines

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Background and aims: The CAPTAIN trials have demonstrated the benefit of Cerebrolysin in moderate to severe traumatic brain injury (TBI) in global outcomes and attention and executive function. In the Philippine ecosystem of care, healthcare is minimally socialized and largely out of pocket, and access to care and care practices vary in regions. The challenge of prompt medical care in TBI is also a stark reality in the Philippines due to unpredictable traffic situations and un-systematized patient transfer during emergencies. Therefore, replicating CAPTAIN II is difficult in the local situation. This investigator-initiated project aimed to adapt CAPTAIN II but make a protocol feasible in the real-world setting in the Philippines (CAPTAIN-PH).

Methods: The original version of CAPTAIN II was reviewed and adapted by a multi-disciplinary team comprised of the neurosurgeons and neurologist who know the protocol from their orientation in previous CAPTAIN trial. The team represents private and public hospital settings. Dafin Muresanu (P.I., CAPTAIN II) was advisory. The team identified necessary adaptations to be introduced in CAPTAIN-PH.

Results: Adaptations in CAPTAIN-PH are: 1) time to needle was adjusted from 4 to 24 hours to allow for qualified patients delayed in traffic; 2) multicenter single-blind (outcomes assessor) design; 3) at least 2 of 3 infusions will be allowed 4) use of multicomponent intervention (Cerebrolysin plus Cognitive Rehabilitation); and 5) addition of optional resting state and cognitive task-based magnetic resonance imaging (MRI) as exploratory outcomes.

Conclusion: CAPTAIN-PH is a multicenter, single-blind, multicomponent TBI intervention (Cerebrolysin and Cognitive Rehabilitation) designed for the real-world situation in the Philippines.

Disclosure: Nothing to disclose

EPO2121

Stress glycemia in patients with ischemic stroke.

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Background and aims: The development of hyperglycemia is one of manifestations of severity of critical state. To assess the incidence of 1 and 2 types of diabetes mellitus and frequency of development of stress hyperglycemia in IS patients.

Methods: A prospective observational study was conducted in 88 IS patients admitted to the NICU. The patients were divided into 2 groups: 1 - 78 surviving patients and 2 - 10 died. Age in 1 group was 66.1±10.9 years and 2 group 71.5±14.8 (p≤0.05). Patients were assessed the presence and type of diabetes mellitus, level of glycemia determined in 1st, 3rd and 5th day. Control of blood sugar was carried out at least 6 times a day with correction by introduction of Insulin.

Results: Patients of the 1st group had a history of diabetes of type 2 in 18 patients (23%), there was no data for 1 type. In the 2nd group was not history of diabetes 1 and 2 type (p≤0.05). The values of blood sugar at the study stages are presented in the table. The patients in 2 group had a statistically significant higher level of blood sugar at all stages of the study compared with patients in 1 group, although there were no patients who had a history of diabetes.

Table 1
Blood sugar level, mmol/l, M [25%; 75%]

	Ambulance	1day	3 day	5 day
1 group	8.3 [4.1; 10.3]	4.1 [3.9; 5.1]	5.1 [4.8; 5.6]	5.2 [4.8; 6.8]
2 group	10.2 [5.8; 12.1]	5.3 [4.5; 7.4]	7.6 [5.9; 9.1]	7.7 [6.1; 9.5]
p	≤0.05	≤0.05	≤0.05	≤0.05

Blood sugar level, mmol/l, M [25%; 75%]

Conclusion: Development of stress hyperglycemia is typical for patients with severe stroke but we did not find the effect of having a history of diabetes mellitus on outcome of disease.

Disclosure: Nothing to disclose

EPO2122

Results of plasmapheresis treatment due to neurological disease in a hospital-based series

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Background and aims: Plasmapheresis is an extracorporeal plasma filtration method that aims to remove immunoglobulins and pro-inflammatory factors. Several studies show a similar efficacy when compared with other acute-phase treatments in varied immune-mediated diseases. However, it is often not used due to low availability and fear of adverse events. The most common complications are related to vascular access and hydro electrolytic disturbances.

We aim to characterize the patients that underwent plasmapheresis due to neurological disease, the frequency and severity of adverse events, and the functional impact of treatment.

Methods: Retrospective, observational study, including all patients that underwent plasmapheresis due to neurological disease between January 2014 and August 2019. Adverse events were graded according to their severity. The treatment outcomes were evaluated with appropriate scales for each disease.

Results: We analyzed 28 treatments (average 6 cycles/treatment), corresponding to 23 patients. The main indications were: CNS demyelinating disease (N=11), myasthenia gravis (N=8), and inflammatory polyneuropathy (N=4). A total of 53 adverse events were registered. The most common were fibrinogen deficiency (N=12), catheter-related infection (N=11), arterial hypotension (N=7), and electrolytic imbalance (N=6). While most were not serious, two severe adverse events were identified (acute pulmonary edema). No deaths related to adverse events occurred. 6 treatments were suspended due to complications. Most patients (70%) had a functional benefit from the treatment.

Conclusion: Although the adverse events were frequent, most are mild, with minimal intervention required. In patients without the desired initial response, plasmapheresis may be useful in achieving a better clinical outcome.

Disclosure: Nothing to disclose

EPO2123

Tapia's Syndrome – is the mechanism neuropraxia from intubation or is it more complex?

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Background and aims: An otherwise well 23-year-old lady had a septorhinoplasty with bilateral implants under general anaesthesia for nasal blockage and right sided nasal deviation unresponsive to conservative therapy.

The operation was successful but 6 hours later the left side of her tongue felt odd, she had dysphonia and 'it felt funny to swallow'. She had deviation of the tongue to the left on protrusion; was unable to move the tongue quickly from side to side; and had altered sensation of the left side of the tongue. There was no obvious tongue swelling or haematoma and no weakness or numbness in the face or limbs. Naso-endoscopy confirmed a left vocal cord paralysis.

Methods: This was recognised as a left sided hypoglossal and vagal nerve palsy. The ENT and anaesthetic teams, felt that it might have been due to over-packing of the throat causing compression and neuropraxia.

This case will be discussed with reference to both the 1st described and more recent case reports of Tapia's syndrome along with the hypothesised mechanisms of injury. Tapia's syndrome is a thought to be due to pressure during intubation but most case reports follow surgeries with hammering and other sudden applications of force, rather than in emergency situations which would be expected to have more problems resulting from intubation.

Results: The patient was admitted for observation, and dexamethasone. Her symptoms substantially improved after 5 days. Later neurophysiological studies didn't find any abnormalities.

Conclusion: It seems important that those who resuscitate patients are aware of this potential complication.

Disclosure: Nothing to disclose

EPO2124

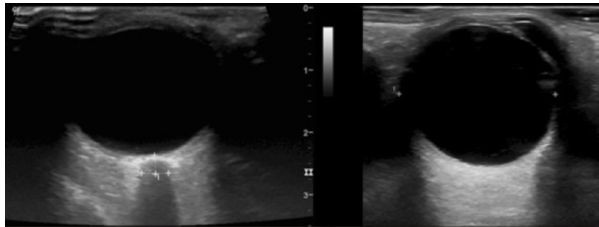
ONSD/ETD as a prognostic ratio of intracranial hypertension in traumatic brain injury patients in the emergency department

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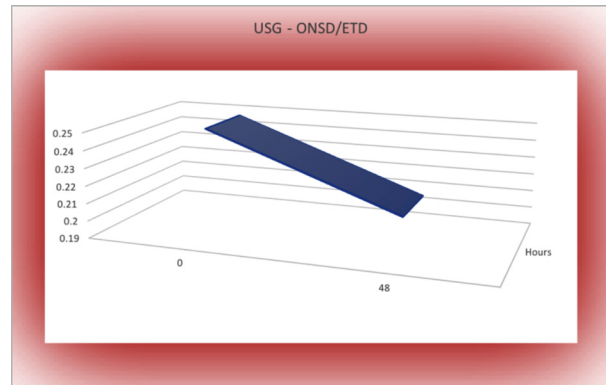
Background and aims: Our objective is to determine the ultrasonographic measurement ratio (ONSD/ETD) can accurately predict the computed tomography findings as a marker for evaluation and prognostication of intracranial pressure in traumatic brain injury.

Methods: We conducted a prospective, blinded observational study of seventy adult patients at the Department of Emergency Medicine between (2017-2018) having moderate to severe TBI and GCS <8. Using a 7.5 MHZ ultrasonographic probe on the closed eyelids, the eyeball transverse diameter(ETD) and optic nerve sheath diameter(ONSD) were performed bilaterally at the ED and after 48 hours of admission, following a 20% Mannitol infusion. ONSD/ETD ratio was calculated. Cranial CT findings (acc. to Marshall Classification) suggestive of elevated intracranial pressure were used to evaluate optic nerve sheath diameter accuracy.

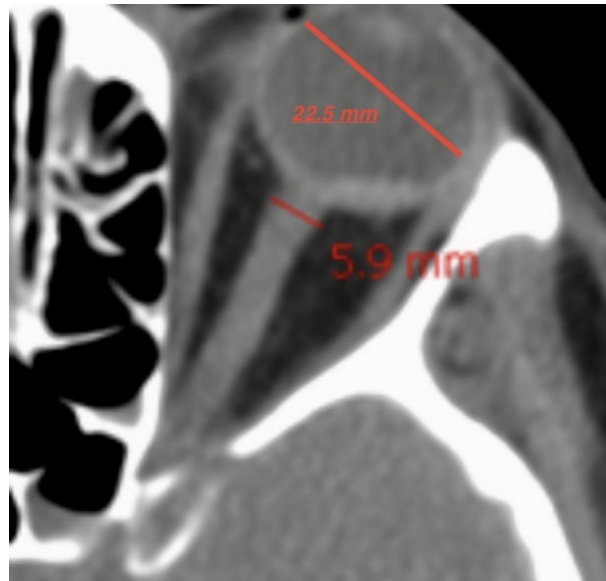


ONSD and ETD measurement

Results: USG-ONSD was greater than 5.7mm and decreased after mannitol infusion from 6.3 (6.1–6.7) to 5.2mm (5.5–6.3) ($p=0.0007$). ONSD/ETD has dropped from 0.25 till 0.21 (0.18-0.18). Median and Mean ETD was 22.85mm and 22.91 ± 0.93 mm. Enlarged right/left CT-ONSDs were $6.5 \pm 1.5/6.4 \pm 1.3$ mm at 3mm and $6.6 \pm 0.8/6.6 \pm 0.6$ mm at 8-10mm from the globe (cut-off value > 5.5mm). ONSD/ETD ratio was 0.29 ± 0.05 compared with 0.19 ± 0.02 in healthy adults ($P < 0.01$). The sensitivity of ultrasonography for detection of any traumatic intracranial injury found by CT was 85% (95% CI 60% to 97%) and specificity was 75% (95 %CI 59% to 86%).



ONSD/ETD analysis



ONSD/ETD (CT) measure

Conclusion: ONSD/ETD has potential as a sensitive screening test for elevated intracranial pressure in traumatic brain injury.

Disclosure: Nothing to disclose

EPO2125

Comparing efficacy of pedicle screw fixation methods for treating thoracolumbar burst fractures with neurological deficit

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Background and aims: Short-segment posterior fixation (SSPF) is the most common method for treating thoracolumbar burst fractures (TLBF). Posterior short-segment fixation including the fractured vertebra (PSFFV) is a means of pedicle screw fixation failure prevention. This study presents the comparison of outcomes of SSPF and PSFFV for TLBFs with neurological deficit.

Methods: 69 patients aged 37±19 years with TLBFs. The neurological deficit was found in all patients and classified on ASIA scale (B – 15, C – 32, D – 22). Pain severity was 7.3±0.5 points on VAS10. CA before surgery was 16.7±5.10. The canal compromise was 50±12%. SSPF was performed on group 1 (n=35) and PSFFV on group 2 (n=34). No statistical differences in age, height, weight, type or injury level as well as the severity of canal compromise or neurological deficit were observed (p>0.05). Outcomes were registered on post-surgery day 7, in 6 and 12 months.

Results: The regress of neurological deficit in 7 days was identical in both groups (p>0.05), and in 6 and 12 months it was higher in group 2 (p=0.04). There were no differences in CA and canal compromise correction in 7 days in both groups (p>0.05), but in 6 and 12 months the results in group 2 showed better stability (p=0.02) suggesting that using PSFFV facilitates stabilization for long-term outcomes.

Conclusion: PSFFV is efficient for treating TLBFs with neurological deficit.

Disclosure: Nothing to disclose

EPO2126

Observational study of infectious complications in a Neurological Intensive Care Unit

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Background and aims: Infections in patients admitted to the neurological intensive care unit (NeuroICU) require often an empirical, prolonged and combination antibiotic therapy due to the initial uncertainty of the etiological diagnosis and/or the frequent multi-drug resistance (MDR) of causal bacteria. Since the duration of infections and antibiotic therapy can affect the mortality and disability of patients in NeuroICU, we investigated the role of infections and duration of subsequent antibiotic therapy on the patients' outcome and on bacterial MDR infections occurrence.

Methods: 120 patients (mean age 67.4±18.7 yrs) were admitted to our NeuroICU between June 2017 and June 2018. Clinical, biological and infection-related data during entire hospitalization were collected. Good outcome was defined a modified Rankin Scale score 0-2 at discharge.

Results: About 40% of patients developed infections during hospitalization. Infections were associated with a lower probability of good outcome (OR 0.01, 95% CI 0.00-0.26) and a tendency towards greater mortality (OR 8.37, 95% CI 0.97-73.32). Longer duration of antibiotic therapy was associated with a greater probability of good outcome (OR 1.11, 95% CI 1.02-1.22) without modifying mortality. MDR agent infections (25.5% of all infections) were more frequent in patients with longer antibiotic therapy and hospitalization as well as in those with medical devices.

Conclusion: On the 1 hand a longer duration of antibiotic therapy is associated with a better outcome, while on the other it is more frequent in patients with MDR infections. Further studies are needed to define a safety cut-off for antibiotic therapy duration in this setting.

Disclosure: Nothing to disclose

EPO2127

Reversible Locked-in Syndrome After a Voluminous Hematoma in The Posterior Fossa

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Background and aims: The locked-in syndrome (LIS) is a state characterized by tetraplegia, anarthria and preservation of the level of consciousness, besides a certain ocular movement through which the patient communicates. We present a case of a woman with quadriplegia and bulbar palsy after suffering a large haemorrhagic stroke in the posterior fossa, and a diagnosis of locked-in syndrome was established.

Methods: Woman, 61-year-old, admitted with thunderclap headache and rapid deterioration of the sensorium. CT scan revealed a voluminous hematoma in the posterior fossa, caused by warfarin intoxication (she had atrial fibrillation, novel anticoagulants were ruled out due to metallic mitral valve). After surgical decompression, she displayed quadriplegia and bulbar palsy, maintaining some extrinsic ocular movements. Conscience was spared - she blinked to answer questions of “yes” and “no”. Presented no respiratory drive, being intubated, later evolving to tracheostomy. CT reading was unclear due to artefacts, and MRI was opted out due to clinical instability and some concern of disturbance of the cardiac valve. After a few weeks, she partially recovered some body movements and the bulbar muscles strength, maintaining dysarthria. MRI, then performed, showed no lesions in the brainstem, except for sequels in the void hematoma area, in the left cerebellar hemisphere.

Results: LIS was caused by the hematoma compression and the subsequent effect of post-manipulation edema.

Conclusion: The compression by the hematoma and subsequently effect of post-manipulation edema might have caused a neuropraxia of the motor pathways, causing a reversible locked-in syndrome.

Disclosure: Nothing to disclose

EPO2128

The use of Medical grade cannabis in Italy

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Background and aims: In Italy, Medical Grade Cannabis (MGC) can be prescribed for different medical conditions, whenever standard and approved therapies have failed, or caused non-tolerable side effects.

Here we describe our 5-year clinical experience in the management and prescription of MGC.

Methods: This is a retrospective observational study. MGC was prepared according to Italian laws and administered as either an olive oil extract (OOE), or as an oral non activated form. Cannabis was prescribed as either Bedrocan (22% THC, <1% CBD), Bediol (6.5% THC, 8% CBD), or Bedrolite (0.4% THC, 9% CBD). Responders were classified as patients showing $\geq 20\%$ reduction in the Numeric Rating Scale (NRS).

Results: We treated 111 patients (63% female; mean age 47.4 years). Median FU for responders was 19 months. Prescription indications are reported in Figure 1. 70% of patients were treated with Bedrocan, 10.8% with Bediol, and 2.7% with Bedrolite. 57% of patients responded to MGC, whereas 43% dropped out for lack of response. Mean baseline NRS was 8.12 ± 1.6 and decreased at FU to 5.27 ± 2.4 ($p < 0.001$; Figure 2). Patients receiving MGC for pain showed the best effect with -3.3 points NRS reduction. Patients with baseline NRS > 8 had a higher therapy persistence (HR=0.19; $p < 0.001$; Figure 3), and higher response to (OR= 4.8; $p = 0.001$). MGC was overall safe and well tolerated.

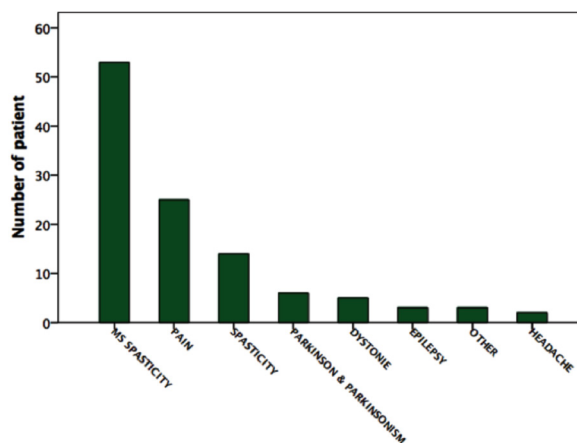


Figure 1. Prescription indications

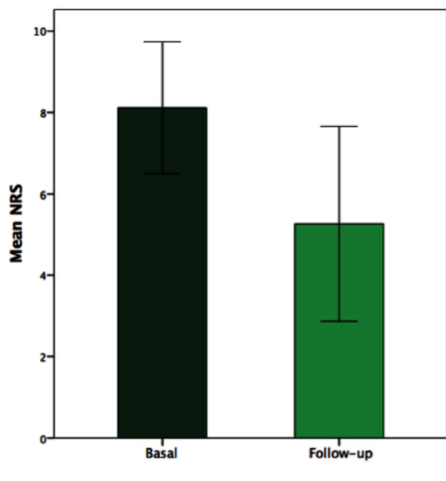


Figure 2. NRS at baseline and FU

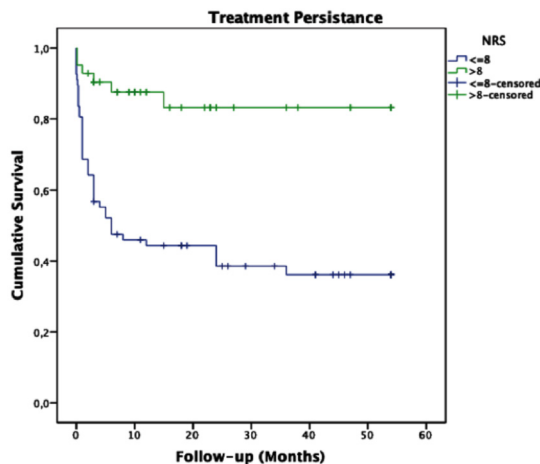


Figure 3. Therapy persistence

Conclusion: Our experience shows that MGC can be successfully used in a neurological setting and that it is safe and well tolerated. Patients with higher NRS had a higher response probability and treatment persistence.

Disclosure: Nothing to disclose

EPO2129

Correlation of clinical symptoms and neuroimaging indicators in aggressive vertebral hemangiomas.

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Background and aims: Aggressive hemangiomas of the vertebrae are characterized by a complex of neurological and radiological changes.

Methods: 42 patients with an average age of 41+1.8 years with aggressive hemangiomas of the vertebrae were examined. Conducted: pain assessment on a visual analogue scale (VAS), on a scale of DN4, neurological status, level of anxiety and depression on a scale of HADS, CT of the vertebrae, calculation of possible changes in vertebral support using a computer program.

Results: All patients had chronic local pain syndrome on average about 2 years. On the VAS scale, an average of 5.6 points, on the DN4 scale, an average of 6.3 points. Patients with hemangiomas occupying more than 80% of the vertebral body according to the VAS scale had 1.7 points. Objectively: muscle-tonic syndrome (85.7%), radicular disorders (57.1%), dysfunction of the pelvic organs (42.8%), chronic venous insufficiency (76.1%), autonomic, trophic disorders of the lower extremities (69%). According to the HADS scale, moderate anxiety in 83.3% of patients, depression in 11.9% of cases. It was found that the likelihood of a decrease in support ability by more than 50% correlated with the localization of hemangiomas at the level of Th12 and L1 vertebrae, by 30% at the level of L3-L5 vertebrae.

Conclusion: Aggressive hemangiomas of the vertebra are accompanied by chronic local pain, with an increase in the size of the hemangioma, severe pain decreases, there is also a neurological deficit, changes in the morphometric parameters of the vertebral body, which increases the risk of a pathological fracture.

Disclosure: Nothing to disclose

EPO2130

Diffuse brain edema as a result of generalized seizures caused by acute hyperglycemia, from new introduced olanzapine therapyV. Shala¹, F. Jashari²¹Peja, ²Prishtina, Albania

Background and aims: Olanzapine can cause both generalized seizures and hyperglycemia. Aim of this paper is to present a case with transient diffuse brain edema, after taking olanzapine tablet, as a result of seizures induced by high level of blood sugar.

Methods: 57-year-old female patient without consciousness and with serial generalized seizures was admitted to the neurology intensive care unit. Glasgow Coma Scale scored 7 points. Heteroanamnesis revealed that the patient was chronically suffering from depressive psychosis, and olanzapine was newly introduced in the treatment scheme. The condition was developed within short period, with dramatic manifestation.

Results: CT scan displayed diffuse brain edema. Lab values indicated a post-generalized seizure activity and hyperglycemic state. The health status has been improved within 48 hours. The main treatment included anti edematous, Ringer's solution, anti-diabetic and anti-epileptic medications.

Conclusion: This case report warns medical professionals regarding adverse effects olanzapine can induce, including hyperglycemia, seizures, ultimately diffuse brain edema. Based on the fact brought above, it is of crucial importance to take a detailed history from family members, because an early and correct diagnosis can save lives.

Disclosure: Nothing to disclose

EPO2131

Secondary traumatic brain injury in rats: Evolution of damage in the neocortex and hippocampus during acute period

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Background and aims: Traumatic brain injury (TBI) induces damage both in the neocortex (primary lesion) and hippocampus (distant lesion). Morphological changes develop gradually and represent secondary mechanisms of damage. The purpose of the study was to assess evolution of morphological damage in the neocortex and hippocampus and its behavioral correlates during acute period of TBI in rats.

Methods: The experiment was performed on 48 adult male Wistar rats. TBI was modeled using lateral fluid percussion in the right sensorimotor cortex. Rats were sacrificed on day 3 after TBI, or on day 7, after behavioral assessment in open field and elevated-plus maze tests. Cortical damage was estimated with semiquantitative analysis of Nissl stained sections using unfolded maps. Pro-inflammatory microglial activation was assessed using anti-IBA staining.

Results: Gliosis and necrosis developed in functional neocortical areas: primary somatosensory, parietal, secondary auditory and secondary visual ones. The degree of neocortical damage increased from day 3 to 7. Microglial activation was seen only in CA3 area of the ipsilateral hippocampus on day 3 after TBI, while on day 7 it was also seen in dentate gyrus (DG) in the ipsilateral and contralateral hippocampus. Morphological changes were accompanied by behavioral abnormalities in both tests.

Conclusion: Secondary damage in acute period of TBI develops in cortex (enlarging necrotic changes in primary and secondary sensory area) and hippocampus (evolving microglial activation in ipsilateral CA3 and bilaterally in DG). The behavioral changes in rats in acute TBI period may result from sensory deficit in rats.

Disclosure: Supported by RFBR, grant №19-015-00258

EPO2132

Late sequelae of TBI in rats: Anxiety and hippocampal sclerosis

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Background and aims: Traumatic brain injury (TBI) is a serious risk factor for neurological and psychiatric disturbances in late period of trauma, including depressive/anxiety and cognitive disorders. Distant chronic neuroinflammation, neuronal loss and gliosis in the hippocampus may explain cognitive deficits and emotional disturbances in late period of TBI.

Methods: The study was performed on 20 male Wistar rats aged 6 months, sham and TBI groups. TBI was modeled using lateral fluid percussion in the right sensorimotor cortex. Anxiety behavior was assessed in the elevated plus maze, open field and forced swim tests 1 week before and 6 months after TBI. Morphological changes were evaluated by Nissl and GFAP staining.

Results: Morphological findings both in TBI and sham rats included astrogliosis in the hippocampus (DG and CA3), notably asymmetrical and much more pronounced in TBI group. TBI induced ipsilateral thinning of pyramidal layer (pl) in CA3 which correlated with astrogliosis. Dispersion in CA3pl was noticed in 11 rats in both groups. 6 months after TBI all rats showed lower activity and signs of anxiety behavior, more significant in TBI group.

Conclusion: 6 months after TBI rats showed asymmetrical hippocampal astrogliosis with neuronal loss in CA3pl. These changes are similar to human hippocampal sclerosis type 3. All rats demonstrated anxiety behavior, significant more expressed after TBI. The results show the validity of the TBI model to study mechanisms of late posttraumatic pathology.

Disclosure: Supported by RFBR, grant №19-015-00258

EPO2133

Case Series: Sensorineural Anosmia Post-Traumatic Brain Injury

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Background and aims: Olfactory dysfunction (OD) is common after traumatic brain injury (TBI). Its incidence ranges from 4-60%, yet it is often undiagnosed, usually recognized later, impacting quality of life. Mechanisms underlying post traumatic OD includes sinonasal tract disruption, direct shearing or stretching of olfactory nerve fibers, and focal contusion of olfactory bulb or cortex, causing conductive or sensorineural OD. We present three cases of patients who sustained motor-vehicle accidents with signs and symptoms of OD.

Methods: The cases are adult-aged males sustaining moderate brain injuries from motorcycle collisions. Each had good cognitive functions therefore was evaluated. Olfactory function was tested using nasoendoscopy, Sniffin' Sticks test (SST) and intravenous olfactory (IVO) test, correlating the results with clinical manifestation and head computed tomography (CT) to interpret the biomechanism of injury.

Results: Case 1: examined on day-22, had nasal bone fracture, frontal lobe fracture and contusion. Case 2: examined on day-16, had frontal lobe fracture and contusion, temporal lobe epidural hematoma (EDH). Case 3: examined on day-16, had nasal and frontal bone fractures, frontal lobe EDH and intracerebral hemorrhage (ICH), temporal lobe ICH. All 3 cases had low SST score, undetectable IVO and was assessed as sensorineural anosmia.

Conclusion: The cases presented shows that post traumatic OD can be recognized and should be detected not long after the onset of injury. The biomechanism and location of lesion in the brain, as well as other structures of the head correlates with the risk of OD. Most head injuries cause severe damage to the olfactory pathways therefore causes sensorineural anosmia.

Disclosure: Nothing to disclose

Epilepsy 3

EPO2134

Gender effect on Juvenile Myoclonic Epilepsy

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Background and aims: Juvenile myoclonic epilepsy (JME) is a widely recognized, presumed genetic, electroclinical generalized epilepsy syndrome. Previous studies evaluated electroclinical prognostic factors with controversial results and only few studies addressed the influence of sex in the long-term prognosis. Objective of the study was to evaluate the long-term outcome in a group of patients and to assess the presence of prognostic factors which could be linked to sex.

Methods: We retrospectively selected a group of patients with JME evaluated in our epilepsy center with at least 5 years of follow-up. We considered the clinical and EEG features at the 1st (T1) and the last follow-up (T2) visit. Seizure-freedom was defined as the absence of any type of seizure for at least 2 years. Patients were stratified into two groups according to sex.

Results: 105 patients with JME were included (67 females [63.8%]; mean age 36.6±9.4). The mean age of seizures onset was 14.2±3.9 years. The mean disease duration was 18.9±9.1 years with a mean follow-up time of 13.1±6.0 years. At the last follow-up, 21 males (55.3%) and 33 females (49.2%) were seizure free with a mean time to reach seizure-freedom of 19±8.7 years for males and 17.3±9.7 years for females, with no significant differences. Negative prognostic factors were weekly seizures and arms myoclonia at onset in males, absences and lower age at onset in females.

Conclusion: The results of our study reveal that some prognostic factors are sex-specific in JME.

Disclosure: Nothing to disclose

EPO2135

Severity and stability of drug resistant focal epilepsy

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Background and aims: A proportion of patients with drug resistant epilepsy (DRE) experience long (>1 year) periods of seizure freedom (PoSF). This may reflect comparatively lower intrinsic severity of the disease.

Methods: The study included 104 patients with focal DRE referred to a epilepsy surgery center. The history was analyzed basing on patients' recollection and previous medical records. In order to assess current disease severity, QOLIE-31, LSSS and NNDI-E questionnaire were used. For the statistical analysis we used the Mann-Whitney test.

Results: PoSFs were observed in 27% (28/104) of the studied patients. Duration of PoSFs varied from 1 to 12 years. In three cases (11%) the patients took no antiepileptic drugs during the PoSF. One patient (3%) had a PoSF twice. There were no statistically significant differences between the patients with and without history of PoSF in terms of current disease severity ($p>0.05$). Patients who had no seizures during one month before the assessment had lower NNDI-E scores (9.2 (6.0–12.0) vs. 12.6 (6.0–21.0), $p<0.01$) and, surprisingly, lower cognitive functioning score in the QOLIE-31 (11.8 (0–27.0) vs. (15.7 (0–27.0), $p=0.04$) than patients with uncontrolled seizures.

Conclusion: Drug resistance in focal epilepsy may be remittent in 27% of the cases. The history of periods of seizure freedom seems to have no influence on overall disease severity. In contrast, the presence of ongoing seizures affect cognitive functioning and emotional well-being.

Disclosure: Nothing to disclose

EPO2136

Cognitive functions in children with temporal and frontal epilepsy

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Background and aims: Frontal Lobe Epilepsy (FLE) and Temporal Lobe Epilepsy (TLE) are the 2 most frequent types of localization – related epilepsies and they are connected with difficulties in cognitive functioning. The main aim of conducted study was to compare cognitive functioning among children with newly diagnosed FLE or TLE at the beginning of the disease and during its course and to compare them with control group.

Methods: Study included 39 patients with newly diagnosed TLE and 24 with FLE and 24 healthy children. Neuropsychological examination was carried out in the moment of diagnosis and after 2 or 3 years from the diagnosis, by using validated and standardized to the patient's age diagnostic tools.

Results: In children with focal epilepsy accomplished worse results in most of the tasks compared to the control group already in the 1st examination. Patients with FLE presented difficulties in memorizing verbal and visual material, attention, and in learning new information. Patients with TLE had difficulties in tasks engaging verbal and non-verbal memory and attention. In long – term analysis group of patients with FLE presented more severe cognitive impairment comparing with other groups. Despite similar tendencies among children with TLE, in group of patients with FLE significant worse results in tasks engaging verbal memory and attention were observed.

Conclusion: Conducting full assessment of cognitive functioning in children suffering from epilepsy is essential not only at the moment of making diagnosis but also during the disease due to introduce, as quick as possible, individual system of support.

Disclosure: Nothing to disclose

EPO2137

Surgical outcomes in patients with Refractory Epilepsy after CNS infection

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Background and aims: Epilepsy is a frequent complication of CNS infections. Analysis of the subset of post-CNS infection refractory epilepsy cases in surgical series is scarce. We aim to characterize this subgroup and compare surgical outcomes with other etiologies.

Methods: Retrospective review clinical, imaging and EEG data of adult patients evaluated on our Reference Centre for Refractory Epilepsy since 2006.

Results: Out of 312 patients evaluated, 38 had past history of CNS infection. After pre-surgical evaluation 23 were surgically treated (9 prior meningitis/14 prior encephalitis). Most patients had seizures in the acute phase (94%) and encephalitic patients had seldom “silent period”. Comparing with patients surgically treated without past infection (n=89): more patients had focal sensory seizure (17% vs 5%) and focal cognitive seizure (22% vs 14%, p-value=0.745); 35% patients had normal brain MRI (vs 10%, p-value=0.001) and 9 had hippocampal sclerosis; on video-EEG monitoring, 29% had focal interictal discharges (vs 59%, p-value=0.016), 48% a focal ictal onset (vs 79%, p-value=0.000) with temporal onset in 75% (vs 78%); 2 patients had invasive-EEG recordings. Resective surgery was performed in 19 patients (83% vs 92%) and VNS in 4 (17% vs 8%, p-value=0.082). Only 6 patients achieved Engel Ia (33% vs 57%, p-value=0.007) and 1 patient didn't improve. Logistic regression showed that younger age at occurrence of meningitis and clear latency period were related with favorable surgical outcome.

Conclusion: As previously reported, our series demonstrated that patients with epilepsy following CNS infection may be good candidates for surgical treatment, although with less favorable outcomes.

Disclosure: Nothing to disclose

EPO2138

Transcranial magnetic stimulation as a tool for the evaluation of neuromodulatory effects of transcutaneous vagus nerve stimulation

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Background and aims: The combination of transcranial magnetic stimulation and electromyography (TMS-EMG) allows to study the modulation of motor-evoked potentials (MEPs). As MEPs reflect the excitability of the entire corticospinal pathway, they are subject to cortical, subcortical and spinal modulation. The combination of TMS and electroencephalography (TMS-EEG) allows a direct read-out of cortical reactivity by means of TMS evoked potentials (TEPs), avoiding this interference. As MEPs and TEPs are reproducible within subjects, they may be useful to study neuromodulatory interventions, like transcutaneous auricular vagus nerve stimulation (tVNS).

Methods: In this prospective cross-over study, 15 healthy male subjects underwent 2 sessions, at least one week apart. During each session, tVNS or sham stimulation was delivered at the maximum tolerated amplitude during one hour. MEPS and TEPs were measured over the right primary motor cortex before and after the intervention. For these measurements, 120 single TMS pulses, 120 paired TMS pulses with an interstimulus interval of 3ms and 120 paired TMS pulses with an interstimulus interval of 100ms were delivered over the motor hotspot.

Results: MEPs and TEPs were compared at the single subject level before and after each neuromodulatory intervention. Preliminary results show no statistically significant difference in mean MEP morphology after real tVNS compared to sham stimulation. TMS-EEG data analysis is still ongoing.

Conclusion: In contrast to previous research, our preliminary results show that active tVNS, as compared to sham stimulation, was not able to modify excitability measured by TMS-EMG. The analysis of the neuromodulatory effect of tVNS on TMS-EEG is currently ongoing.

Disclosure: Nothing to disclose

EPO2139

Role Of Vascular Endothelial Growth Factor in Arteriovenous Malformation Associated-Seizures

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Purpose: This study was designed to evaluate the role of vascular endothelial growth factor in AVM associated seizures

Methods: A case-control study conducted on 40 patients subdivided into 3 groups on Mansoura university hospital. The patients subdivided into 3 groups: 10 patients: AVM with seizures. 16 patients: AVM without seizures. 14 patients (control): patient without AVM. Plasma samples were collected from 40 patients to detect the basal level of VEGF. The serum samples were immediately centrifuged and frozen at -80 C, VEGF were measured by commercially available ELISA (double-antibody sandwich enzyme linked Immunosorbent Assay) kits (Human vascular endothelial cell growth factor ELISA Kit, SUNRED Biological Technology) Data were fed to the computer and analyzed using IBM SPSS software package version 22.0. Significance of the obtained results was judged at the 0.05 level.

Results: There was statistically significant higher mean of VEGF among AVM cases in comparison to control group, also the VEGF mean value was statistically significant higher among epileptic cases than cases without epilepsy

Conclusion: Our results confirmed the role of VEGF in both AVM and epilepsy and it may be used in future as a reliable and valid predictor. Regarding the debate of the role of VEGF in epilepsy, whether if it's a neuroprotective or it's epileptogenic, our study tilting the balance heavily in favour of the epileptogenic effect of VEGF. This study not only gives a hope for using VEGF as a predictor tool in AVM and epilepsy but also VEGF may have a role in future treatment.

Disclosure: Nothing to disclose

EPO2140

The effect of additional antiepileptic drugs for epilepsy in glucose transporter 1 deficiency syndrome

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Background and aims: Glucose transporter 1 deficiency syndrome (GLUT1DS) leads to cerebral energy failure and causes refractory epilepsy, intellectual disability and several complex movement disorders. Although the ketogenic diet (KD) is the only effective treatment, it does not effective for some patients. We studied the efficacy of KD and additional antiepileptic drugs for epilepsy in GLUT1DS.

Methods: We retrospectively reviewed the medical records of GLUT1DS patients who visited our hospital from 2004 to 2019. The diagnosis was confirmed by genetic analysis of the SLC2A1 gene or the erythrocyte glucose uptake test.

Results: The study enrolled 43 patients (19 males and 24 females; age range: 1–53 years [median: 14 years]), and 39 (91%) patients had epilepsy. The seizure types were generalised tonic-clonic (23, 53%), focal tonic (25, 58%), focal clonic (19, 44%), focal impaired consciousness (25, 58%), focal to bilateral tonic-clonic (24, 56%), absence (23, 53%) and infantile spasms (1, 2%). The KD was introduced in 38 (88%) patients. The average age at diet initiation was 6 years, and the average diet duration was 7 years. 2 patients dropped out owing to refusal. Convulsive seizures and absence were eliminated by KD alone in 9 (26%) and 8 (35%) patients, respectively, and antiepileptic drugs along with KD in 1 (3%) and 4 (17%) patients, respectively. Valproate, lamotrigine, levetiracetam and nitrazepam were sometimes effective to reduce seizure frequency after KD introduction.

Conclusion: Our findings indicate the efficacy of the KD and show that appropriate addition of antiepileptic drugs is sometimes efficacious for seizure control.

Disclosure: Nothing to disclose

EPO2141

Incidence of post-stroke epilepsy in Umbria: population study based on administrative regional health data

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Background and aims: Depending on the underlying cerebrovascular disease, 3–30% of patients who have had a stroke develop post-stroke epilepsy (PSE). According to the present ILAE definition, a single late seizure (>7 days) after stroke qualifies as structural epilepsy (PSE). This project aims to estimate the incidence of PSE in Umbria using administrative healthcare data.

Methods: In this retrospective study, population consists of all patients with a hospitalization due to acute stroke (ischaemic and haemorrhagic) in Umbria between 2013 and 2017. Patients with strokes were identified in the administrative databases using ICD-9-CM codes. Post-stroke epilepsy was identified with the prescription of at least one EEG and one or more AEDs seven days after stroke, according to Franchi and colleagues.

Results: During the study period, 9465 incident cases of acute stroke were identified. Most of our cerebrovascular events were ischaemic strokes (n=6642, 80.2%). Following these patients until 2018, 228 people presented PSE (56.1% males/ 43.9% females; median age 67 years). Multivariable Cox regression showed that onset of PSE was associated with intracerebral and subarachnoid haemorrhagic stroke, younger age and longer duration of hospital stay. Levetiracetam was the most commonly prescribed AED (56.6%) for the management of PSE. Diabetes, hypertension and heart failure were not associated with PSE in the multivariable model.

Conclusion: This is the 1st study of incidence of epilepsy after stroke using administrative healthcare data in Italy. The data collected showed that PSE was associated with haemorrhagic strokes and younger age, as reported in previous studies and hospital stay

Disclosure: Nothing to disclose

EPO2142

Epilepsy and women: reproduction

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Background and aims: Epilepsy is one of the widespread diseases.

Purpose: To research reproductive indicators in women with epilepsy (WWE).

Methods: 155 WWE aged 18-45y.o. were included in the prospective observational research of antiepileptic drugs (AEDs) reproductive side effects. Reproductive strategy (RS), endocrine complication (REC), the fertility rate (FR) were compared into 3 groups: 1gr. - AEDs monotherapy, 2gr. - polytherapy, 3gr. - without AEDs.

Results: 1gr. - 68 (44%), 2gr. - 67 (43%), 3 gr. - 20 patients (13%). The average age was 25y.o. with the prevalence of patients in optimal reproductive age (20-30y.o.) 62%. 47% of women were married, 31% had children without differences in groups. Women planning pregnancies were 45%. The majority of patients interviewed in 2012 planned to have one child, in 2017 - 2 children. New RS was early repeated pregnancies. RS "without children" remained the actual problem among patients in late reproductive age. The common frequency of REC - 53%, due to AEDs side effects -40%. Polytherapy enlarged REC frequency in comparison with 1gr - 30%, 3gr - 10% and made 60% ($p < 0,001$). The fertility rate was 0,3 in the cohort. New generation AEDs (perampanel, brivaracetam) allowed achieving remission at first and second polytherapy. The fertility rate among women with epilepsy was lower optimal due to medical and social reasons. The reproductive strategy was changing at the present time. It is necessary to use an integrated approach to women with epilepsy.

Conclusion: The reported study was funded by RFFR according to the research project № 18-013-00222

Disclosure: The reported study was funded by RFFR according to the research project № 18-013-00222

EPO2143

Real-world experience with perampanel at low doses in a secondary center

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Background and aims: Our aim is to review the efficacy and tolerability of perampanel at 4mg dose after at least 6 months of use.

Methods: We carried out a retrospective 5-year review of all patients receiving perampanel in our center.

Results: A total of 22 patients received perampanel at a dose of 4mg. The mean age was 48 (25-78) years, 50% being males. 7 had a diagnosis of idiopathic generalized epilepsy, 14 of focal-onset epilepsy, and 1 remains undetermined. The mean previous antiepileptic drugs (AEDs) used were 4 (2-7). 2 patients were in monotherapy (9%), 7 in double therapy (32%), 8 in triple therapy (37%), and 5 (22%) had more than 3 other AEDs. The mean time of use of treatment was 18 months (6-39 months). 13 (60%) patients continue treatment at the time of last follow up. The mean seizure reduction rate was 36,4%, with 6 (27%) patients free of seizures. 10 patients presented adverse effects (AEs). The most common were behavioural changes (4), followed by somnolence (2) and dizziness (2). None showed suicidal thoughts, and only 4 (18%) had to discontinue treatment due to AEs.

Conclusion: Perampanel is an effective AED with good response and retention rates at a dose of 4mg. The occurrence of AEs is usually well tolerated, and the number of serious AEs that require suspension of the treatment is within reasonable margins. No patients presented suicidal thoughts reaching the 4mg dose, which favours the use of this drug at low doses, while maintaining good efficacy and tolerability.

Disclosure: Nothing to disclose

EPO2144

Music and seizures: does it change something after glioma surgery?

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Background and aims: Association between music and seizures is complex and intriguing. Musical processing within the human brain recruits a network involving many cortical areas that could be activated as part of temporal lobe seizure. Changing in music perceptions and emotions have been described during epilepsy surgery, but less is known regarding the same aspects in case of surgery for primary brain tumours (PBTs). We reported our monocentric experience, in a cohort of patients with PBTs and seizures characterised by auditory hallucinations.

Methods: Retrospective analysis of 155 patients affected by PBTs and tumour-related epilepsy, surgically treated in our Department, between 2007 and 2017. Inclusion criteria were: tumour-related epilepsy with auditory hallucinations or sound misperception; 1st diagnosis of brain tumour; no previous chemotherapy or radiotherapy; 18 months follow-up.

Results: Among 155 patients, 13 (7 males and 6 females, mean age: 50 years) were enrolled. They all presented seizures with musical hallucination or sound misperception and underwent surgery for gliomas located within the temporal lobe (10/13) and the insula (3/13). After surgery, 8/13 were in Engel class Ia; 5/13 presented new emotional reaction to music, described as increased sensitivity to high pitch and loud music. 2 subjects, both with musical education, developed musicophilia. No relations with seizure outcome, tumour histology and extent of resection were observed, while there was a statistically significant relation with pre-operative seizure frequency ($p=0.002$) and EEG/electrocorticographic epileptic pattern ($p=0.001$).

Conclusion: Assessment of music perception and emotions should be considered in glioma surgery and post-operative changing should be screened.

Disclosure: Nothing to disclose

EPO2145

Fitting in: seizure presentations over 12 months

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Background and aims: With an estimated 37000 people live in Ireland with a diagnosis of epilepsy, seizures are a common presentation to emergency departments. Symptomatic seizures, secondary to acute medical or surgical illness, alcohol and drug intoxication, further compounds the situation. Diagnosing, identifying triggers and management of these patients often requires neurology input. A previous study performed at our institution showed that 28% of referrals to neurology services were for seizures. We aimed to analyse all seizure presentation over a 12 month period and to identify triggers, their inpatient course and management.

Methods: We conducted a retrospective review of all seizure related admissions between January 1st 2018 and December 31st 2018. Seizures were identified based on based on ICD coding criteria for seizures and convulsions. Non epileptic seizures and alternative aetiologies were excluded. Data was analysed on demographics, background, length of stay, triggers, EEG and referral to neurology.

Results: 304 patients were enrolled with an age range of 15-95 years. 53% were male. 27% presented as a 1st onset unprovoked seizure. 22% had a diagnosis of epilepsy. 7% had more than 1 seizure related admission. Neurologist department was consulted on 62%. 55% had an EEG, with 3 having seizures captured. Alcohol was the most obvious trigger (10%). Drugs, stroke, and medication non-compliance were also identified.

Conclusion: Seizures only comprise a significant proportion of patients presenting to emergency services. Early intervention from neurologists can guide investigations and treatment. Improving outpatient resources and providing nurse led services can help in reducing seizure presentations.

Disclosure: Nothing to disclose

EPO2146

Clinical, behavioral and sociodemographic profile of non-psychotic patients with epilepsy and suicidal ideation

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Background and aims: People with epilepsy (PWE) have a higher risk of suicidal ideation (SI) and attempts (SA) than the general population. At the same time, for PWE there is a knowledge gap on prevalence of variables that were found to be associated with increased risk of suicide in general population. We aimed to identify variables that may be associated with epilepsy in patients with non-psychotic mental disorders (NPMD) and SI.

Methods: The study was a case-control: 40 PWE with NPMD and SI were compared to similar patient without epilepsy 1:2. Patients underwent a psychiatric examination and self-injurious thoughts and behaviors interview. Information on demographic, biographical, clinical, and behavioral features was collected. Mann-Whitney and Pearson's chi-squared were used.

Results: There were no differences between groups in terms of gender identity, education, marital status, family history of mental disorders and suicidal behavior, history of physical violence, bullying, sexual behavior, drugs use experience, smoking, eating disorders, piercing, tattoos, severe body modifications (al:p>0.05). Significantly lower number of PWE had a history of sexual abuse (10/40vs36/80; $\chi^2=4.51$, p=0.03) and homosexual experience (5/40vs23/80; $\chi^2=3.93$, p=0.04). Regarding suicide plan, SA, non-suicidal self-injury (NSSI), age at onset of SI, first SA and first NSSI as well as number of SA no differences were found between groups (al:p>0.05). Suicide gestures were significantly less prevalent in PWE (4/40vs32/80; $\chi^2=11.42$, p<0.001).

Conclusion: Patients with NPMD share many common features for suicide, but a history of sexual abuse and homosexual experience as well as suicide gestures are less prevalent in PWE.

Disclosure: Nothing to disclose

EPO2147

Alteration of brain oxygen metabolism triggered by the interictal epileptiform discharges (IEDs) in patient with primary generalized (PGE) epilepsies. Assessment of Blood Oxygenation Level Dependent (BOLD) signal changes - EEG-fMRI preliminary study

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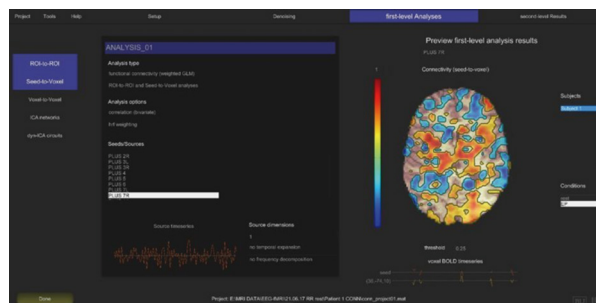
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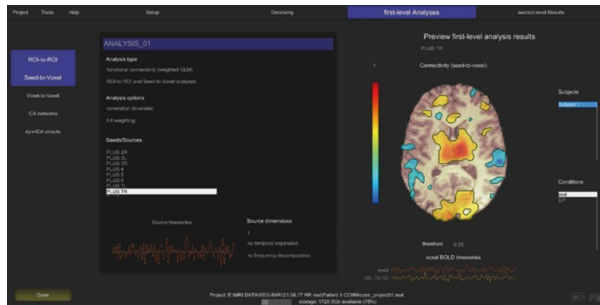
Background and aims: IEDs are the phenomena that occur in patients with PGE without evident clinical manifestations. Little is known about its pathophysiological importance. There are no conclusive data on how much IEDs may affect brain metabolism and whether or not they require more intensive antiepileptic treatment. We hypothesize that IEDs may influence brain metabolism in epileptic foci and in distant brain regions and affect resting brain functional network connectivity (FNC).

Methods: We have analyzed 5 patients with PGE. Simultaneous EEG and fMRI recordings were used to evaluate BOLD signal changes during IED's. For each patient three 10 min resting state runs were acquired with 3T GE Discovery MR750w scanner and 64-channel Neuroscan EEG. IEDs events were detected by neurophysiologist from EEG recordings and subsequently used as an event onset times in General Linear Model (GLM) in fMRI analysis. Additionally FNC with thalamus was calculated with CONN toolbox between rest and IEDs condition.

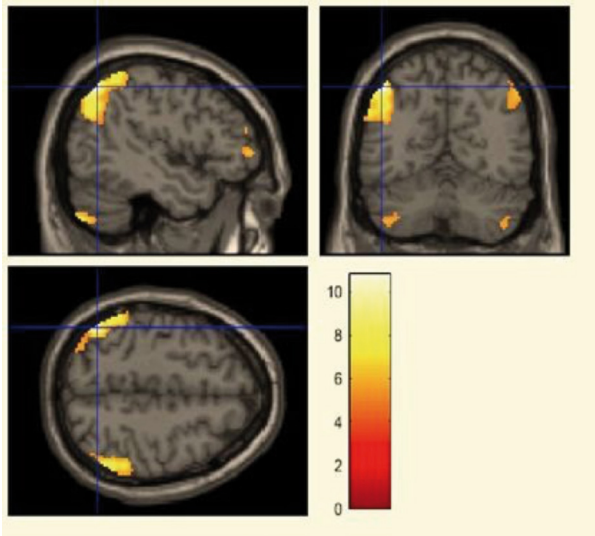
Results: In patients with PGE during IED's we identified regions (parietooccipital junctions and cerebellum) of significant reduction of BOLD signal that may be secondary to the hypoperfusion or metabolism reduction. The analysis of FNC revealed significant disturbances between thalamus and visual and frontal cortex connectivity resulting in negative correlation of the thalamus activity and frontal regions and loss of correlation with visual cortex.



Functional network connectivity of thalamus and other brain regions during IEDs



Functional network connectivity of thalamus in resting condition



Regions of negative BOLD signal during IEDs

Conclusion: During repetitive IEDs some brain regions have altered oxygen metabolism and brain resting mode connectivity is disturbed. These changes may contribute to long term complication of epilepsy such as cognitive function decline and attention deficits.

Disclosure: Nothing to disclose

EPO2148

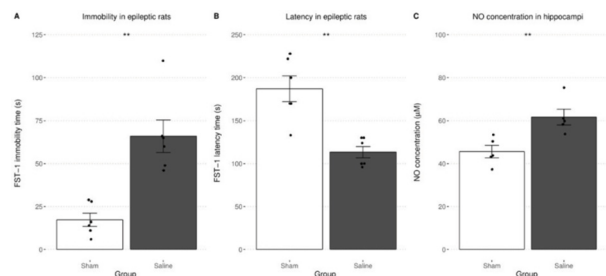
Overcoming Resistance to Fluoxetine in a Rat Model of Epilepsy-associated Depression by Suppression of Neuronal Nitric Oxide Synthase (nNOS)

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Background and aims: Depression is the most frequent psychiatric comorbidity of epilepsy. Increased nitric oxide (NO) levels in the hippocampi of epileptic rats has been linked to neuronal cell damage, possibly leading to the development of depressive symptoms. Unfortunately, epilepsy-associated depression is commonly resistant to conventional SSRI treatments. Therefore, we hypothesized that inhibition of the nitrergic system may augment the treatment efficacy of such SSRIs.

Methods: Epilepsy was induced in rats using the pilocarpine status epilepticus (SE) model. 45 days after SE induction, development of depression was verified by measurement of latency and immobility times in the forced swim test (FST-1). Following verification, the animals underwent a 10-day treatment regimen of either chronic fluoxetine (Flxc) or saline, followed by a second FST (FST-2) on the 10th day. A single dose of one of the following treatments was also administered 30 minutes prior to FST-2: acute fluoxetine (Flxa), 7-NI, Flxa + 7-NI, or saline. The effectiveness of treatment types was assessed using 2-way ANCOVA. Furthermore, the hippocampi were extracted following FST-2 for molecular analysis.

Results: NO concentrations were increased in the hippocampi of post-SE rats concurrently with the presentation of depressive symptoms. Of all the single and combination therapies, only Flxc+7-NI treatment significantly reversed depressive behaviors in FST-2 in post-SE rats. This improvement corresponded to increased expression of cFOS and BDNF mRNAs in the hippocampi.



Evaluating depression in post-SE rats (Saline) compared to the pilocarpine-naïve rats (Sham) in FST-1. (A & B) Immobility times were increased and latency to 1st immobility times were decreased in the Saline group. (C) NO concentrations in hippocampal tissue were increased in the Saline group.

EPO2149

Analysis of Patients with Nonconvulsive Status Epilepticus required videoEEG monitoring in the Intensive care Unit

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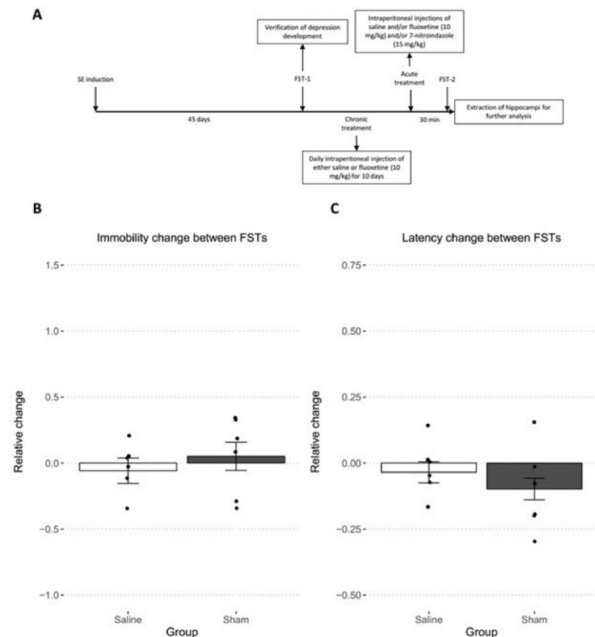
Background and aims: Nonconvulsive status epilepticus (NCSE) is diagnosed in critically ill patients with increasing frequency. NCSE can lead to neuronal damage and is associated with neurological deterioration and increased morbidity and mortality, especially with delayed treatment. Our study aimed to evaluate the clinical predictors of poor clinical outcome in NCSE patients.

Methods: Retrospective monocentric analysis of patients with NCSE with prolonged continuous VideoEEG monitoring treated at comprehensive stroke centre intensive care unit from January 2013 to June 2019. Analysed parameters were categorised by phenomenology, treatment, EEG patterns, NIHSS, age, medical history, morbidity, trigger and acute and chronic lesion. All analysed patients met Salzburg consensus criteria for NCSE. Favourable functional outcome at discharge was defined as mRS 0-2, poor outcome as mRS 3-6.

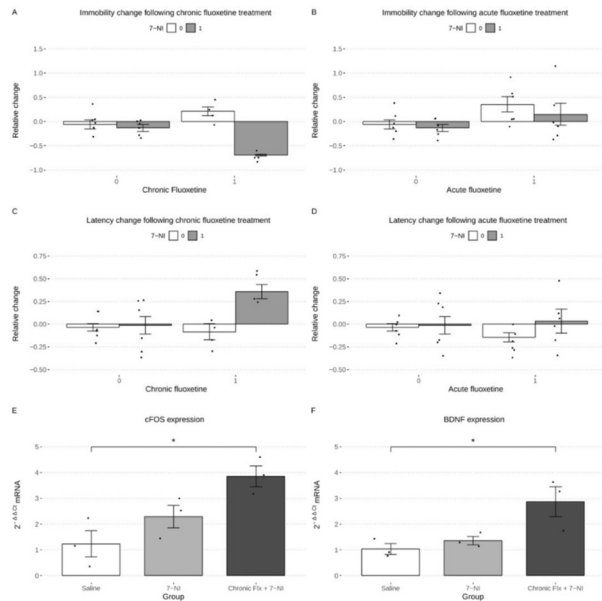
Results: 46 patients, 21 (45.7%) men, mean age 63.9 years were included. Mean NIHSS on admission was 9.7, duration of NCSE was 13.6 days, time of hospitalisation was 25 days. Good outcome at discharge occurred in 14 (30.5%) patients. Poor outcome was 32 (69.5%) including 13 (22.2%) deaths. All patients with positive symptoms (e.g. rhythmic twitching of one or more muscle groups, tonic eye deviation, hippus or nystagmoid eye jerking) had poor outcome (p=0.026). Predictors for the poor outcome were atrial fibrillation, ischemic heart disease and history of stroke.

Conclusion: The phenomenology of NCSE was demonstrated as the only significant predictor in our cohort. Our findings warrant detailed clinical follow-up of patients with NCSE for subtle signs.

Disclosure: Nothing to disclose



Evaluating the possible behavioral effects of the study design in the Sham and Saline groups. (A) The experimental timeline. (B & C) Relative changes in immobility and latency times between FST-1 and FST-2 calculated as (FST-2 – FST-1)/FST-1 following chronic and acute saline treatment. All changes were statistically insignificant.



Assessing the effect of different treatment regimens on post-SE depression. For each treatment, 1 indicates administration and 0 shows no administration. (A - D) Relative changes in immobility and latency times between FST-1 and FST-2. (E - F) BDNF and cFOS mRNA expression in hippocampal tissue.

Conclusion: Inhibition of nitric oxide production may be a plausible way of countering resistance to SSRIs in epilepsy-associated, and possibly other types of, depression.

Disclosure: Nothing to disclose

Headache and pain 2

EPO2150

Could metabolic syndrome and insulin resistance have a role in frequency and severity of migraine headache attacks?

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Background and aims: The relationship between migraine headache and both metabolic syndrome and insulin resistance is still a matter of debate. Controversy exists regarding the presence of specific characteristics for migraine headache in patients with metabolic syndrome or insulin resistance. The aim of this work was to detect the frequency of metabolic syndrome and insulin resistance in patients with migraine headache and to study their impact on frequency and severity of migraine headache attacks.

Methods: This is a case-control study that was conducted on 30 patients diagnosed as having migraine headache and 30 healthy controls. History regarding migraine headache characteristics was taken from all included patients. Assessment of migraine was done using Migraine severity scale (MIGSEV) and Headache Impact Test-6 (HIT-6). Fasting blood glucose, fasting insulin level, lipid profile and Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) were measured for all included patients and controls.

Results: Patients with migraine headache had significantly higher fasting insulin level (p-value=0.049) and HOMA-IR (p-value=0.01) than controls. The frequency of metabolic syndrome and insulin resistance was higher in migraine patients compared to controls (p-value=0.024, 0.012). There were statistically significant positive correlations between both fasting insulin level and HOMA-IR and frequency of headache attacks/month (p-value <0.001, <0.001), MIGSEV severity grade (P-value=0.003, <0.001), and HIT-6 scale (p-value=0.031, <0.001).

Conclusion: The incidence of both metabolic syndrome and insulin resistance is higher in patients with migraine headache than healthy controls, and their presence significantly affect frequency and severity of migraine headache attacks.

Disclosure: Nothing to disclose

EPO2151

Lower glucose level associated with increased risk for post-dural puncture headache

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Background and aims: Post-dural puncture headache is the most common significant adverse event following lumbar puncture. In this study, we investigated the possible systemic factors associated with risk for post-dural puncture headache

Methods: We consecutively enrolled 969 patients who underwent diagnostic lumbar puncture following a standardized protocol. We compared the clinical and laboratory profiles of the post-dural puncture headache group and the non-headache group. Logistic regression analysis was conducted to identify any independent associations with post-dural puncture headache.

Results: A total of 48 patients (5%) reported headache; 12 of these patients (25%) received a therapeutic epidural blood patch (and the remaining 36 patients improved with conservative treatment. After adjusting for other variables, younger age and lower serum glucose levels were independently associated with post-dural puncture headache, whereas other factors showed no statistical significance. Serum glucose levels were persistently lower in all age groups of patients who experienced headache

Conclusion: Low glucose levels were inversely associated with risk for post-dural puncture headache. Patients with low serum glucose should be carefully monitored for headache after lumbar puncture.

Disclosure: Nothing to disclose

EPO2152

Improvements in Headache-related Disability With Fremanezumab in Patients ≥ 60 Years of Age With Migraine: Pooled Results of 3 Randomised, Double-blind, Placebo-controlled Phase-3 Studies

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Background and aims: Migraine is one of the leading causes of disability worldwide in patients of all ages. Fremanezumab, a fully-humanised monoclonal antibody (IgG2 Δ) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for preventive treatment of migraine in adults. The impact of fremanezumab on headache-related disability in a subgroup of patients ≥ 60 years of age was evaluated in this pooled analysis.

Methods: This analysis of fremanezumab in patients ≥ 60 years of age with episodic migraine (EM) or chronic migraine (CM) included data from three phase-3 trials (HALO EM, HALO CM, FOCUS), in which patients were randomised 1:1:1 to subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Improvements in headache-related disability, as measured by reductions from baseline in the 6-item Headache Impact Test (HIT-6) score (FOCUS and HALO CM) or Migraine Disability Assessment (MIDAS) score (FOCUS and HALO EM), during the 12-week double-blind treatment period were evaluated.

Results: HIT-6 scores were analysed for 177 patients ≥ 60 years of age and MIDAS scores were analysed for 162 patients ≥ 60 years of age. Baseline HIT-6 and MIDAS scores were similar across treatment groups (Table). Reductions from baseline in the HIT-6 and MIDAS scores over 12 weeks of treatment were greater with both fremanezumab dosing regimens versus placebo, with significant differences for monthly fremanezumab versus placebo ($p < 0.01$; Table).

Conclusion: Pooled data from three phase-3 trials demonstrate that fremanezumab treatment over 12 weeks improved headache-related disability in patients ≥ 60 years of age with EM or CM.

EPO2153

Comparison of Magnesium, Sodium Valproate, and concurrent Magnesium-Sodium Valproate therapy in prevention of migraine headache: a randomized, double-blind study

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Background and aims: This study is aimed to access the efficacy of combination magnesium - sodium valproate compares with either magnesium or sodium valproate alone for migraine prophylaxis.

Methods: In a randomized, double-blind, clinical trial, 222 migraine patients aged 18-65 years were randomly assigned sodium valproate (A group, n= 82), magnesium- sodium valproate (B group, n= 70), or magnesium (C group, n=70). The characteristic of migraine headache (severity, frequency, number of attacks, duration of the attack and the number of painkillers taken per month were recorded monthly in each visit. MIDAS and HIT-6 scores were recorded at baseline and after 3 months of treatment in each group. Within and between-group analyses were done in this study.

Results: A significant reduction in all migraine characteristics in all groups ($p < 0.05$). Intragroup data analysis indicated there was no statistically significant difference in headache frequency between A and B group but three other parameters show a significant reduction in B compared with A ($p \leq 0.001$). Conversely, the C group cannot effectively reduce measured parameters in the patient as compared to A and B groups ($p \leq 0.001$). MIDAS and HIT-6 scores were significantly lower in all treatment groups in comparison with baseline ($p < 0.05$). Also, MIDAS and HIT scores were diminished similarly in the A and B group and they have a significant difference with the C group ($p < 0.05$).

Conclusion: This study demonstrates that magnesium could enhance anti-migraine properties of sodium valproate in combination therapy and reduced the valproate dose required for migraine prophylaxis.

Disclosure: Nothing to disclose

Table. BL Scores and Changes From BL in Headache-related Disability Scores in Patients ≥ 60 Years of Age During 12 Weeks of Double-blind Treatment

	Placebo (n=57)	Quarterly fremanezumab (n=61)	Monthly fremanezumab (n=59)
HIT-6			
BL score, mean (SD)	63.3 (5.46)	62.9 (5.11)	63.1 (5.20)
Change from BL, LSM (SE)	-2.7 (0.92)	-4.3 (0.89)	-6.8 (0.94)
Change from BL, LSMD (SE) versus placebo	—	-1.6 (1.15)	-4.2 (1.17) ^a
MIDAS			
BL score, mean (SD)	43.2 (44.92)	52.0 (41.58)	40.9 (42.16)
Change from BL, LSM (SE)	-11.0 (3.85)	-21.7 (4.37)	-24.0 (3.56)
Change from BL, LSMD (SE) versus placebo	—	-10.7 (5.40)	-13.0 (4.53) ^a

BL, baseline; LSM, least-squares mean; SE, standard error; LSMD, least-squares mean difference; HIT-6, 6-item Headache Impact Test; Migraine Disability Assessment, MIDAS.

^a $P < 0.01$ versus placebo.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPO2154

Cavernous malformation with ipsilateral headache like hemicrania continua.

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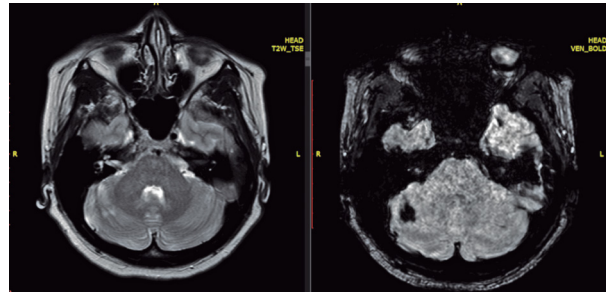
Background and aims: Hemicrania Continua refers to primary headaches classified as trigeminal autonomous cephalgia. According to the international classification of headache disorders 3rd edition, it is characterized as prolonged unilateral pain with autonomic symptoms and sensitive to treatment with indomethacin.

Methods: we present 2 clinical cases.

Results: 1. A man of 24 years without previous medical history. Appealed due to persistent left-sided headache with nasal congestion and lacrimation without nausea or vomiting. The pain was rated at 7 out of 10 by visual analog scale (VAS). The pain bothered for more than 30 days for 3 months. On examination, the neurological status is normal. MRI revealed a small cavernous malformation in the left temporal lobe.

2. Woman 33 years old. At the age of 13, she suffered a subarachnoid hemorrhage. Appealed due to a new persistent headache in the right part of the head for 4 months. Pain rated at 8/10 VAS. During the examination, slight swelling of the right half of the face, anisocoria D>S. An MRI revealed cavernous angioma in the left temporal lobe and left cerebellar hemisphere.

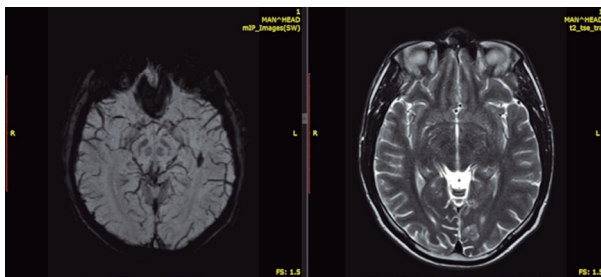
In both patients, pain regressed after taking indomethacin 150mg/day.



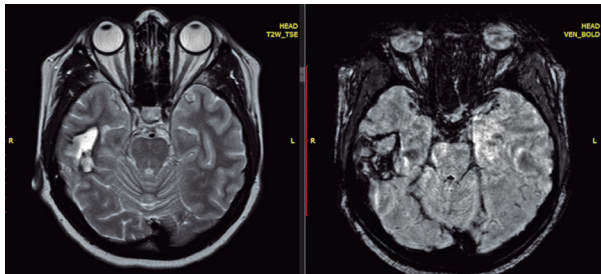
Woman MRI T2 and SWI

Conclusion: There are described cases of cluster headache with ipsilateral cavernomas. Perhaps there may be a connection in the development of trigeminal autonomous cephalgia and cavernous angiomas.

Disclosure: Nothing to disclose



Man MRI SWI and T2



Woman MRI T2 and SWI

EPO2155

Does postdural puncture headache influence the clinical course of previous chronic headache? One-year follow-up study

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Background and aims: The incidence of postdural puncture headache (PDPH) in relation to the pre-existing chronic headache (CH) was assessed as well as the effects of PDPH on the clinical course of CH (days with headache per months, duration of attacks, efficacy of therapy) 3, 6 and 12 months after PDPH.

Methods: The study was conducted as a single center, cohort prospective study which included 252 patients (105 men and 147 women), average age of 47.3±15.0 years, in which lumbar puncture (LP) was performed with traumatic needles of different caliber (20G vs. 18G, p=0,167).

Results: PDPH was reported in 133 (52.8%) patients. In the studied group, 82 (32.5%) patients had CH. Patients with CH were more likely to have PDPH (p=0.003). The individual clinical type of CH did not have an effect on the incidence of PDPH (p=0.128). Patients with PDPH and CH had a clinical deterioration of CH after 3, 6 and 12 months of LP in terms of higher days per months and/or incomplete efficacy of performed therapy regarding baseline values (p=0.047, p=0.027, p=0.030, respectively). Multivariate analysis confirmed the direct association of female sex and duration of CH and worsening of CH after 12 months of LP (OR 4.785 [95% CI: 1.248-14.322], p=0.033; OR 1.788 [95% CI: 1.332-1.988], p=0.032).

Conclusion: The presented results can be significant for the prediction of PDPH occurrence in patients having CH and for the prevention of clinical worsening of CH in patients having PDPH.

Disclosure: Nothing to disclose

EPO2156

Habituation study in visual evoked potentials in migraine patients with Ehlers-Danlos syndrome, hypermobility type

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Background and aims: Migraine is one of the most frequent clinical manifestations in Ehlers-Danlos syndrome, hypermobility type (hEDS). The comorbidity between these 2 diseases has been only partially investigated. The aim of our study was to observe whether neurophysiological alterations described in migraineurs in visual evoked potentials (VEP), namely habituation deficit, were present in hEDS migraineurs.

Methods: We enrolled 22 hEDS migraineurs with and without aura (according to ICHD-3 criteria), 22 non-hEDS migraineurs with and without aura, and 22 healthy controls (HC) matching gender and age. Repetitive pattern reversal (PR) stimulation in basal conditions was studied in all participants. During uninterrupted stimulation, 250 cortical responses were recorded (4000Hz sample rate) and divided into epochs of 300ms after the stimulus. Cerebral responses were divided in 5 blocks. We expressed habituation as the amplitude change (%) between the 1st and the 5th block of averages in N75-P100 and P100-N145 components of PR-PEV.

Results: We observed a trend towards a habituation deficit in both components of PR-PEV in non-hEDS migraineurs compared to HC. Unexpectedly, we observed a significant habituation deficit in hEDS migraineurs compared to HC in the P100-N145 component of PR-VEP (respectively Δ 93.44%±167.30 vs -11.00%±27.77, p = 0.011).

Conclusion: The PR-VEP habituation deficit in the P100-N145 component observed in hEDS migraineurs might be explained by functional alterations of extrastriate cortical areas in relation to the chronic pain experienced by these patients due to the underlying disease. Functional neuroimaging studies are needed to confirm this hypothesis.

Disclosure: Nothing to disclose

EPO2157

Medication overuse Headache: Clinical features and treatment approach

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Background and aims: Medication Overuse Headache (MOH) is defined as a complication of another primary headache. The level of evidence to support different treatment strategies (early discontinuation alone vs discontinuation plus preventive treatment) is still low. Our aim is to describe patients' characteristics and evaluate the response to different strategies.

Methods: Retrospective analysis of the clinical features of patients diagnosed with medication overuse headache attended for the 1st time in a Headache Clinic from May 2017 to April 2018. Clinical outcome over 3 successive visits and response to Onabotulinumtoxin A were assessed. Response is defined as $\geq 50\%$ reduction of headache days from baseline.

Results: 51 patients with MOH were included. 46 (88%) were women, with a median (IQR) age of 47 (14). 10 (19.6%) patients had opioid overuse and 13 (25%) were smokers. 22 (43.1%) had psychiatric comorbidities. The main associated primary headache was chronic migraine (CM), diagnosed in 37 patients (72.5%). 26 patients were treated with Onabotulinumtoxin A at first visit. Compared to those who received withdrawal strategy alone, patients who were treated with Onabotulinumtoxin A presented higher response rate (22.2% vs 50%, $p=0.147$)

Conclusion: Our results suggest that discontinuation of the overused medication with the addition of Onabotulinumtoxin A could lead to a better outcome than discontinuation alone.

Disclosure: Nothing to disclose

EPO2158

Medical Cannabis in the Treatment of Patients with Trigeminal Neuralgia: An Ongoing Retrospective Study

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Background and aims: Presently, those clinically diagnosed with Trigeminal Neuralgia (TN) have few treatment options. With up to 50% of patients employing traditional pharmacologic approaches becoming refractory, surgical intervention is often the only remaining option. A growing body of evidence; however, suggests that medical cannabis (MC) is an effective option in treating a wide array of neuropathic pain syndromes including TN.

Methods: This retrospective chart review included patients clinically diagnosed with TN and were certified to use MC via New York State's Medical Marijuana Program. Patients were certified and followed in a neurologic outpatient setting in Buffalo, NY, USA.

Results: 85 patients (16=male, 69=female) with an average age of 60.5 years (range 33-93), were included in this study. Improvement in TN symptomology was self-reported by 87.1% of patients with the most common treatment modality being an oral tincture, which was utilized by 85.8% of patients. Type II chemovar products were most prevalent, with 77.65% of patients utilizing a 1:1 (THC:CBD) ratio. Adverse events (AEs) were reported by 30 patients (35.3%) with only 1 patient opting to discontinue MC treatment. The most common side effects were: fatigue, cognitive difficulty, dry mouth, and increased appetite. 30% of the 36 patients reporting opioid use upon initiation of MC treatment reduced their consumption.

Conclusion: This study suggests that MC is generally well-tolerated in the treatment of TN, with 87.1% of patients reporting improvement(s) in symptomology. While promising, future randomized placebo-controlled trials are needed to determine MC's place in a comprehensive treatment plan.

Disclosure: This study was supported by The Harry Dent Family Foundation, Inc., a 501(c)(3) Non-for-profit organization dedicated to supporting neuroscience research.

EPO2159

The use of Medical Cannabis in the Treatment of Neuropathies: An Ongoing Retrospective Study

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Background and aims: In recent years many governments have shifted their stance on the use of medical cannabis (MC) due to its wide array of medical benefits. With anti-inflammatory and neuroprotective properties MC presents as a probable option in the treatment of neuropathies, which, are estimated to affect more than 168 million individuals worldwide.

Methods: This retrospective chart review included patients clinically diagnosed with neuropathies and that were certified to use MC via New York State's Medical Marijuana Program. Patients were certified and followed in a neurologic outpatient setting in Buffalo, NY, USA.

Results: 265 patients (138=male, 127=female) with an average age of 60.3 years (range 22-95), were included in this study. Improvement in neuropathic symptomology was self-reported by 78.5% of patients with the most common treatment modality being an oral tincture, which was utilized by 83.4% of patients. Type II chemovar products were most prevalent, with 64.9% of patients utilizing a 1:1 (THC:CBD) ratio. Adverse events (AEs) were reported by 73 patients (27.5%) of which only 2 patients opting to discontinue MC treatment. The most common side effects were: somnolence, fatigue, and cognitive difficulty.

Conclusion: This study suggests that MC is generally well-tolerated in the treatment of neuropathies, with 78.5% of patients reporting improvement(s) in symptomology. While promising, future randomized placebo-controlled trials are needed to determine MC's place in a comprehensive treatment plan of those with neuropathies.

Disclosure: This study was supported by The Harry Dent Family Foundation, Inc., a 501(c)(3) Non-for-profit organization dedicated to supporting neuroscience research.

EPO2160

Semiology of Pain in Headache Diagnosis

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Background and aims: To describe the location and quality of pain and other associated symptoms and its relationship with the final headache diagnosis.

Methods: Observational retrospective study of 1st-time-attending patients of a Headache Unit between May 2017 and April 2018. Patients were diagnosed by a headache specialist of a 3rd level hospital following the International Classification of Headache Disorders 3rd edition.

Results: 360 diagnoses were made for a total of 283 patients. Mean age was 47.7±16.3 and 222 (78.3%) were women. Overall, migraine was the most common diagnosis, with 181 cases, representing the 64.6% of bilateral headache, 48.9% of side-locked pain and 88.6% side-shifting headache. Tension-type headache (TTH) represented 29.1% of bilateral pain. Trigeminal autonomic cephalgias (TAC) were responsible of 19.1% of side-locked headaches. Throbbing headache was most commonly diagnosed as TTH (35%), closely followed by migraine (34%). 61% of oppressive pain cases were classified as cervicogenic headache. Migraine represented 37% of this kind of pain and TTH, only 24%. Shock-like headache was most commonly described in neuropathies. Photophobia and phonophobia was most commonly seen in migraine, but it was also frequent in other headaches, particularly TTH. 10% of migraines, 26% of TTH and 64% of TAC showed trigeminal autonomic features. Psychomotor agitation was most common in TAC and worsening with Valsalva manoeuvre, in cervicogenic headache.

Conclusion: Migraine is the most frequent diagnosis in the Headache Unit and its semiology is fairly diverse. Symptoms traditionally associated to migraine may be present in other primary headaches and vice versa.

Disclosure: Nothing to disclose

EPO2161

Treatment response to erenumab in refractory migraine patients

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Background and aims: Recent randomised studies reported a positive effect of erenumab in migraine prevention. Aim of our study was to investigate real-life efficacy and safety of erenumab in refractory migraine patients.

Methods: Patients received erenumab 70mg monthly for 3 months. At month 3 (M3), the dose of erenumab was increased to 140mg following patients' response. Changes in monthly migraine days (MMD), intake of acute medications, 50% responders rate, Headache Impact Test (HIT-6) and Allodynia Symptom Checklist (ASC-12) scores were assessed at M3 and after 6 months of treatment (M6).

Results: 58 patients with a mean age of 51 were enrolled in the study. The MMD at baseline was 19 (SD 8.0). 41 patients had chronic migraine and 44 patients had medication overuse headache (MOH). Before starting erenumab, patients have tried an average of 5 preventives (range: 1-10). 17 patients received erenumab 140mg at M6. The MMD was reduced by 3.9 at M3 and by 5.0 at M6 ($p < 0.001$). The number of days of acute medication intake was reduced by 3.6 at M3 and by 5.3 at M6 ($p < 0.001$). At M6, a 50% or greater reduction in the MMD was achieved for 39% of patients. Mean HIT-6 and ASC-12 scores were reduced by 7.4 ($p = 0.002$) and 2.9 ($p = 0.03$), respectively, at M6. MOH was not confirmed in 29% of patients at M6. 25% of patients had side effects.

Conclusion: 6-month treatment of Erenumab is effective in reducing migraine severity and patients' disability in refractory migraine in a daily-life setting.

Disclosure: Nothing to disclose

EPO2162

Which treatment is considered most effective in the treatment of trigeminal neuralgia? A survey on 106 Spanish Neurologists

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Background and aims: European guidelines include a number of prophylactic therapies for Trigeminal Neuralgia (TN); however, evidence is limited for most of the treatments. Clinical experience might give some light about the perceived efficacy of the different options. We aim to analyze clinicians' personal opinion about which therapies are the most effective in the treatment of TN.

Methods: We invited Spanish Neurologists to complete an online survey (carried out by the scientific committee of the Spanish Society of Neurology) evaluating the top-3 most effective treatments for TN in their opinion. We gave them a list including all TN therapies mentioned in the official local guidelines. We describe frequency and percentage of each election.

Results: The survey was completed by 106 neurologists, 48.6% of them focused on headache disorders, with a mean of 11.4±8.4 years of experience and seeing a mean number of 6.8±6.8 TN patients per month. Participants listed 6 different drugs as the most effective TN treatment, being eslicarbazepine the most frequently mentioned (59.4%), followed by carbamazepine (22.6%) and baclofen (9.4%). 14 and 15 different drugs were selected as the 2nd and 3rd most effective. The most frequently listed 2nd choice were baclofen (19.8%), followed by lamotrigine (17.9%) and eslicarbazepine (13.2%). The most frequently selected drugs as 3rd choice were lamotrigine (17.9%), topiramate and levetiracetam (12.3% each).

Conclusion: Eslicarbazepine was judged as the most effective drug in TN treatment, however there was significant heterogeneity. The drugs that were considered as most effective do not coincide with the guidelines and evidence supporting these choices is limited.

Disclosure: Nothing to disclose

EPO2163

Use of onabotulinumtoxin A in the treatment of Trigeminal Neuralgia in Spain: a nationwide survey on 106 Spanish Neurologists

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Background and aims: Several oral prophylactic drugs can be used in Trigeminal Neuralgia (TN); however, some patients might experience adverse effects or be treatment resistant. Some authors have reported positive results with the use of onabotulinumtoxin A (onabotA). In this study we aim to describe the opinion and pattern of use of onabotA among Spanish Neurologists.

Methods: We invited all the Spanish Neurologists to complete an online survey about TN management carried out through the scientific committee of the Spanish Society of Neurology and specifically asking about the use of onabotA, frequency of use, preferred scheme, number of units and when they considered it.

Results: The survey was completed by 106 neurologists, 48.6% of them focused on headache disorders, with mean age of 43.2 ± 10.5 years and 48.1% of female participants. Mean monthly number of TN patients was described of 6.8 ± 6.8 patients. OnabotA was used in monotherapy by 39.6% and as add-on treatment by 56.6%. Frequency of onabotA use is represented in figure 1. Mean number of prior treatments was 2.4 ± 1.5 . Preferred injection scheme was creating a “mesh” for 56%, 26.6% of responders also used a personal scheme and 22.7% injected trigger points. The number of employed units ranged from 10 to 75. Contralateral side was also injected by 19.8% of responders. Half of the users estimated that onabotA benefited most of the patients. The most frequently experienced adverse event was facial weakness.

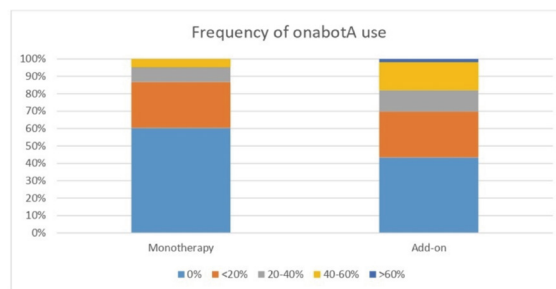


Figure 1. Frequency of onabotA use.

Conclusion: Onabotulinumtoxin A is considered for the therapy of treatment resistant TN patients by half of the Spanish neurologists, but the pattern of use is variable.

Disclosure: Nothing to disclose

EPO2164

The burden of migraine in the Netherlands: results from the My Migraine Voice survey

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Background and aims: The My Migraine Voice survey aimed to investigate the migraine patient's journey through the Dutch healthcare system as well as the functional, emotional and economic impact of migraine, with a focus on patients who suffered from at least 4 monthly migraine days and reported use of prophylactic medication.

Methods: The My Migraine Voice online worldwide survey was conducted in partnership with the European Migraine and Headache Alliance (EMHA) in 31 countries, including Netherlands, from September 2017 until February 2018. In the Netherlands, survey respondents were recruited via online panels and patient advocacy organizations. Study participants were adult patients (≥ 18 years) suffering from migraine. The survey investigated the patient journey, functional and emotional burden of migraine from the patient's perspective. Additionally, the impact of migraine on work productivity and activities during the past 7 days (prior to survey completion) was evaluated using the Work Productivity and Activity Impairment (WPAI) questionnaire. Descriptive survey results are presented and compared for 4 subgroups; prophylactic treatment naive, no prior prophylactic treatment failure (TF), 1 TF and ≥ 2 TF patient subgroups.

Results: A total of 340 Dutch people with migraine completed the survey. The results describe the patient's journey through the healthcare system and employment environment and demonstrate the often considerable social, emotional, functional and economic impact of migraine.

Conclusion: The Dutch results of the My Migraine Voice survey demonstrate that migraine is associated with a significant functional, emotional and economic burden. Results show a trend towards a higher burden as patients fail an increasing number of prophylactic treatments.

Disclosure: This abstract is fully funded by Novartis. The original publication is 'My Migraine Voice survey: a global study of disease burden among individuals with migraine for whom preventive treatments have failed. *J Headache Pain.* 2018; 19(1): 115.' This abstract is about the outcome of the Dutch survey data.

Motor neurone diseases 2

EPO2165

Neuroinflammation gene expression analysis in patients with amyotrophic lateral sclerosis

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Background and aims: There is growing evidence on the role of immune reactions in disease development and progression in ALS but it's still not clear whether they bring more benefit or harm and what are the most important immunological features during various stages of the disease. This study aimed to analyze the expression of a wide range of neuroinflammation genes in patients with different stages, progression rates and duration of ALS.

Methods: The study included 23 patients with ALS (PALS) and 12 healthy controls (HCs). Gene expression was examined in patients PBMC RNA using the Neuroinflammation gene expression panel consisting of 770 genes for the Nanostring nCounter platform. Data was processed with the nSolver Analysis Software 4.0 and compared with clinical features.

Results: 2 patterns of gene expression in PALS were observed which differed mostly on genes related to innate and adaptive immune response, autophagy, matrix remodeling, oligodendrocyte function and Wnt pathways. PALS with distinct patterns differed among themselves in the duration of the disease. Median disease duration was 16.5 months for pattern 1 and 33 months for pattern 2 ($p < 0.05$). Other clinical features such as age, stage and form of the disease, ALS-FRS-R scores, rates of progression were similar. Pattern 2 differed more significantly from the expression pattern observed in HCs.

Conclusion: 2 distinct patterns of neuroinflammation gene expression depending on disease duration but not stage or disease progression rate were detected in PALS.

Disclosure: Nothing to disclose

EPO2166

Synaptic proteins in neuromuscular synapses at the presymptomatic and symptomatic stages of pathology in ALS model

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Background and aims: Dysfunction of neuromuscular synapses is 1 of the earliest and most important events in the pathogenesis of amyotrophic lateral sclerosis (ALS). The aim of the present study is to investigate the molecular mechanisms of neuromuscular synapses dysfunction in ALS model. Presynaptic proteins, that mediate processes of synaptic vesicles recycling and its exocytosis, and neurotransmitter reception were studied for the 1st time. This study was supported by the Russian Science Foundation Grant #19-15-00329.

Methods: We have used transgenic mSOD1 (G93A) mice as a model of ALS. We used three groups of mice: mSOD1 mice at the presymptomatic and symptomatic stage of the disease, and wild-type mice as a control. The immunoexpression of synaptophysin, synapsin-1, SNAP-25, and nicotinic acetylcholine receptors was evaluated in the diaphragmatic muscle by the immunofluorescent method. Preparations of the diaphragmatic muscle were stained with primary and secondary antibodies. The preparations were studied on a confocal microscope. The fluorescence intensity and area of each protein in synapses were evaluated.

Results: A significant decrease in SNAP-25 and synapsin-I was found in the neuromuscular synapses of mSOD1 mice at the presymptomatic stage of pathology. In the symptomatic mSOD1 mice, the immunoexpression of all studied presynaptic proteins was markedly decreased, as well as a decrease in the degree of co-localization of the areas of expression of synaptophysin, and nicotinic acetylcholine receptors was shown.

Conclusion: The molecular aspects of neuromuscular synapses dysfunction in different stages of modeled ALS in mSOD1 mice were described, which expands our understanding of the mechanisms of the ALS pathogenesis.

Disclosure: Nothing to disclose

EPO2167

Treatment with nusinersen in adult patients with spinal muscle atrophy in Slovenia

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Background and aims: Nusinersen is the 1st approved drug for the treatment of spinal muscular atrophy (SMA). There is still lack of data about efficacy of treatment with nusinersen in adult SMA patients. So far, a few papers reported on feasibility, safety and some clinical effects of this treatment (Stolte, 2018, Bortolani, 2019, Walter, 2019, Veerapandiyam, 2019). We have started treating adult SMA patients in Slovenia in April 2019.

Methods: From the Register of neuromuscular disorders, all patients with genetically confirmed SMN1 (5q-SMA) were invited to receive treatment with nusinersen. Those who responded to the invitation were tested and divided in 6 groups according to their functional capabilities (Table 1). Patients with less disabilities were 1st to receive treatment.

Results: 44 out of 106 (42%) invited patients responded to the invitation letter. They were divided into functional groups (Table 1). First 27 patients with the best functional score were recruited for the treatment so far; however, 7 of them wished to postpone the beginning of treatment. Until January 2020, 20 patients (8 female) received between 1 to 8 nusinersen doses (Table 2). CT guided application was used in five patients.

Table 1 Patients who responded to invitation letter for treatment with nusinersen.

Group	Number of patients	Age (years)	Scoliosis operation	Non-invasive ventilation
1 (walking)	12	23-69	0	0
2 (walking with aids)	0			
3 (no gait, arms lifted to the head)	6	20-50	0	0
4 (no gait, arm movements but not reached to the head, VC>30% of predicted)	13	23-61	3	0
5 (no gait, distal arm movements, VC>30% of predicted)	7	24-66	5	3
6 (no gait, distal arm movements, VC<30% of predicted)	6	26-49	6	4

VC – vital capacity

Table 1 Patients who responded to invitation letter for treatment with nusinersen

Table 2 Adult SMA patients receiving nusinersen treatment

SMA type	Group	Number of patients	Age: median, range (years)	Disease duration: median, range (years)	Scoliosis operation, (number of pts)	CT guided administration, (number of pts)
SMA2	3, 4	4	22, 20-40	21, 19-36	3	3
SMA3	1, 3	16	42, 19-69	33, 4-53	0	2

Table 2 Adult SMA patients receiving nusinersen treatment

Conclusion: Intrathecal nusinersen can be successfully delivered in adult SMA patients, even in patients with severe scoliosis. Significant proportion of patients has not responded to treatment invitation. Some of those, who are interested in treatment, prefer to wait for further information before initiating treatment.

Disclosure: Nothing to disclose

EPO2168

Detection of speech dysfunction due to ALS based on acoustical analysis of sustained vowel phonation test

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Background: Detection and assessing of speech impairments associated with ALS using acoustical analysis of speech signal is actual theoretical and practical problem. Development of such analysis methods could significantly simplify and standardize procedure of assessing speech dysfunction of ALS patients and may also contribute to early diagnosis of ALS.

Aims: In this study we have assessed suitability of sustained vowel phonation test for detection of speech dysfunction related to ALS.

Methods: There are 4 groups of voice signal parameters obtained using fundamental frequency (fo) analysis have been considered: 1) jitters; 2) shimmers; 3) statistical parameters of fo; 4) time-frequency parameters of fo contour. For classification of feature vectors to normal/pathology groups 2 approached have been used: 1) linear discriminant analysis and 2) k Nearest Neighbors (kNN). Accuracy of classifiers was assessed using K-fold cross validation method (K=6).

Results: The voice data of 54 speakers (39 healthy controls (HC) – 23 males, 16 females and 15 ALS patients – 6 males, 9 females) used in this study was collected in Republican Research and Clinical Center of Neurology and Neurosurgery (Belarus). The average age in HC group was 41.9 years, in ALS group – 57.7 years. Best classification results with 95.7% of accuracy (sensitivity 91.5% and specificity of 97.4%) have been obtained using kNN method.

Conclusion: We have presented an approach to automatic detection of bulbar ALS changes using acoustical analysis of speech signal with high levels of sensitivity 91.5% and specificity of 97.4%.

Disclosure: This study received the funding from the Ministry of Health of the Republic of Belarus.

EPO2169

SUNFISH Part 2: Efficacy and safety of risdiplam (RG7916) in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA)

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On Behalf Of The Sunfish Working Group¹⁵

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions and/or mutations of the SMN1 gene. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (RG7916) is an orally administered, centrally and peripherally distributed SMN2 pre-mRNA splicing modifier that increases the levels of functional SMN protein. Part 2 of the SUNFISH study (NCT02908685) aims to determine the safety and efficacy of risdiplam in patients with Type 2 or non-ambulant Type 3 SMA.

Methods: SUNFISH is a multicentre, 2-part, randomised, placebo-controlled, double-blind study (randomised 2:1, risdiplam:placebo) in patients, aged 2–25 years, with Type 2 or Type 3 SMA.

Part 1 (n=51) is a dose-selection study assessing the safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam dose levels in patients with Type 2 and

Type 3 SMA (ambulant and non-ambulant); confirmatory Part 2 (n=180) assesses the safety and efficacy of the risdiplam dose level that was selected from Part 1 compared with placebo in patients with Type 2 and non-ambulant Type 3 SMA. The primary objective of Part 2 is to evaluate the efficacy of risdiplam compared with placebo in terms of motor function as assessed by the change from baseline in the 32-item Motor Function Measure total score at month 12.

Results: Here we will report data from SUNFISH Part 2 including baseline demographics, safety and novel efficacy data in participants treated with risdiplam or placebo for 12 months.

Conclusion: SUNFISH Part 2 is ongoing.

Disclosure: Study sponsored by F. Hoffmann-La Roche AG, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media, UK, in accordance with Good Publication Practice (GPP3) guidelines.

EPO2170

Role of routine Cerebrospinal Fluid (CSF) and serum parameters in adult 5q- SMA type 2/3 treated with Nusinersen: a prospective observational study

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Background and aims: The anti-sense oligonucleotide drug nusinersen was recently approved for spinal muscular atrophy (SMA). Our aim was to examine CSF routine parameters determining a prognostic marker for this treatment.

Methods: Consecutive SMA type 2-3 undergoing nusinersen were included in a single-center study. They were sampled for CSF and serum at baseline (T0), after loading dose (T1) and after one maintenance dose (T2). Serum/CSF albumin, oligoclonal IgG bands (OB), Neurofilament light chain (NFL), Tau, p-Tau, pTau/Tau, beta-amyloid 1-42 were evaluated. Motor function was assessed using HFMSE, RULM. Paired sample T-test and Pearson correlations were used.

Results: 9 patients whose clinical characteristics were described in Table 1 were recruited. BBB dysfunction was detected in 3 patients from T0 to T2 and in 1 more patient during the follow-up. Persistent OB systemic synthesis (OSS) were found in 4 patients from T0; 3 patients developed OSS in the follow-up; 1 patient had intrathecal OB from T0 to T2. Serum creatinine at T0 were much lower than normal values. Table 2 summarized serum/CSF parameters. HFMSE and RULM improved significantly between T0 and T1 (CI:95% p=0.032 and p=0.017 respectively). At T0 serum creatinine values strongly correlated to HFMSE and RULM, respectively r=0.93, p<0.001 r=0.799, p=0.001. Neuronal biomarkers did not correlate with functional scales at T0, T1 and T2.

Patients characteristics	Values
Number of patients	9
Age (mean ± SD), years	42,78 ± 13,95
SMA type 2:3	2:7
Disease onset (mean ± SD), years	6,89 ± 5,92
Gender male: female	6:9
HFMSE T0 (mean ± SD)	14,78 ± 20,87
RULM T0 (mean ± SD)	17,5 ± 13,89
HFMSE T1 (mean ± SD)	16,22 ± 20,87
RULM T1 (mean ± SD)	19,22 ± 14,08
HFMSE T2 (mean ± SD)	16,55 ± 22,01
RULM T2 (mean ± SD)	19,11 ± 14,24

Table 1 Clinical characteristics of SMA patients

Parameter	CSF	Serum	OB	CSF NFL (pg/ml)	CSF p-Tau (pg/ml)	Tau (pg/ml)	CSF p-Tau (pg/ml)	CSF p-Tau/Tau
T0	6,21 ± 0,8	5,91 ± 0,8	1 patient with intrathecal OB	39 patients with OSS	36,101 ± 13,636	27,023 ± 10,278	17,623 ± 10,342	36,123 ± 10,342
T1	6,28 ± 0,5	6,38 ± 1,0	3 patients with intrathecal OB	43 patients with OSS	32,28 ± 10,576	404 ± 12,018	18,6 ± 10,426	12,1 ± 0,927
T2	6,28 ± 0,8	6,40 ± 1,2	1 patient with intrathecal OB	43 patients with OSS	30,897 ± 10,837	39,665 ± 10,642	30,083 ± 10,42	10,87 ± 0,848

Table 2 Serum and CSF parameters in SMA patients (T0, T1, T2) (Oligoclonal antibody synthesis (OSS), Oligoclonal bands (OB))

Conclusion: In a mixed cohort of adult patients with SMA type 2-3, neuronal biomarkers did not have prognostic role during initial phase of treatment. The development of Ig-OSS related to the treatment need to be further confirmed.

Disclosure: Nothing to disclose

EPO2171

Sensory disturbances in the SOD1G93A murine model of ALS: the satellite glial cells as a new non-motor neuron target

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Background and aims: Several clinical and preclinical studies have shown sensory disturbances in both amyotrophic lateral sclerosis (ALS) patients and murine models of the disease. We aimed to evaluate sensory abnormalities in the transgenic SOD1-G93A mouse model of ALS, focusing on the satellite glial cells-sensory neuron functional units (GCSNFU) as a potential non-motor neuron target of the disease.

Methods: 24 SOD1-G93A transgenic and 24 control mice were used in the study. The presence of sensory disturbances was evaluated with specific sensory tests. Additionally, cell biology analysis was carried out at days 75 and 95, including conventional histology, immunofluorescence and electron microscopy on mechanically dissociated GCSNFU and tissue samples of sensory ganglia. Complementary biochemical analysis with western blot and qPCR were performed at day 95 of age.

Results: By day 75 of age, von Frey and hot plate tests demonstrated clear sensory disturbances in ALS transgenic mice in comparison with control mice. Histological studies demonstrated that in the transgenic mice the sensory neurons had a marked loss of glial coating. In addition, the GCSNFU had a severe accumulation of mutated SOD1 protein, enlarged lysosomal compartment and significantly increased levels of oxidative stress. Intriguingly, these alterations were much more pronounced within satellite glial cells than in sensory ganglion neurons.

Conclusion: In addition to the widely known motor symptomatology, SOD1G93A murine model of ALS, exhibit early sensory disturbances. In these alterations, the involvement of the GCSNFU, particularly of the satellite glial cells, seems to play an important role, thus emerging as a new target in ALS.

Disclosure: Nothing to disclose

EPO2172

ALS-derived fibroblasts exhibit reduced proliferation rate, cytoplasmic TDP-43 aggregation and a higher susceptibility to DNA damage

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Background and aims: Dermic fibroblasts have been proposed as a potential genetic-ALS cellular model. This study aimed to explore whether dermic fibroblasts from patients with sporadic-ALS (sALS) recapitulate alterations typical of ALS motor neurons and exhibit abnormal DNA-damage response.

Methods: Dermic fibroblasts were obtained from 8 sALS patients and 4 control subjects. Cellular characterization included proliferation rate analysis, cytoarchitecture studies and confocal immunofluorescence assessment for TDP-43. Additionally, basal and irradiation-induced DNA damage was evaluated by confocal immunofluorescence and biochemical techniques.

Results: sALS-fibroblasts showed decreased proliferation rates compared to controls. Additionally, whereas control fibroblasts exhibited the expected normal spindle-shaped morphology, ALS fibroblasts were thinner, with reduced cell size and enlarged nucleoli, with frequent cytoplasmic TDP-43 aggregates. Also, baseline signs of DNA damage were evidenced more frequently in ALS-derived fibroblasts (11 versus 4% in control-fibroblasts). Assays for evaluating the irradiation-induced DNA damage demonstrated that DNA repair was defective in ALS-fibroblasts, accumulating more than double of gH2AX-positive DNA damage foci than controls. Very intriguingly, the proportion of fibroblasts particularly vulnerable to irradiation (with more than 15 DNA damage foci per nucleus) was 7 times higher in ALS-derived fibroblasts than in controls.

Conclusion: Dermic-derived ALS fibroblasts recapitulate relevant cellular features of sALS and show a higher susceptibility to DNA damage and defective DNA repair responses. Altogether, these results support that dermic fibroblasts may represent a convenient and accessible ALS cellular model to study pathogenetic mechanisms, particularly those related to DNA damage response, as well as the eventual response to disease-modifying therapies.

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EPO2173

Impact of the disease on Quality Of Life in patients with Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a degenerative disease that involves progressive muscle weakness with gradual loss of physical abilities in which quality of life (QoL) can be a parameter of special interest in determining the effectiveness of Nusinersen administration in advanced stages. We analyzed the impact of this disease on the QoL of patients diagnosed with SMA types III and IV.

Methods: Structured interviews measuring the EuroQol-5D, SF 36, ALSFRS, mRs, Hamilton and PRISM scales in patients diagnosed with SMA in a third-level hospital prior to Nusinersen administration.

Results: We identified 9 cases (66.6% male and 33.3% female) with ratio III/IV of 7/2 whose median years of evolution was 29 and median age 40. Although 55.6% were unable to walk, the score at EuroQol was 0.67 and 55.5% reported having no problems in carrying out domestic activities. More than half of patients did not see interference from the disease in their social or emotional relationships. 77.7% did not report psychic symptoms and 66% had no pain or discomfort, data consistent with those obtained on the SF 36 and Hamilton scales, being these responses equitable in terms of ages and years of evolution.

Conclusion: QoL in SMA could be related to the ability to adapt to the degree of motor impairment, so that they retain as much functional independence as possible, rather than this one itself. Its emotional impact is less than expected by its motor impairments and does not seem to be strictly related to age or years of evolution.

Disclosure: Nothing to disclose

EPO2174

Objective and Subjective impact of Nusinersen in Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by degeneration and loss of spinal cord motoneurons leading to weakness and progressive muscular atrophy. Nusinersen's approval in June 2017 has opened a door to the treatment of this disease. We analyzed the objective and subjective impact of treatment in patients diagnosed with SMA III.

Methods: Structured interviews with measurement of subjective rating scales and Hammersmith (HFNSE), CHOP-Intend and RULM objective scales in patients diagnosed with SMA III in two third-level hospitals before and after the start of the treatment with Nusinersen.

Results: We identified 4 cases (1 male and 3 women) whose median years of evolution were 23.5 and the mean of age 35. 1 patient received 7 doses according to established protocol. 2 received 6 and 1 just four. 2 of them walked with support. The average improvement in HFNSE and CHOP-Intend was 1 point. Almost 2 points was achieved in RULM. The subjective improvement in health status was 40%, scoring an average of 2 on the EVA scale of satisfaction grade assessment (high degree). The areas of greatest improvement were the ability to perform activities and in problems with hands and feet, followed by mobility, fatigue, shortness of breath, weakness in the back, chest or abdomen and in problems in the hips, thighs or knees. There was no worsening in the other items evaluated.

Conclusion: Despite the short period of treatment, our patients experienced both objective and subjective improvement. Both should be taken into account in SMA therapeutic decision-making.

Disclosure: This research was suggested by Biogen.

EPO2175

Sensory nerve fiber involvement in amyotrophic lateral sclerosis (ALS)A. Rosenbohm¹, A. Calderaro¹, I. Katona², J. Weis², A.C. Ludolph¹¹Neurology, University of Ulm, Ulm, Germany,²Neuropathology, University Hospital RWTH Aachen, Aachen, Germany

Introduction: We investigated the involvement of sensory nerve fibers in ALS and compared small intraepidermal nerve fiber involvement in skin biopsies with quantitative sensory testing.

Methods: The cohort consisted of 51 patients with ALS (23 women, 28 men) according to the Revised El Escorial criteria. Sensory involvement was examined using neurography of the sural nerve, sensitive evoked potentials (SEP) of the tibial and median nerves, quantitative sensory testing (QST), and small fiber neuropathy in skin biopsy.

Results: Mild sensory symptoms including diffuse dysesthesias, paresthesias, and hypesthesia were inconsistently reported in patients. Skin biopsies could be evaluated in 44/51 patients. 63.6% showed small fiber neuropathy (SFN) in the biopsy. No significant correlation between SFN and onset type (bulbar, spinal), disease duration, age or ALSFRS-R could be detected. Histologically confirmed SFN cases were all detected in QST (n=28). Normal skin biopsies (n=16) had a pathological QST measurement in n=14 (87.5%) cases. When QST was completely normal, no SFN was detected in biopsy (n=2). When SFN was proven in the biopsy, QST measurement displayed an affection of A δ fibers in most of cases (86.4% versus C fibers 59.1% and A β fibers 41.0%).

Conclusion: These results indicate that small, distal epidermal nerve fibers are frequently involved in ALS, detected by skin biopsy. Noninvasive QST measurement of small sensible fiber involvement has a poor predictive value compared to skin biopsy since specificity is low. Fiber type involvement, especially A δ fibers, cannot be distinguished histologically due to lack of characterizing stainings.

Disclosure: Nothing to disclose

EPO2176

The Terminal Complement Pathway Is Markedly Activated in the Cerebrospinal Fluid and Plasma of Amyotrophic Lateral Sclerosis Patients

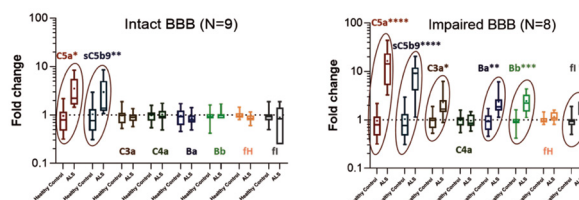
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Ra Pharmaceuticals, Cambridge, USA

Background and aims: Hyperactivation of the complement system is observed in several neurodegenerative diseases. Amyotrophic lateral sclerosis (ALS) is a progressive and fatal disease characterized by degeneration of motor neurons leading to loss of muscle action. In this study, we examine levels of complement activation markers in the cerebrospinal fluid (CSF) and plasma from ALS patients compared to healthy controls and investigate correlations of complement split-products with markers of blood-brain barrier (BBB) permeability, neurodegeneration and neuroinflammation.

Methods: We sourced commercially CSF and plasma samples from ALS patients and age-matched healthy controls (PrecisionMed). Analytes were measured using multiplex and singleplex ELISAs.

Results: C5a and soluble C5b-9 (sC5b-9), markers of terminal complement (TCC) pathway activation, were significantly elevated in both CSF and plasma of ALS patients versus age-matched controls. Using albumin-quotient (CSF/plasma) as a measure of BBB permeability, we demonstrate additional elevation of markers of the alternative activation pathway including C3a, Ba and Bb, in CSF of patients with impaired BBB (Figure 1). Interestingly, markers of classical or lectin activation pathway, but not alternative pathway, were observed in plasma. Finally, we examine the correlation of markers of axonal neurodegeneration (NFL and pNFH) and neuroinflammation (CHIT1) in CSF with TCC levels.



Whiskers indicate 5-95 percentile and "f" within boxes denotes mean. Albumin-quotient (Albumin-Q) was assessed by calculating the ratio of CSF to plasma human serum albumin levels. 8 of 17 ALS CSF patient samples (47%) showed Albumin-Q >9.0 indicating BBB impairment whereas only 1 of 14 healthy donors had an Albumin-Q >9.0. Data from all healthy controls were therefore included in both intact BBB and impaired BBB analyses. Statistical analysis performed using Kruskal-Wallis test; *p<0.05, **p<0.01, ***p<0.001

Figure 1: CSF of ALS patients with impaired BBB shows elevated activation markers of TCC and alternative complement activation pathway

Conclusion: These studies provide comprehensive characterization of the activation of the terminal complement pathway in ALS patients and support additional studies aimed at investigating the utility of these markers as potential pharmacodynamic and mechanism-specific

biomarkers in an upcoming multicenter ALS platform trial investigating zilucoplan, a convenient, subcutaneously self-administered macrocyclic peptide inhibitor of complement component 5.

Disclosure: All authors are employees and shareholders of Ra Pharmaceuticals

EPO2177

Amyotrophic lateral sclerosis and Curcumin: a double-blind, placebo-controlled clinical trial.

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Background and aims: Literature data show that oxidative stress plays an important role in amyotrophic lateral sclerosis (ALS) pathogenesis.

Methods: The current study was designed to determine whether curcumin oral supplementation (1500mg/day) may be efficacious in the treatment of ALS. Patients had a diagnosis of definite/probable ALS. Clinical parameters such as ALS-Functional Rating Scale (ALS-FRS), Medical Research Council (MRC), body mass index, and oxidative stress markers including oxidative protein products (AOPPs), ferric reducing ability (FRAP), total thiols (T-SH) and lactate, were evaluated, before and after 3 months of curcumin/placebo treatment.

Results: A total of 33 ALS patients were evaluated before the introduction of experimental therapy, a subgroup of 10 patients were reevaluated after 3 months of placebo/curcumin supplementation. Compared to controls, the whole ALS population showed a greater oxidative stress valued by increased AOPP ($p<0.001$), and decreased FRAP and t-SH ($p<0.001$) levels.

After 3 months of curcumin administration, a positive trend was observed regarding lactic acid levels that were improved, with a borderline p-value ($p=0.06$) with respect to placebo group. A small not significant difference was observed between groups, in AOPP, FRAP levels and in ALS-FRS and MRC scales.

Conclusion: Curcumin is a potent scavenger of reactive chemical species as observed in ALS mouse models. Related to this ongoing trial, the obtained results indicate a possible therapeutic effect of this compound in ALS, may be in add on or combined treatments, in any case worthy to be further studied on more consistent case histories as well as for a longer follow-up.

Disclosure: Nothing to disclose

EPO2178

Sema3E in CSF works as a diagnostic biomarker of amyotrophic lateral sclerosis (ALS)

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Background and aims: Increasing evidence suggest that hypo-perfusion/hypoxia in the spinal cord is deeply involved in the pathogenesis of ALS. We previously showed that novel prostaglandin I₂ agonist ameliorated the motor function of ALS model mice by mitigating hypoxia in the spinal cord of ALS mice (Tada et al., *Scientific Reports*, 9(1), 5252., 2019). Based on this result, we speculated that hypo-perfusion/hypoxia in the spinal cord could initiate ALS, and hypothesized that Semaphorin 3E (Sema3E), which suppresses angiogenesis, might be involved in the pathogenesis of ALS. In order to further elucidate the possible contribution of hypo-perfusion/hypoxia to ALS, we measured the concentration of Sema3E in the cerebrospinal fluid (CSF) of ALS patients and compare it with that of control patients.

Methods: We measured the concentration of Sema3E in the CSF of 11 ALS patients (8 males and 3 females, average age at collection; 67.1 years old) and 11 control patients (8 males and 3 females, average age at collection; 64.8 years old) by ELISA.

Results: The concentration of Sema3E in CSF of ALS patients was significantly increased compared to that of control patients (2311±448.2pg/ml and 1071±171.6pg/ml, respectively, average ± SD). A cutoff value of 1036pg/ml confirmed the diagnosis of ALS with the sensitivity of 63.6% and the specificity of 81.8%.

Conclusion: We showed here that the concentration of Sema3E in CSF is elevated in ALS patients, and it could serve as a diagnostic biomarker for ALS. Sema3E could be a therapeutic target in ALS by regulating hypo-perfusion/hypoxia in the spinal cord.

Disclosure: Nothing to disclose

EPO2179

Integrated Safety Report for Intravenous (IV) Onasemnogene Apeparvovec Clinical Development Programs in Spinal Muscular Atrophy (SMA) Type 1 (SMA1)

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Background and aims: IV onasemnogene apearvovec (formerly AVXS-101) gene therapy addresses the genetic root cause of SMA, survival motor neurone 1 gene (SMN1) deletion/mutation. This report describes the safety of IV onasemnogene apearvovec in SMA1 across 4 clinical trials.

Methods: Symptomatic or pre-symptomatic SMA1 patients (2–3xSMN2) received a single IV onasemnogene apearvovec dose. Adverse events (AEs) were assessed per Common Terminology Criteria for Adverse Events and monitored/reported in accordance with study protocols.

Results: As of 8 Mar 2019, 75 patients received IV onasemnogene apearvovec (therapeutic dose [1.1e14 vg/kg]; mean [SD, range] age: 2.5 [1.8, 0.3–7.9] months [mos]; weight: 5.33 [1.33, 3.0–8.4] kg). Two deaths were reported: patient aged 7.8mos, respiratory arrest 5.7mos post-treatment (unrelated to treatment); patient aged 6.8mos, hypoxic/ischemic encephalopathy and an acute illness. 64 (85%) patients reported ≥1 AE; 33 (44%) patients had treatment-related AEs; 29 (39%) patients had serious AEs. Vomiting and pyrexia have been reported as treatment-emergent AEs at rates of >5% in the clinical development program (considered treatment-related). Increased liver transaminase (>upper limit of normal): 8 (11%) patients (considered treatment-related, clinically asymptomatic, and generally resolved with prednisolone. Transient thrombocytopenia was reported, without clinically significant bleeding/bruising. There is no consistent evidence of cardiac safety concerns associated with onasemnogene apearvovec. Anticipated safety update: Q1 2020.

Conclusion: As of 8 Mar 2019, the IV onasemnogene apearvovec safety profile remains consistent with the United States package insert and continues to be monitored across multiple settings.

Disclosure: These studies were sponsored by AveXis, Inc., a Novartis Company.

EPO2180

Cerebrospinal fluid phosphorylated neurofilament heavy chain and chitotriosidase in primary lateral sclerosis

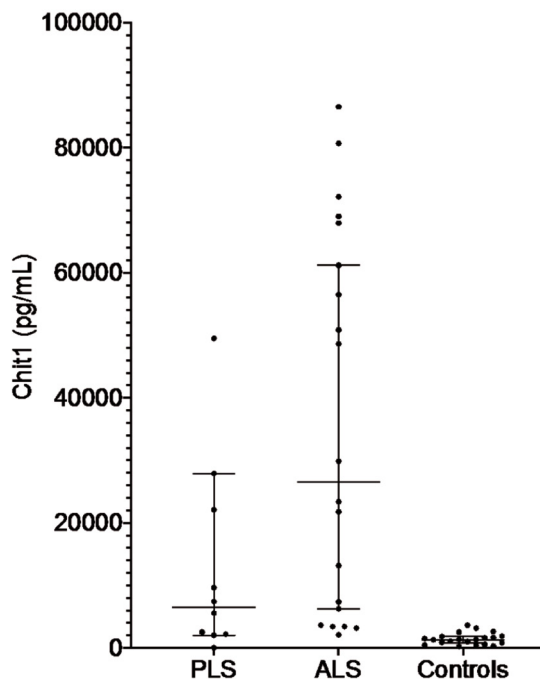
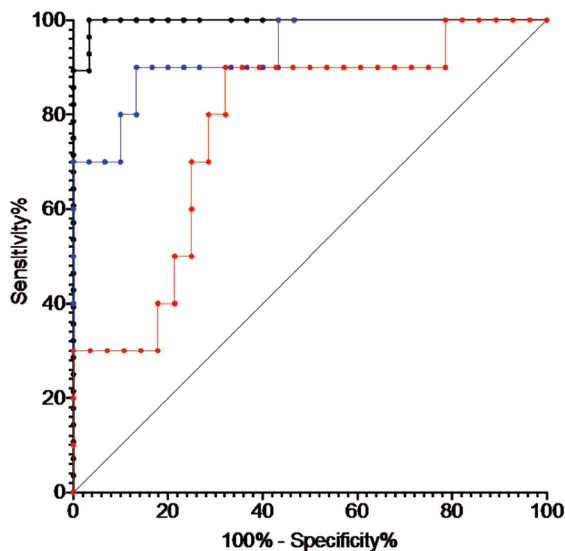
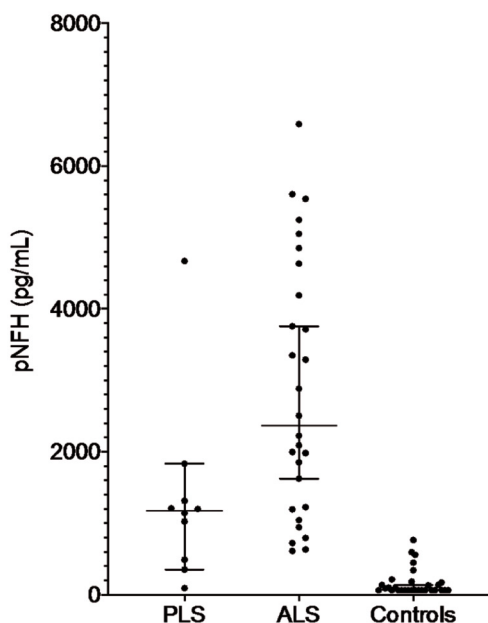
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Background and aims: The upper motor neuron disease primary lateral sclerosis (PLS) accounts for a small proportion of motor neuron disease cases. Early differentiation from ALS is difficult and there are no supporting biomarkers.

Methods: We measured the 2 ALS biomarkers phosphorylated neurofilament heavy chain (pNFH) and chitotriosidase (Chit1) in the CSF of 10 PLS patients, 28 ALS patients, and 30 controls.

Results: pNFH was significantly higher in ALS and in PLS patients in comparison with controls, but also higher in ALS vs. PLS (Figure 1). Accordingly, it discriminated between ALS and controls with AUC 0.996, between PLS and controls with AUC 0.933, and between PLS and ALS with AUC 0.77 (Figure 2; black, ALS vs. controls; blue, PLS vs. controls; red, PLS vs. ALS). Chit1 differed in a similar but weaker way between the same categories (Figure 3) (AUC for ALS vs. controls, 0.981; AUC for PLS vs. controls, 0.848; AUC for PLS vs. ALS, 0.74). pNFH was moderately correlated with progression rate in the ALS cohort ($r=0.529$), and ALS patients with higher levels displayed a shorter survival (HR, 4.95). Chit1 had a moderate correlation with progression rate in the entire MND cohort ($r=0.504$).



Conclusion: We confirm that pNFH and, to a lesser extent, Chit1 are promising diagnostic and prognostic biomarkers for ALS. Most importantly, we suggest a role for pNFH and possibly for wChit1 for the differentiation between PLS and ALS, which has important diagnostic, prognostic, and therapeutic implications.

Disclosure: Nothing to disclose

Movement disorders 4

EPO2181

Dystonia treatment with ultrasound-guided botulin toxin injection in a Niemann-Pick type C patient

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Background and aims: Niemann-Pick type C (NP-C) is a genetic and progressive disease characterized by an inability of the body to transport fatty acids inside the cells. Neurological symptoms are frequent in NP-C and include movement disorders such as dystonia, as well as psychosis and cognitive deficits. For dystonia treatment, ultrasound-guided botulin toxin (BT) injections allow for improved accuracy of the BT application, including the ones applied to deeper muscles, which are not easily accessible by palpation.

Results: A 27-year-old man, diagnosed with NP-C with neurological symptoms, namely a refractory epilepsy and generalized dystonia, was 1st examined on a movement disorders consultation because of a generalized dystonia. Since he had a progressive disease, he was not eligible for deep brain stimulation surgery and application of BT injections to the more affected dystonic muscles was started. He presented bilateral and persistent upper limb pronation and wrist flexion, beginning treatment with BT injections (50 Botox[®] units) in both flexor digitorum profundus muscles, showing a mild improvement. On a subsequent consultation, the same dose of BT was then applied to the pronator teres muscles, this time with an ultrasound-guided approach, leading to a much more significant improvement of the dystonic postures.

Conclusion: Through this case, we aim to show the benefit of ultrasound-guided BT injections in patients with NP-C disease associated dystonia. The application of BT to deeper muscles might show additional benefits, thus justifying the use of an ultrasound-guided approach for improved therapeutic success.

Disclosure: Nothing to disclose

EPO2182

Salivary proteome in Parkinson's disease

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Background and aims: Parkinson's disease (PD) is a progressive neurodegenerative disorders. Lewy pathology involves numerous organs. Submandibular glands are affected in about 75% of in vivo cases, with higher rates of positive findings in post-mortem histopathological studies. Salivary microbiome composition in PD patients is also different than in healthy controls. Therefore, saliva may serve as a promising source of biomarkers of PD.

Methods: 39 subjects (24 PD patients and 15 healthy controls) were recruited for the study. Saliva was collected 30 minutes after rinsing mouths with tap water, in morning hours, using RNA- Pro Sal kits. Samples were frozen immediately after collection in -80°C. Label-free LC-MS/MS mass spectrometry was performed to comprehensively characterize the proteome of saliva.

Results: A total of 530 proteins and peptides were identified. We observed 10-fold change in concentrations of protein S100-A16 in PD group vs healthy control. We also observed about 4-fold change in concentrations of proteins from annexin family: annexin A2 and annexin A8, and in resistin concentration in PD vs control. Due to variability of expression of these proteins, q-value <0.05 was not reached.

Conclusion: To our knowledge very limited data on salivary proteome of PD subjects is available. The results of our analysis indicate that salivary proteome of PD patients might be different that in healthy controls. This could be caused by oral inflammatory process, reflected by increased concentration of S100-A16 protein and resistin. The main limitations of the study are variability of expression of proteins between subjects in two groups and variations caused by external factors.

Disclosure: Research was funded by Medical University of Warsaw grant NZZ/PM1/17

EPO2183

Personality changes after deep brain stimulation for Parkinson's disease

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Background and aims: Parkinson's disease (PD) patients frequently experience difficulties in social adjustment, especially in family relationships after subthalamic nucleus deep brain stimulation (STN-DBS). The reason may be in personality changes after DBS.

Methods: We applied the Iowa Rating Scales of Personality Change (ISPC) questionnaire to 27 patients and their caregivers for evaluation of personality changes after DBS. ISPC is an instrument that allows retrospective evaluation of personality changes after medical procedure. It consists of five composite scales: 1. Executive Deficits; 2. Disturbed Social Behavior; 3. Diminished Motivation; 4. Emotional Reactivity and 5. Distress. We used the Wilcoxon signed-rank test for the statistical analysis of perceived differences in personality traits before and after the operation.

Results: By applying the ISPC questionnaire to caregivers to evaluate personality changes in patients before and after DBS operation we found significant worsening in 2 composite ISPC scales: 1. Executive Deficits (Mdn=3.05 vs. Mdn=3.61, $Z=-2.32$, $p=0.01$) and 2. Disturbed Social Behavior (Mdn=2.52 vs. Mdn=2.99, $Z=-2.00$, $p=0.02$). There were no changes on any of the ISPC scales when presented to the patients themselves. On the ISPC sub-scale for Impulsivity there was also a significant change after DBS (Mdn=3.07 vs. Mdn=3.85, $Z=-2.02$, $p=0.03$), but no change on the ISPC sub-scale for Apathy, both perceived by the caregivers

Conclusion: In contrast to the caregivers, patients did not perceive significant changes in their personalities after STN-DBS operation according to ISPC questionnaire. This result may reflect a lack of patients' insight and may be one of the causes for family frictions after otherwise successful STN-DBS operation.

Disclosure: Nothing to disclose

EPO2184

Deep brain stimulation of the subthalamic nucleus in advanced Parkinson's disease: life quality beyond 15 years of follow-upA. Gamaleya¹, S. Omarova¹, A. Tomskiy¹, E. Bril², V. Shabalov¹

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Background and aims: STN-DBS appeared to improve dramatically motor and nonmotor dopamine-sensitive symptoms in advanced PD-patients. However, a disease-modifying effect of STN-DBS was not proved and most of the patients deteriorate over time. We describe the longest follow-up after STN-DBS for PD-patients in our center.

Methods: In the 1st patient, PD manifested at the age of 32 years. He developed disabling dyskinesias soon after beginning of levodopa-treatment. Considering accompanying fluctuations, he underwent STN-DBS at 39 years (UPDRS-3 OFF/ON:46/19, LEDD:1200mg). The other man had a 9-year PD-history. By the age of 57 years, he suffered severe dyskinesias and motor fluctuations, hence he was assigned to STN-DBS (UPDRS-3 OFF/ON:42/13, LEDD:625mg). We assessed patients annually with maximal follow-up of 15 years.

Results: Following STN-DBS, we observed a significant amelioration of PD-symptoms in OFF-state and decrease in levodopa-induced complications in both patients. In the 1st patient, correction of right-electrode position was needed. By 8th-year of STN-DBS, patient retained moderate improvement in functioning and mobility in OFF-state, however, condition of ON-state deteriorated. By 15th-year, QoL deteriorated compared to preoperative (PDQ-39:112→139), though LEDD remained decreased by 33% and cognitive function preserved (MoCA:29). In the other patient, quality of ON-state got worsen after 10-year follow-up accompanied by progression in cognitive decline. By 15th-year, beside sufficient overall mobility, patient suffered pronounced dementia (MoCA:5) and became depend in most daily activities requiring admission to nursing home. LEDD remained reduced by a half.

Conclusion: Our observation demonstrates long-term effect of STN-DBS. Overall long-term outcome varies individually. Nevertheless, PD-progression with augmentation of dopamine-nonresponsive symptoms and cognitive decline over time remains challenging.

Disclosure: Nothing to disclose

EPO2185

Features of Parkinson's disease associated with mutation in the glucocerebrosidase A (GBA) gene in Russian population

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Background and aims: Mutation in the GBA gene is quite common among the patients with Parkinson's disease (PD). Its prevalence varies significantly in various populations. Pronounced cognitive decline is the most prominent feature of GBA+ PD.

Aim: To identify the prevalence of GBA gene mutation in patients with PD in Russia and assess its effect on disease course.

Methods: To assess prevalence, 506 PD patients were examined for 2 most common mutations in GBA gene (N370S, L444P). 2 groups were formed, comparable by gender, age, and duration of disease: the main group that had the mutation in GBA gene (as shown on screening + 10 with pre-identified mutation) and control group GBA-. Patients of both groups were assessed for parkinsonism symptoms severity (UPDRS), cognitive state (MoCA), presence of autonomic, psychotic disorders, RBD, motor fluctuations and dyskinesias.

Results: Of 506 patients with PD a mutation was only identified in 8 patients (prevalence of 1.85% in Russian populace). There was a lower score in the 3rd section of a scale UPDRS in GBA-PD group compared to control (31.3±12.8 vs 40.8±9.2 respectively), but patients of GBA-PD group demonstrated higher score in the 4th section of UPDRS (p<0.05). Cognitive state was comparable in both groups (MoCA 25.8±2.9 vs 24.8±3.6 respectively).

Conclusion: Mutation in GBA gene in Russian PD patients is rare with prevalence of 1.85%. GBA+ PD patients have more mild motor features but more prominent motor fluctuation and dyskinesias. Our data showed no influence of this mutation on cognitive state.

Disclosure: Nothing to disclose

EPO2186

Cerebellar ataxias: clinical and molecular description – a case series in a centre of Buenos Aires, Argentina

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Background: The new genetic diagnostic techniques allowed a huge knowledge expansion of hereditary ataxias. Classically, a regional distribution is described. There is a lack of a national registry in Argentina, with only case reports published in the literature.

Aim: To characterize a series of hereditary ataxias at a specialized centre of Buenos Aires, Argentina

Methods: Data was obtained from the medical records of 50 patients with diagnosis of ataxia. The positive molecular diagnosis was prioritized in order to typify the demographic and clinical characteristics

Results: 25 women and 25 men compose the sample, with a mean time of disease evolution of 3.18 years. 38% (n=19) had a positive family history. 22 patients agreed to the molecular study: SCA3 (9, corresponding to 4 families), SCA1 (1), SCA2 (4), SCA10 (1), Friedreich's ataxia (4), Episodic Ataxia type 1 (1); Stub 1 (1), FMR-1 (1). The predominant initial symptoms were gait instability and falls. A proportion of cases had another neurological sign (5.5%) with pyramidalism and lower limb polyneuropathy as the most frequent ones. Anti-GAD antibodies were identified in one patient with SCA2, with intravenous immunoglobulins positive response. A triplet expansion for Kennedy disease was identified in one member of a family with SCA3.

Conclusion: SCA3 was the most prevalent variant in our centre. Although the small sample we need to mention 2 unusual observations 1) the coexistence of genetic and immunomediated causes and 2) the presence of 2 different triplet expansions in siblings of the same family

Disclosure: Nothing to disclose

EPO2187

A Predominant Ataxic Syndrome in a Patient with both Huntington's Disease (HD) and Spinocerebellar Ataxia 35 (SCA 35)?

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Background and aims: SCA 35 is characterized by a slow, progressive course of trunk/limb ataxia and hand tremors. It has been associated with mutations in the transglutaminase 6 gene (TGM6), however the pathogenicity of TGM6 in SCA has been questioned.

Methods: Case report

Results: A 37-year-old caucasian woman presented with symmetrical and progressive upper limb postural and intentional tremor since the age of 25. 5 years later she complained of gait imbalance. By the age of 35, she started with voice tremor, slurred speech, and abnormal movements with twitching/tics and chorea affecting upper limbs, trunk and neck; and dystonic movements of the extremities. She has family history of tremor and gait imbalance from the father's side.

Neurological examination revealed mild executive impairment, increased latency in saccade initiation, slow saccadic movements, dysarthria, a pancerebellar syndrome with pyramidal signs; abnormal movements with mild chorea affecting the extremities, trunk and neck, twitching/tics of the trunk and neck, and dystonic posture of her left hand. Her scale for the assessment and rating of ataxia (SARA) score was 17/40.

Imaging studies showed diffuse cortico-subcortical and cerebellar atrophy. Blood tests revealed the presence of acanthocytes. Serum iron kinetics, serum and urinary copper, and ceruloplasmin levels were normal. Genetic testing revealed one HTT allele with 49 CAG repeats and a heterozygous frameshift mutation in the TGM6 gene with a possible deleterious effect.

Conclusion: This case may highlight the inflation of TGM6 mutations in its causation in SCA 35, despite the absence of typical imagiological findings of HD and the more predominant ataxic features.

Disclosure: Nothing to disclose

EPO2188

Detecting promoter methylation pattern of apoptotic genes as a key of inverse comorbidity of Huntington's disease and cancer

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Background and aims: Many of epidemiological studies have shown a lower than expected incidence of cancer in patients with Huntington's disease (HD). Such decrease of co-occurrence of 2 diseases in 1 person is called an inverse comorbidity. Molecular mechanisms of this phenomenon are still unknown. Cancer is characterized by evasion of apoptosis, while, HD is characterized by an increase of apoptosis. Thus, apoptosis is 1 of relevant biological pathways crucial for both pathologies. Of particular interest in this study is identification of apoptotic genes that can inhibit cancer in patients with HD.

Methods: Reconstruction of associative gene network was carried out using "ANDSystem" (Ivanisenko V.A., 2015). The gene network of HD included 140 genes/proteins which were prioritized by standard methods of gene prioritization (ToppGene) and special criteria of prioritization, integrated in ANDSystem, such as: betweenness centrality, closeness centrality, stress centrality, cross-talk specificity and cross-talk centrality (Saik O. et al., 2018).

Results: As a result of prioritization according to prioritization criteria, 10 genes with highest ranks were determined, including APOE, PSEN1, INS, IL6, SQSTM1, SP1, HTT, LEP, HSPA4, BDNF. The next step of analysis was a search of CpG islands. In 8 of 10 genes CpG islands were observed, except INS and IL6. CpG islands in promoter regions were determined for 5 genes, including: SQSTM1, SP1, HTT, HSPA4, BDNF.

Conclusion: Identified genes implicated in apoptotic pathways may be possible cause of inverse comorbidity of cancer and neurodegeneration disease. DNA methylation patterns requires a further research.

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Disclosure: Nothing to disclose

EPO2189

Anomalies of serum antibodies to nerve tissue antigens in Parkinson's disease (PD)

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Background and aims: The system of natural autoantibodies (auto-AB) is the basis of the functioning of the human immune system. Looking at its changes it is possible to judge the role of neuroinflammation in pathogenesis, including neurodegenerative diseases.

The aim was a multiparameter evaluation of abnormal autoantibodies content, reflecting the state of the nervous system microstructures in PD.

Methods: The study has been conducted on the basis of Rostov State Medical University clinic and included 139 patients with diagnosis of PD (main group) and 31-as a control. We have assessed the following indicators of autoimmune inflammation: AB to NF-200, GFAP, S100, MBP proteins, β -Endorphin, voltage-dependent-Ca-channel, Na-Choline, GABA, glutamate, dopamine, Mu-Opiate and serotonin receptors in blood serum using ELI-test kits. The significance of differences has been determined by the Mann-Whitney test (U), the correlations - by the Spearman correlation coefficient.

Results: We have revealed significant differences in the immunoreactivity profiles between the patients and the control (Table 1). At the early stage of the disease, we have found significant differences in the level of auto-AB to dopamine receptors compared with the control (U=79.5, p=0.01).

We have revealed the correlations of auto-AB values with the severity of non-motor symptoms (assessed by the NMSS-scale) and with the severity of motor disorders (on the third part of the UPDRS-scale) (Table 2).

Table 1. Differences of the immunoreactivity profiles between the patients and the control group (by the Mann-Whitney test)

Auto-AB parameters	U-test	p-value
GFAP	428	p \leq 0,01
Vd-CaChannel	221	p \leq 0,01
GABA-R	541,5	p \leq 0,01
Ser-R	449,5	p \leq 0,01
Mu-Opiate_R	506	p \leq 0,01
beta-Endorphine	462,5	p \leq 0,01
Glut-R	583	p \leq 0,05
DOPA-R	611,5	p \leq 0,05
NF200	529	p \leq 0,05

Table 1. Differences of the immunoreactivity profiles between the patients and the control group (by the Mann-Whitney test)

Table 2. The correlations of the clinical characteristics of the main group with the values of auto-AB (by the Spearman correlation coefficient).

Auto-AB parameters	NMSS point	UPDRS point
GABA-R	r = - 0,25 (p \leq 0,01)	-
DOPA-R	r = - 0,23 (p \leq 0,01)	-
Ser-R	r = - 0,23 (p \leq 0,01)	r = 0,24 (p \leq 0,05)
NF200	-	r = - 0,26 (p \leq 0,05)

Table 2. The correlations of the clinical characteristics of the main group with the values of auto-AB (by the Spearman correlation coefficient).

Conclusion: Thus, the autoimmune response has a specific character, which manifests itself in wide range of auto-AB, progressive changes depending on the stage of the disease, which may reflect destructive and inflammatory processes in the nervous system tissues.

Disclosure: Nothing to disclose

EPO2190

Possible Early Markers of Parkinson's Disease (PD)M. Gelpy¹, Z. Goncharova¹, O. Oksenjuk², A. Tanova²¹Department of diseases of nervous system and neurosurgery, Rostov State Medical University, Rostov-on-Don, Russian Federation, ²Rostov-on-Don, Russian Federation

Background and aims: No reliable serum markers still have been identified to diagnose PD in early stages. Along with studying the possible role of auto-antibodies to antigens of nervous tissue, it is important to study the role of inflammatory processes and free radical oxidation in the pathogenesis of neurodegenerative diseases, including PD. The aim was to reveal clinically significant markers of early diagnosis of PD.

Methods: The study was conducted on base of Rostov State Medical University Clinic on 139 patients with PD (main group), and 31-as the control. We determined the following parameters in blood serum: the total antioxidant activity (TAS), malondialdehyde's (MDA) level, small, medium, large, giant circulating immune complexes (CICs) and medium-weight molecules (MWM) at 254nm, 260nm and 280nm wavelengths on the Hitachi-U-2900 spectrophotometer. The significance of differences has been determined by the Mann-Whitney test (U), the correlations - by the Spearman coefficient.

Results: We revealed significant differences in neuroinflammation and endogenous intoxication profiles of patients and control, and the same - between the early-staged disease and control (Table1). When comparing the groups of early and late stages, significant differences were revealed in the MWM260 and TAS indices (U=147.5; U=137, respectively, p<0.05). The correlations of mCIC and TAS with the severity of motor disorders (on the third part of the UPDRS-scale) have been revealed (r=0.29; r=0.26 respectively, p<0.05).

Table 1. Differences of the neuroinflammatory and endogenous intoxication parameters between the patients and the participants of the control group (by the Mann-Whitney U-test), p<0,01

Parameters	Full main group	Early stage of PD
gCIC	301	52
mCIC	232	70,5
MDA	370,5	74
MWM 254	253,5	49
MWM 260	238	30,5
MWM 280	159,5	15
TAS	502	67

Differences of the neuroinflammatory and endogenous intoxication parameters between the patients and the participants of the control group (by the Mann-Whitney U-test), p<0.01

Conclusion: The revealed statistically significant changes in markers of neuroinflammation and endogenous intoxication in early stages of PD could be an argument for considering them the potential markers of early diagnosis of the disease.

Disclosure: Nothing to disclose

EPO2191

Voluntary posture control impairment in motor neuron disease and Parkinson's disease

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Background and aims: Balance impairment is a symptom of several neurodegenerative diseases.

Aims: To study voluntary control of vertical posture (VCP) in patients with Parkinson's disease (PD) and motor neuron disease (MND).

Methods: We studied a group of 52 MND patients, from 22 to 82 (median 60) years old, and a group of 86 PD patients, from 33 to 79 (median 59.5) years old, and median Hoehn-Yahr stage 2.5.

We assessed VCP, utilizing videomotion analysis with biofeedback. A patient followed on-screen target by changing torso position. For the acquired positions of patient and target, VCP quality coefficients CVCPf and CVCPs were calculated as Spearman correlation, and phase shifts PSf and PSs were estimated using cross-correlation, in frontal and sagittal planes respectively.

Results: CVCPf and CVCPs in bulbar onset ALS are significantly lower, and absolute values of PSf and PSs are significantly higher (bigger lag between patient and target) compared to other forms of MND (U, p<0.05). 7 MND patients had CVCPf and CVCPs less than 10th centile, 5 of them had bulbar onset ALS with no weakness or spasticity in lower limbs and axial muscles.

In PD, CVCPf and CVCPs, PSf and PSs negatively correlate with Hoehn-Yahr stage (Spearman, p<0.05).

Conclusion: PD patients and MND patients may have impaired voluntary control of posture. Increased phase shift may reflect bradikinesia and increased response time. Impairments in bulbar onset ALS may be profound, therefore such patients may have an increased risk of falls, and may benefit from interventions like balance training and barrier-free environment.

Disclosure: This work has been partially funded by the Ministry of Health of the Republic of Belarus

EPO2192

Pilot study of memantine hydrochloride effectiveness in correction of falls in vascular parkinsonismE. Gracheva¹, T. Usenko², I. Miliukhina¹¹Center for Neurodegenerative Disease, Institute of Experimental Medicine, Saint-Petersburg, Russian Federation, ²Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation

Background and aims: Vascular parkinsonism (VaP) is a rare condition in which clinical features of parkinsonism are caused by cerebrovascular disease. Most commonly VaP is a symmetrical lower-body parkinsonism with gait disturbance, postural instability, falls and poor response to levodopa which makes it a challenging condition to treat. Patients with VaP often suffer from cognitive decline. Modern researches consider cognitive impairment to add to falls which makes use of antidementia drugs perspective.

Aim of our study was to assess the effectiveness of memantine hydrochloride in correction of falls in VaP.

Methods: 13 patients with VaP and cognitive impairment were recruited for the current study. Each patient received 20mg/day of memantine hydrochloride alongside levodopa treatment. In order to objectify changes in gait parameters before and after 3 months of memantine treatment all patients underwent neuropsychological assessment (MMSE, MoCA, FAB, CDT), examination with the use of treadmill with integrated measurement platform. Statistical analysis was performed using R packages (version 3.6.2). Significance was established at $p < 0.05$.

Results: After 3 months of treatment with memantine hydrochloride several patients admitted less frequent falls, but no significant differences in comparison to baseline were shown in most gait parameters ($p > 0.05$) except for the duration of "heel off" phase of stride ($p = 0.0019$).

Conclusion: This is the 1st report to show changes in "heel off" phase after 3 months of administering 20mg/day of memantine hydrochloride. We plan to conduct further research with bigger group of patients in order to proof or refute effectiveness of memantine hydrochloride in reducing falls in VaP.

Disclosure: Nothing to disclose

EPO2193

Validation Turkish version of the simple screening tool for early diagnosis of advanced Parkinson's disease in daily practice: the CDEPA questionnaireS. Güler¹, N. Turan²¹Istanbul, Turkey, ²Department of Biostatistics, Trakya University Faculty of Medicine, Adrianople, Turkey

Background and aims: We aimed was to modify to validate a simple screening tool, the CDEPA questionnaire (Cuestionario De Enfermedad de Parkinson Avanzada [Questionnaire for Advanced Parkinson's Disease (APD)], for the identification of APD in daily practice and to analyse the validity and reliability of the questionnaire.

Methods: 120 consecutive patients with APD (45% were women, mean age was 69.3 ± 11.6 years) included in the study and stratified according to the Hoehn and Yahr scale. Permission regarding the translation and validation of the CDEPA questionnaire was obtained. The CDEPA questionnaire defined APD as the presence of severe disability requiring help for activities of daily living, motor fluctuations with limitation or inability to perform ADL, severe dysphagia, recurrent falls or dementia.

Results: PD was categorized as advanced in 45 (37.5%) patients when using the gold standard and in 75 (62.5%) patients when the CDEPA questionnaire was used. The CDEPA questionnaire and the gold standard agreed moderately ($P < 0.001$). The CDEPA classified APD with a sensitivity of 98%; specificity of 58%; total accuracy of 74.6%; and area under the curve of 78.5%. The internal consistency determined by Cronbach's alpha indicated an extremely good correlation (0.975). Significant differences were found between the groups created by the CDEPA in several usual PD evaluations (HY Scale, SCOPA Motor Scale, Non-motor Symptoms Scale for PD, Clinical Impression of Severity Index for PD, Clinical Global Impression Severity Scale).

Conclusion: These findings suggest, Turkish version of the CDEPA questionnaire is a valid, reliable and useful instrument for easily screening APD.

Disclosure: Nothing to disclose

EPO2194

The Prevalence of Essential Tremor (ET) in Edirne and Its Districts Concomitant Comorbid ConditionsS. Güler¹, A. Caylan², N. Turan³¹*Istanbul, Turkey*, ²*Department of Family Medicine, Trakya University Faculty Of Medicine, Adrianople, Turkey*,³*Department of Biostatistics, Trakya University Faculty of Medicine, Adrianople, Turkey*

Objective: ET has negative impacts on the quality of life in patients. This condition is the subject of an increasing number of epidemiological studies. While it is recognized that genes play a major role in ET with $\geq 50\%$ of the affected individuals having a positive family history.

Methods: To assess the prevalence of ET in Edirne and its districts, 3008 volunteers, including 1518 men and 1470 women, were included in the study. To account for the possibility of missing cases of ET in our study population, we added an additional 10% to the estimated number of individuals needed, for a total of 3367. However, ultimately, only 3008 individuals were included.

Results: The study population consisted of 3008 participants, including 50.8% men (n=1518) and 49.2% women (n=1490). The ET prevalence was 5.8 % and 173 participants were evaluated as ET positive. 135 (47.9%) of the ET patients were men, and 147 (52.1%) were women. There was a statistically significant difference in the presence of thyroid disease between those who received ET and those who did not (p=0.000).

Conclusion: As a result, in many countries and regions, despite many efforts and studies regarding the prevalence, epidemiology, mechanisms and treatment of the disease, ET has not been sufficiently elucidated. We determined family history of ET high frequency of positive. The field of essential tremor (ET) genetics remains extremely challenging. Thus, for the determination of the prevalence and mechanisms of the disease, additional detailed and comprehensive studies are needed.

Disclosure: Nothing to disclose

EPO2195

Varying Phenotypic Spectrum in Paroxysmal Exercise-Induced Dystonia: A Turkish family with SLC2A1 pathogenic variantM. Gültekin¹, R. Bayramov², G. Sımsır³, A.N. Basak³¹*Department of Neurology, Erciyes University Faculty of Medicine, Kayseri, Turkey*, ²*Department of Medical Genetics, Haseki Education Research Hospital, Istanbul, Turkey*, ³*Molecular Biology and Genetics, Koç University School of Medicine, Istanbul, Turkey*

Introduction: Paroxysmal exercise-induced dyskinesia (PED, OMIM #612126) is characterized by recurrent episodes of involuntary movement disorders usually precipitated by sustained walking or running, with or without a history of epilepsy. SLC2A1 (OMIM *138140) pathogenic variants were associated with a wide spectrum of clinical features of autosomal dominant inherited PED. We present varying phenotypic spectrum of PED in a Turkish family with a synonymous SLC2A1 pathogenic variant.

Material and methods: After examination and preliminary diagnosis of patients with clinical symptoms of PED, family members were tested for mutations in the SLC2A1 gene by whole exome sequencing.

Results: In all 5 family members with PED symptoms SLC2A1 NM_006516.3:c.972G>A, (p.Ser324=), rs796053254 heterozygous pathogenic variant was detected which is not previously reported in healthy population. Case-1 (mother) had not any symptoms after the third decade of her life. Case-2, M, 39 years, has bilateral foot dystonia, dyskinesia, weakness, and chorea during PED attack. Also, he has psychiatric disorder. Case-3, F, 20 years, has unilateral foot dystonia, epileptic seizure and mild cognitive disorder. Case-4, M, 24 years, has just unilateral foot dystonia. Case-5, M, 26 years, has bilateral foot dystonia during the attack of the PED.

Conclusion: Despite of carrying same SLC2A gene p.Ser324= variant and being first degree relatives all PED diagnosed family members had varying symptoms. Clinicians should be aware of this phenomena while examining patients with PED symptoms.

Disclosure: Nothing to disclose

EPO2196

Cancelled

EPO2197

The relation between the self-reported and objective motor symptoms and the health-related quality of life in functional movement disorders

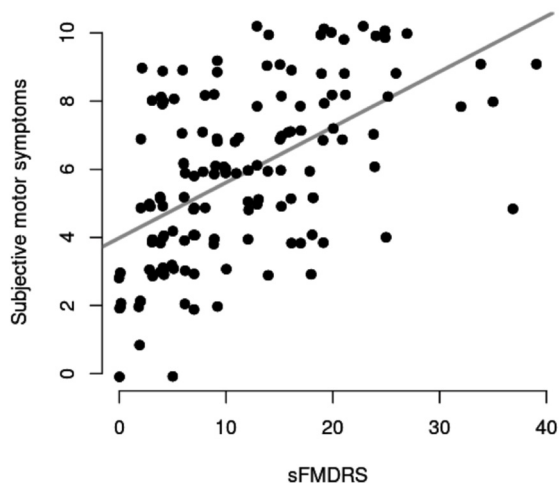
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Background and aims: Multiple self-reported non-motor symptoms, but not objectively measured motor symptom severity correlated with impaired health-related quality of life (HRQoL) in a small sample of patients with functional movement disorder (FMD). This study aimed to analyse the relation between objective and self-reported motor symptoms measures and HRQoL in FMD patients.

Methods: In 144 patients with clinically established FMD 101 female, mean age 47 (21-81) years, mean FMD duration 6.7 (0.1-39) years, we measured motor symptom severity using The Simplified FMD Rating Scale (s-FMDRS) and number of different motor symptoms types (i.e. tremor, dystonia, gait disorder, myoclonus, and weakness). All patients evaluated each motor symptom type severity on Likert scale and completed questionnaires for depression, anxiety, pain, fatigue, cognitive complaints, and HRQoL (SF-12).

Results: The sum of self-reported motor symptoms severity correlated with s-FMDRS and the number of motor symptoms ($p < 0.001$). Both the self-reported motor severity and s-FMDRS ($p < 0.001$) but not the number of motor symptoms and FMD duration correlated with HRQoL. All non-motor measures strongly correlated with self-reported motor severity and HRQoL ($p < 0.001$) and weakly with s-FMDRS ($p < 0.01$). Multiple linear regression revealed pain ($p < 0.001$), subjective motor severity ($p < 0.01$), and depression ($p < 0.01$) were the leading factors affecting the HRQoL while the effect of s-FMDRS was not significant.



Correlation between s-FMDS and self-reported motor symptoms severity

Conclusion: In this group of FMD patients, both subjective and objective measures of motor symptom severity were related to HRQoL. However, only subjective measures of symptom severity jointly predicted the HRQoL in FMD patients.

Disclosure: Supported by the grant AZV 16-29651A.

EPO2198

Effect of an increase in dose of istradefylline, an A2A receptor antagonist, in levodopa-treated patients with Parkinson's Disease (PD)

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Background and aims: Istradefylline is an oral adenosine A2A receptor antagonist for adjunctive treatment to a levodopa/decarboxylase inhibitor in adults with PD experiencing OFF time. Istradefylline significantly reduced OFF time in placebo-controlled, parallel-group studies of 20 and 40mg/day. We investigated whether increasing istradefylline from 20 to 40mg/day improves clinical responses.

Methods: Patients with PD receiving levodopa and experiencing motor fluctuations completing a 12-week, randomized, double-blind trial of istradefylline 20 or 40mg/day vs placebo could enter a 52-week open-label extension study. Initially, all patients received istradefylline 20mg once-daily. After 4 weeks, istradefylline was increased to 40mg/day as needed. Total daily OFF and ON time were assessed using patient-completed diaries, as were Clinical Global Impression-Global Improvement (CGI-I) and Unified Parkinson's Disease Rating Scale (UPDRS). Treatment-emergent adverse events (TEAEs) were recorded.

Results: After 4 weeks of istradefylline 20mg/day, patients previously receiving double-blind placebo had improvements in OFF time and ON time without troublesome dyskinesia (ON-WOTD), and those previously receiving 40mg/day showed worsened OFF time (Table 1). In patients requiring dose increase, OFF time, ON-WOTD, and UPDRS III (ON) improved after 4 weeks of 40mg/day, and a greater % had improved CGI-I, vs patients remaining on 20mg/day (Table 2). Among TEAEs (frequency $\geq 5\%$), nasopharyngitis, dyskinesia, contusion, and constipation became more frequent with dose increase vs maintaining 20mg/day.

Conclusion: Reducing istradefylline dose from 40 to 20mg/day for 4 weeks resulted in increased OFF time/day. Increasing istradefylline from 20 to 40mg/day for 4 weeks improved OFF time, ON time without troublesome dyskinesia, UPDRS III (ON), and CGI-I compared with remaining at 20mg/day.

Table 1. Baseline to Week 4 Change in Study Endpoints in Patients Receiving Open-Label Istradefylline 20mg/day From Baseline to Week 4.

	Prior Placebo		Prior 20 mg/day		Prior 40 mg/day	
	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]
Baseline	5.98 (n=99)		5.39 (n=101)		4.91 (n=107)	
Week 4	5.52 (n=98)	-0.56 [-0.85, -0.27]	5.28 (n=96)	-0.09 [-0.37, 0.20]	5.07 (n=105)	0.11 [-0.17, 0.38]
Mean Total Daily OFF Time						
	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]	Hours/day	Baseline to Week 4 Change, LS Mean [95% CI]
Baseline	9.92 (n=99)		10.36 (n=101)		10.99 (n=107)	
Week 4	10.46 (n=98)	0.47 [0.14, 0.79]	10.57 (n=96)	0.21 [-0.11, 0.54]	10.92 (n=105)	-0.02 [-0.34, 0.29]
Mean UPDRS III (ON)						
	Score	Baseline to Week 4 Change, LS Mean [95% CI]	Score	Baseline to Week 4 Change, LS Mean [95% CI]	Score	Baseline to Week 4 Change, LS Mean [95% CI]
Baseline	18.12 (n=99)		17.80 (n=100)		16.08 (n=106)	
Week 4	16.40 (n=98)	-1.69 [-2.58, -0.81]	16.34 (n=98)	-1.27 [-2.16, -0.39] (n=97)*	15.42 (n=104)	-0.92 [-1.78, -0.06]

*n = number of subjects having a value at both Baseline and Week 4. CI, confidence interval; LS, least squares; UPDRS, Unified Parkinson's Disease Rating Scale.

Table 2. Week 4 to Week 8 Change in Study Endpoints in Patients Remaining on Istradefylline 20 mg/day vs Patients Increasing to 40 mg/day.

	Remained on 20 mg/day		Increased to 40 mg/day	
	Hours/day	Week 4 to Week 8 Change, LS Mean [95% CI] (n=130)	Hours/day	Week 4 to Week 8 Change, LS Mean [95% CI] (n=160)
Week 4	4.72		5.72	
Week 8	4.96	0.23 [-0.05, 0.51]	5.25	-0.48 [-0.73, -0.22]
Mean Total Daily ON Time Without Troublesome Dyskinesia				
	Hours/day	Week 4 to Week 8 Change, LS Mean [95% CI] (n=130)	Hours/day	Week 4 to Week 8 Change, LS Mean [95% CI] (n=160)
Week 4	11.11		10.33	
Week 8	10.80	-0.30 [-0.59, -0.01]	10.80	0.47 [0.21, 0.73]
Mean UPDRS III (ON)				
	Total Score	Week 4 to Week 8 Change, LS Mean [95% CI] (n=132)	Total Score	Week 4 to Week 8 Change, LS Mean [95% CI] (n=164)
Week 4	15.94		16.45	
Week 8	15.42	-0.51 [-1.05, 0.03]	15.45	-1.00 [-1.48, -0.52]
CGI-I Benefit (≥1 category)^a				
	Remained on 20 mg/day, n (%) (n=132)		Remained on 40 mg/day, n (%) (n=164)	
Week 4 to Week 8	17 (12.9)		38 (23.2)	

^aCGI-I Benefit is ≥1 category improvement to minimally, much, or very much improved at Week 8 relative to Week 4. CGI-I, Clinical Global Impression-Global Improvement; CI, confidence interval; LS, least squares; UPDRS, Unified Parkinson's Disease Rating Scale.

Disclosure: This work was supported by Kyowa Kirin Pharmaceutical Development, Inc.

EPO2199

Pre-existing severe polyneuropathy is not necessary a contraindication for LCIG treatment

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Background and aims: Levodopa/carbidopa intestinal gel (LCIG) administered by a jejunal catheter via gastrostomy connected to the extracorporeal pump is one of the device-aided treatments for advanced Parkinson's disease (PD). One of the serious complications is polyneuropathy, whereas pre-existing neuropathy is considered a relative contraindication for this treatment.

Methods: We present a 61-year-old male with a 26 year history of young-onset PD with a history of hallucinations and severe fluctuations poorly controlled by oral antiparkinsonian medication. The patient was indicated for LCIG treatment despite a severe axonal sensorimotor polyneuropathy of unknown etiology with a relatively high levodopa equivalent daily dose (LEDD) of oral treatment: (2869mg).

Results: The clinical symptoms significantly improved during the LCIG titration period at the price of an increased dosage of LEDD (3308mg). The plasma levels of folate and vitamin B12 supported by oral supplementation remained in a normal range after the LCIG initiation. However, a pre-existing severe sensorimotor polyneuropathy was initially detected with no further progression on an EMG within the next two years. Finally, the LEDD of the LCIG increased to 3484mg enabling very good control of motor symptoms and fluctuations.

Conclusion: A LEDD higher than 2000mg is usually considered to be a risk factor for the development or deterioration of polyneuropathy. Our patient demonstrated that doses of LCIG exceeding this limit in combination with pre-existing polyneuropathy were not automatically associated with its worsening. However, higher caution and regular clinical visits with more frequent EMG examinations and laboratory testing are advised in these patients.

Disclosure: Supported by GAČR 16-13323S and Progress Q27

Movement disorders 5

EPO2200

Movement disorders in NMDA encephalitis

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Background and aims: Since N-methyl-D-aspartate receptor (NMDAR) encephalitis was 1st described in 2007, the clinical phenotype has broadened dramatically. The majority of patients will develop a movement disorder during their illness, with wide variation seen in phenomenology, associated symptoms, severity and response to treatment.

Methods: In this study, we describe 4 cases of anti NMDAR encephalitis presenting to the neurology service at Walton Centre NHS Foundation Trust in Liverpool, UK.

Results: The 1st 2 cases occurred in women with histologically proven ovarian teratomas, 1 with a classical presentation of orofacial dyskinesia requiring aggressive treatment and the 2nd with stereotypies, perseveration and catatonia that was responsive to corticosteroids alone. The 3rd case had a monosymptomatic presentation of chorea. The 4th case had a biphasic presentation, initially with orofacial dyskinesia and chorea and much later developing an encephalopathy.

Conclusion: The cases presented here represent a spectrum of movement disorders associated with NMDAR encephalitis. Although orofacial dyskinesias are the most frequently observed movement disorder in NMDAR encephalitis, a range of hyperkinetic movements have been reported, including chorea, ballismus, athetosis, myoclonus, and dystonia. Monosymptomatic movement disorder presentations are rare, but should be considered in the evaluation of a subacute-onset hyperkinetic movement disorder in the absence of another cause, even without encephalopathy or seizures. NMDAR encephalitis should no longer be considered an afterthought in viral PCR negative syndromes, given its distinct clinical syndrome, as it is 4 times more common than individual infective encephalitides. Early and aggressive immunomodulatory treatment is associated with better outcomes.

Disclosure: Nothing to disclose

EPO2201

Safinamide safety and tolerability in a Spanish elderly population

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Background and aims: Safinamide (Xadago[®]) is a new drug for Parkinson's disease with a double mechanism of action: It is a reversible MAO B inhibitor and a glutamate modulator. In pivotal trials, 016 and SETTLE, patients treated with 100 mg Safinamide were younger than usual clinical practice.

Methods: We decided to study the safety and tolerability profile of safinamide in our population in Yecla Hospital (Spain) which is 15 years older than previous populations included in these studies. We have done a retrospective analysis of our Parkinson's Unit collecting data from 53 patients that have been treated with safinamide. Variables studied are age, Levodopa Equivalent Dose (LED), months of treatment duration, discontinuation rate and causes of safinamide.

Results: These 53 patients are 75.0 ±11.05 years and have received safinamide treatment for 7.67±6.77 months. The LED is 786.83±328.58mg. The starting dose of safinamide was 50mg during the 1st month and then increased to 100mg. Change from prior iMAOB, when applicable, was done overnight without any adverse event. Only 4 patients (7.55%) have presented complications, derived from the introduction of safinamide, that lead to discontinuation. 3 of them were mild complications (food rejection, paresthesias and nocturnal hallucinations), and 1 was of severe degree (hyponatremia) and required hospital admission in the center.

Conclusion: In this elderly population, safety and tolerability profile of safinamide is good and remains similar to the 1% on pivotal trials, demonstrating that safinamide is also safe in people aged above 70s.

Disclosure: Nothing to disclose

EPO2202

Parkinson's disease and cancer

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Background and aims: Parkinson's disease (PD) is 1 of the most frequent neurodegenerative pathologies. In last years some studies have established a lower overall cancer risk in people with PD.

Methods: Retrospective study including 354 PD patients. Demographic features (age, sex, comorbidities), PD characteristics (disease duration, Hoehn and Yahr (HY), non-motor symptoms) and cancer history (histological diagnosis, management, outcome) were analyzed. Patients with and without cancer were compared.

Results: 198 (55.9%) were men. Mean age 71.99 years (DE 10.07). Hypertension was the most frequent comorbidity (48%). Mean time of disease duration was 8.85 years (DE 5.65). 76.8% had at least 1 non-motor symptom being depression the most common (31%). 68 patients (19.2%) had been diagnosed with cancer. A total of 87 malignant neoplasms were analyzed. Skin basal cell epithelioma was the most frequent (20.6% of all cancers) followed by prostatic adenocarcinoma (13.7%) and breast invasive ductal carcinoma (9.1%). All neoplasms received treatment: 80.4% surgery, 29.8% chemotherapy and 12.6% radiotherapy, reaching complete remission in 79.3% of cases.

Comparing patients with and without cancer we observed that the 1st group was older, with a higher rate of men and more frequent history of smoking and pulmonary pathology.

Conclusion: We found a high prevalence of cancer (specially skin cancer) although most had a good outcome. Patients with cancer were older, more frequently men and had a higher incidence of tobacco exposure and pulmonary comorbidity.

Disclosure: Nothing to disclose

EPO2203

Development and Validation of a PSP questionnaire as Screening Tool for early diagnosis of progressive supranuclear palsy (PSP)

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Background and aims: Our aim was to develop a screening questionnaire for progressive supranuclear palsy (PSP) for early clinical detection and differentiation from other parkinsonian syndromes.

Methods: 1 screening questionnaire for patients (PSP-SQ-Patient) and 1 for caregivers (PSP-SQ-Caregiver) with 19 dichotomous questions was developed in German language on the basis of the new clinical diagnostic criteria for PSP (Höglinger et al., *Mov Disord.* 2017;32:853-864.). After cognitive pretesting, PSP-SQ-Patient and PSP-SQ-Caregiver scores were collected from clinically diagnosed patients with PSP and Parkinson's disease (PD; Postuma et al., *Mov Disord.* 2015;30:1591-601) and their respective caregivers, together with demographic information, PSPRS scores and MDS-UPDRS scores.

Results: Demographic data are presented in Table 1. PSP-SQ-Patient and PSP-SQ-Caregiver are presented in Table 2. The mean PSP-SQ-Patient score was 13.16±0.88 SEM (R=19-7) in PSP and 7.15±1.07 SEM (R=14-0) in PD patients, the mean PSP-SQ-Caregiver score was 14.2±0.86 SEM (R=17-9) in PSP caregivers and 9.3±1.26 SEM (R=13-6) in PD caregivers.

Figure 1 shows sensitivity and specificity of the PSP-SQ-Patient (A) and PSP-SQ-Caregiver (B) as a function of different cut-off values.

Receiver operating characteristics showed good discrimination abilities for PSP-SQ-Patient (area under the curve [AUC]: 0.878) and PSP-SQ-Caregiver (AUC: 0.858).

TABLE 1. Demographic and clinical data

	PSP	PD
N	12	13
Gender (female/male)	5/7	2/11
Age	66.8 ± 6.0	66.8 ± 11.1
Disease duration (years)	4.7 ± 2.2	5.8 ± 5.0
PSPRS score (worst=100)	38.8 ± 10.0	-
UPDRS III score (worst=108)	30.9 ± 20.1	41.0 ± 11.3

Legend: PSP: Progressive Supranuclear Palsy; PD: Parkinson's disease; PSPRS: Progressive Supranuclear Palsy Rating Scale; UPDRS III: Unified Parkinson's Disease Rating Scale Part III.

TABLE 2.

PSP-SQ-Patient

Diagnostic domain	Screening questions
Ocular mobility	1 Haben Sie zunehmend Probleme, Ihre Augen nach oben und unten zu bewegen?
	2 Haben Sie manchmal Probleme, Ihre Augen zu öffnen?
	3 Sehen Sie manchmal doppelt?
	4 Sind Ihre Augen lichtempfindlicher geworden?
Postural Instability	5 Fällt es Ihnen zunehmend schwerer von einem Stuhl aufzustehen?
	6 Haben Sie beim Stehen oder Gehen das Gefühl, dass der Boden unter Ihnen schwankt?
	7 Haben Sie zunehmend Schwierigkeiten beim Stehen oder Gehen das Gleichgewicht zu halten?
Akinesia	8 Sind Sie im letzten Jahr mehr als einmal gestürzt?
	9 Sind Ihre Bewegungen zunehmend langsamer geworden?
Cognition	10 Sind Ihre Muskeln zunehmend steifer geworden?
	11 Fällt es Ihnen schwerer Knöpfe an Ihrer Kleidung zu schließen?
	12 Ist Ihre Handschrift zunehmend kleiner geworden?
	13 Fühlen Sie sich beim Gehen manchmal plötzlich wie eingefroren, als würden Sie am Boden festkleben, z.B. wenn Sie durch eine Tür gehen?
	14 Sagen Ihre Angehörigen, dass Ihr Antrieb zunehmend weniger geworden ist (z.B. Hobbies, Freunde, Gespräche)?
Clinical Chars	15 Fällt es Ihnen schwerer, sich gedanklich auf neue Situationen einzustellen?
	16 Meinen Sie, dass Ihr Denken langsamer geworden ist?

Table 1/2

Clinical Chars	17 Fallen Ihnen zunehmend beim Sprechen die Worte nicht ein?
	18 Ist Ihre Sprache zunehmend undeutlicher geworden?
	19 Verschlucken Sie sich in letzter Zeit häufiger?
PSP-SQ-Caregiver	
Diagnostic domain	Screening questions
Ocular mobility	1 Hat Ihr Angehöriger zunehmend Probleme, die Augen nach oben und unten zu bewegen?
	2 Hat Ihr Angehöriger manchmal Probleme, die Augen zu öffnen?
	3 Klagt Ihr Angehöriger manchmal darüber, dass er doppelt sieht?
	4 Klagt Ihr Angehöriger darüber, dass dessen Augen lichtempfindlicher geworden sind?
Postural Instability	5 Fällt es Ihrem Angehörigen zunehmend schwerer von einem Stuhl aufzustehen?
	6 Hat Ihr Angehöriger manchmal das Gefühl, dass beim Stehen oder Gehen der Boden unter ihm schwankt?
	7 Hat Ihr Angehöriger zunehmend Schwierigkeiten beim Stehen oder Gehen das Gleichgewicht zu halten?
Akinesia	8 Ist Ihr Angehöriger im letzten Jahr mehr als einmal gestürzt?
	9 Sind die Bewegungen Ihres Angehörigen zunehmend langsamer geworden?
Cognition	10 Sind die Muskeln Ihres Angehörigen zunehmend steifer geworden?
	11 Fällt es Ihrem Angehörigen schwerer Knöpfe an der Kleidung zu schließen?
	12 Ist die Handschrift Ihres Angehörigen zunehmend kleiner geworden?
	13 Ist Ihr Angehöriger während dem Gehen manchmal plötzlich wie eingefroren, als würde er am Boden festkleben, z.B. wenn er durch eine Tür geht?
	14 Ist der Antrieb Ihres Angehörigen zunehmend weniger geworden (z.B. Hobbies, Freunde, Gespräche)?
Clinical Chars	15 Fällt es Ihrem Angehörigen schwerer, sich gedanklich auf neue Situationen einzustellen?
	16 Meinen Sie, dass das Denken Ihres Angehörigen langsamer geworden ist?
	17 Fallen Ihrem Angehörigen zunehmend beim Sprechen die Worte nicht ein?
	18 Ist die Sprache Ihres Angehörigen zunehmend undeutlicher geworden?
	19 Verschluckt sich Ihr Angehöriger in letzter Zeit häufiger?

Table 1/2

Figure 1

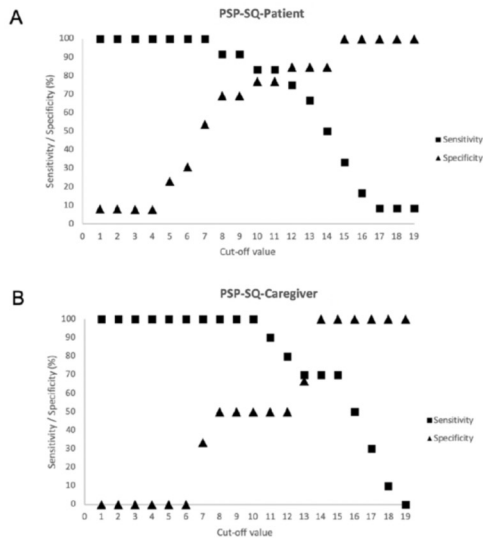


Fig. 2: Sensitivity (squares) and specificity (triangles) of the SQ-Patient (A) and SQ-Relative (B) as a function of the cut-off value (defined as ≥). The best trade-off between sensitivity and specificity is provided with a cut-off of 10 points in the PSP-SQ-Patient and of 13 points in the PSP-SQ-Caregiver.

Figure 1

Conclusion: PSP-SQ-Patient and PSP-SQ-Caregiver are easy, reliable, and sensitive tools to recognize clinically diagnosed PSP and differentiate them from PD. Next, we will evaluate the performance of both questionnaires in very early disease stages.

Disclosure: Nothing to disclose

EPO2204

None of the common tests distinguishes between essential and dystonic head tremor

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Background and aims: In patients with head tremor, it is often difficult to distinguish between essential tremor (ET) and cervical dystonia with dystonic head tremor (DT). We aimed to assess the differential diagnostic value of standard clinical tests and accelerometric measurements.

Methods: 22 patients (66.8±10.7 years) with ET and 36 patients (58.8±10.8 years) with cervical dystonia and DT were included. The patients were examined using routine scales and questionnaires – Tab 1. In addition, head tremor was assessed in the sitting and supine position at rest, during phonation and cognitive tasks with an accelerometer fixed on the patient's forehead, and the power of tremor was calculated. The statistical analyses were performed with the significance level $p < 0.01$.

Results: Significantly higher scores for tremor and ataxia and lower scores for dystonia were found in ET compared to DT patients (Tab. 1). However, no significant intergroup differences in accelerometric tremor amplitude and power were found. In both groups, the tremor power increased significantly with serial subtraction but not with phonation (Tab 2). In none of the groups, the tremor power decreased significantly in the supine compared to sitting position, whereas in 5 ET and 11 DT patients, the supine tremor power persisted above the normal threshold.

	ET	DT	p
Positive family history	11/22 (50.00%)	11/36 (30.56%)	NS
Age at onset (years)	36.05 ± 18.01	40.50 ± 16.96	NS
Effect of alcohol	10/19 (52.63%)	12/26 (46.15%)	NS
TETRAS ADL	21.45 ± 10.35	8.56 ± 8.70	< 0.0001
TETRAS PS	16.23 ± 7.02	7.56 ± 5.17	< 0.0001
TETRAS total score	37.68 ± 16.46	16.11 ± 12.98	< 0.0001
TWSTRS part IA	0.91 ± 0.92	3.00 ± 1.51	< 0.0001
TWSTRS total score	5.77 ± 7.16	23.19 ± 12.93	< 0.0001
SARA	5.16 ± 3.49	2.69 ± 4.43	0.00026

Tab. 1: Results of the questionnaire and scales; ET = Essential Tremor, DT = Dystonic Tremor, TETRAS = The Essential Tremor Rating Assessment Scale, ADL = Activities of Daily Living, PS = Performance Subscale TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale, part IA = the Torticollis Severity Subscale, SARA = Scale for the Assessment and Rating of Ataxia.

Tab. 1: Results of the questionnaire and scales

	SFon	SCog	LFon	LCog
ET	0.426	0.000	0.014	0.001
DT	0.179	0.002	0.196	0.000

Tab. 2: Differences between head tremor power in sitting at rest and in supine position; ET = Essential Tremor, DT = Dystonic Tremor, SFon = tremor in sitting during phonation, SCog = tremor in sitting during cognitive task (serial subtraction), LFon = tremor in supine position during phonation, LCog = tremor in supine position during cognitive task (serial subtraction). Results at significance level $p < 0.01$.

Tab. 2: Differences between head tremor power in sitting at rest and in supine position

Conclusion: Although comparisons between patients with essential and dystonic tremor of the head showed significant differences in the group scores of tremor, dystonia and ataxia, the individual scores did not allow for differential diagnosis. Moreover, neither the accelerometric power of tremor nor the sitting/supine test showed significant differential diagnostic performance.

Disclosure: Nothing to disclose

EPO2205

A possible link between Cisplatin treatment and tau pathology (an overlap between Progressive Supranuclear Palsy and Frontotemporal Degeneration)

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Background and aims: Progressive Supranuclear Palsy (PSP) can frequently overlap symptoms with Frontotemporal Degeneration (FTD), as they are both taupathies. There is still much to discover regarding the etiology and predisposing factors of these neurodegenerative disorders. In a recent study performed on male mice it is postulated that Cisplatin induces taupathy and behavioural abnormalities

Methods: We present the case of a 65-year-old female patient with a history of anexectomy for an ovarian malignancy, followed by 6 cycles of Cisplatin (25 years ago). In the last 3 years she initially presented repeated falls, then scanning speech and dysphagia. Neurological examination revealed limitation of the upright vertical eye movements, slow and hypometric pursue movements, the absence of optokinetic nystagmus, mild axial rigidity, wide-base gait, postural instability with tendency to fall at the pull test. She also had disinhibition, impulsivity, hand automatisms and perseveration. The cerebral MRI showed important mesencephalic, cerebellar, frontal and temporal lobe atrophy.

Results: The clinic and neuroimaging tools point towards a probable PSP. The phenotype is compatible with Richardson syndrome, plus frontal and cerebellar signs. The changes in behaviour and the fronto-temporal atrophy overlap with FTD (behaviour variant).

Conclusion: We presume that in this patient's case the chemotherapy with Cisplatin could have played a role in accelerating a neurodegenerative disorder. It would be a point of interest in the future to assess the connection between Cisplatin treatment in humans and the development of neurodegenerative diseases, especially taupathies.

Disclosure: Nothing to disclose

EPO2206

Impact of baseline dyskinesia on the safety and efficacy of istradefylline, an adenosine A2A receptor antagonist, in patients with Parkinson's disease: a pooled analysis of 8 clinical studies

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Background and aims: Istradefylline, a selective adenosine A2A receptor antagonist that acts via the indirect basal ganglia outflow pathway, is indicated as adjunctive treatment to a levodopa/decarboxylase inhibitor in adults with Parkinson's disease (PD) experiencing OFF time. This updated, posthoc, pooled analysis assessed the effect of baseline dyskinesia on the efficacy and safety of istradefylline.

Methods: The analysis included 8 randomized, placebo-controlled, double-blind, phase 2b/3 trials in which patients received istradefylline (20 or 40mg/day) or placebo for 12 or 16 weeks. The primary endpoint was change from baseline in OFF time (istradefylline vs placebo) based on patient-completed 24-hour ON/OFF diaries. Subgroups of patients with (+BL-dyskinesia) and without (-BL-dyskinesia) baseline dyskinesia were defined using patient-completed baseline ON/OFF diaries. Adverse events (AEs) were recorded throughout as spontaneous reports.

Results: 2719 patients were included (+BL-dyskinesia, n=1515; -BL-dyskinesia, n=1204). There were differences between subgroups in baseline daily levodopa dosage and time since PD diagnosis (Table 1). AEs of dyskinesia were more frequent with istradefylline vs placebo in the +BL-dyskinesia vs -BL-dyskinesia subgroups (Figure). Mean reduction in OFF time and increase in ON time without troublesome dyskinesia (ON-WOTD) were greater with istradefylline than placebo; these were unaffected by the presence of baseline dyskinesia (Table 2). Mean decreases in UPDRS scores were greater in -BL-dyskinesia than in +BL-dyskinesia subgroups (Table 2). Istradefylline was well-tolerated.

Conclusion: Dyskinesia as an AE was more frequent during istradefylline treatment, particularly in patients +BL-dyskinesia compared with -BL-dyskinesia patients. Istradefylline-induced improvements in OFF time and ON-WOTD time were not affected by the presence of baseline dyskinesia.

Table 1. Baseline Characteristics and Demographics.

Baseline Dyskinesia	Placebo		Istradefylline			
	No (n=423)	Yes (n=569)	20 mg/day		40 mg/day	
			No (n=362)	Yes (n=486)	No (n=419)	Yes (n=460)
Age, mean (SD), years	64.6 (8.98)	63.0 (8.98)	64.6 (9.18)	64.2 (8.92)	63.4 (8.91)	63.5 (8.77)
Male gender, n (%)	269 (63.6)	310 (54.5)	228 (63.0)	258 (53.1)	262 (62.5)	250 (54.3)
Daily levodopa dosage at study entry, mean (SD), mg	611.71 (332.90)	742.85 (397.83)	568.62 (279.32)	757.21 (386.23)	545.31 (263.80)	754.53 (450.82)
Time since PD diagnosis ^a						
n	385	409	313	341	378	300
Mean, years	7.46	10.02	7.08	10.67	7.37	9.85
Range, years	0.6-32.3	0.1-27.9	0.6-28.2	1.4-36.8	0.4-28.4	0.7-25.6
OFF time at baseline, mean (SD), hours	6.89 (2.350)	5.81 (2.189)	6.87 (2.577)	5.71 (2.364)	6.75 (2.430)	5.56 (2.178)
ON time without troublesome dyskinesia at baseline, mean (SD), hours	9.39 (2.425)	9.31 (2.558)	9.49 (2.454)	9.44 (2.672)	9.50 (2.409)	9.42 (2.729)

PD, Parkinson's disease; SD, standard deviation.

^aTime since PD onset was only reported by a choice of range of years in one of the studies.

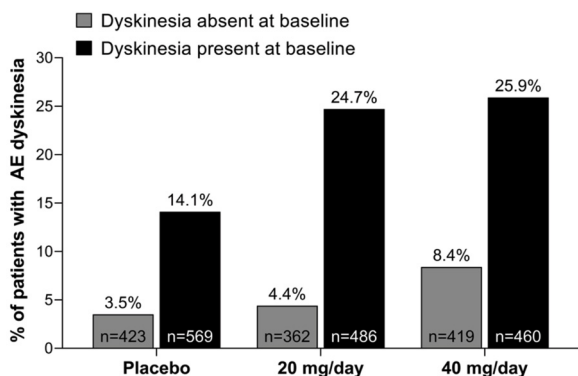


Table 2. Change From Baseline to Endpoint (LOCF) in Hours per Day in Total OFF Time and ON Time Without Troublesome Dyskinesia and in UPDRS Part III by Presence of Baseline Dyskinesia.

Baseline Dyskinesia	Placebo		Istradefylline			
	No (n=423)	Yes (n=569)	20 mg/day		40 mg/day	
			No (n=362)	Yes (n=486)	No (n=419)	Yes (n=460)
Mean change from baseline in total hours in the OFF state (±SD) ^a	-0.79 ±2.703	-0.80 ±2.337	-1.29 ±2.693	-1.18 ±2.394	-1.27 ±2.582	-1.17 ±2.459
Mean change from baseline in total hours in the ON state without troublesome dyskinesia (±SD) ^b	0.62 ±2.658	0.73 ±2.739	1.19 ±2.735	1.03 ±2.791	1.03 ±2.676	0.90 ±2.836
Mean change from baseline in UPDRS Part III score (±SD) ^c	-2.69 ±7.331	-2.01 ±7.451	-3.12 ±7.125	-2.71 ±8.167	-4.72 ±7.716	-2.96 ±8.408

LOCF, last observation carried forward; SD, standard deviation; UPDRS, unified Parkinson's disease rating scale.

^aTreatment x baseline dyskinesia interaction p-value = 0.849.

^bTreatment x baseline dyskinesia interaction p-value = 0.494.

^cTreatment x baseline dyskinesia interaction p-value = 0.167.

Disclosure: This work was supported by Kyowa Kirin Pharmaceutical Development, Inc.

EPO2207

Protective effects of bilirubin toward dopaminergic neuron sufferance in an ex vivo model for Parkinson's disease

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Background and aims: There is no current therapy to slow down the progression of Parkinson's disease (PD). Mildly elevated bilirubin levels are protective against in extra CNS diseases but the protection toward neurological diseases is still scarce. Therefore, we investigated the neuroprotective effects of bilirubin in PD's model.

Methods: We have developed a PD ex vivo model by using the organotypic brain cultures (OBCs) of substantia nigra obtained from Wistar rat at day 5 post-natal challenged with rotenone (Rot). Increasing concentration (0.5µM to 4µM) of unconjugated bilirubin (UCB) was applied to Rot-challenged OBCs and RT-qPCR was used to monitoring alterations of oxidative stress marker genes (Srxn1), inflammation related-genes (Tnf-alpha, Il6, Cox2), and neurotrophic genes (Bdnf). Immunofluorescence staining was used to evaluate the number of dopaminergic neurons (DOPAn)

Results: The mRNA level of Tnf-alpha, Il6, Cox2, Srxn1, and Bdnf was significantly (p<0.05) higher in Rot-treated OBCs compared to DMSO treated controls. UCB 0.5 µM reverted Tnf-alpha expression to control level (p=0.007). UCB 1 µM similarly reverted the expression of Tnf-alpha (p=0.017), Il6 (p=0.001), and Bdnf (p=0.03). UCB 2 µM decreased the expression of Il6 (p=0.003) while UCB 4 µM increased the mRNA level of all the selected markers above the expression in Rot challenged slices (p<0.05). The sufferance of DOPAn was indicated by the reduction of DOPAn number in Rot-treated OBCs (-30%, p=0.003) and was restored by UCB 1µM treatment (p=0.01).

Conclusion: UCB at low concentrations has protective effects on PD model as anti-inflammatory agents. The protective effect is lost at higher UCB concentrations.

Disclosure: This study was supported by the grant from the Italian Liver Foundation and the Lembaga Pengelola Dana Pendidikan (LPDP) of the Indonesian Ministry of Finance.

EPO2208

Levodopa, but not subthalamic deep brain stimulation modulates the resting activity of putamen in Parkinson's disease

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Background and aims: Using a functional MRI, we investigated the effects of levodopa on brain activity during the execution of finger movements in comparison with subthalamic deep brain stimulation (STN-DBS) in Parkinson's disease (PD).

Methods: We investigated 18 patients with an advanced akinetic-rigid type of PD (age 54.6 ± 7.1 years) during the execution of a finger-tapping task using a 1.5T MRI scanner with a gradient-echo echo-planar imaging. The task was performed after medication withdrawal and administration of a single levodopa dose. After STN-DBS implantation, the same group of patients was re-examined with the stimulator switched on and off. A 3-factorial design with within-subject factors Treatment (LDOPA/DBS), State (ON/OFF), and Finger Tapping (LEFT/RIGHT) resulted in 8 scanning sessions for each patient.

Results: While investigating levodopa treatment, we found a significant interaction between both factors of Treatment and State in the bilateral putamen, but not in other motor regions ($p < 0.05$ FWE corrected, Figure 1). Specifically, in the levodopa-off state, the activity in the putamen was higher at rest than during tapping.

Fig 1. Cross-sectional brain slices showing significant brain activity differences with levodopa treatment and STN-DBS in Parkinson's disease using a block-based finger tapping paradigm.

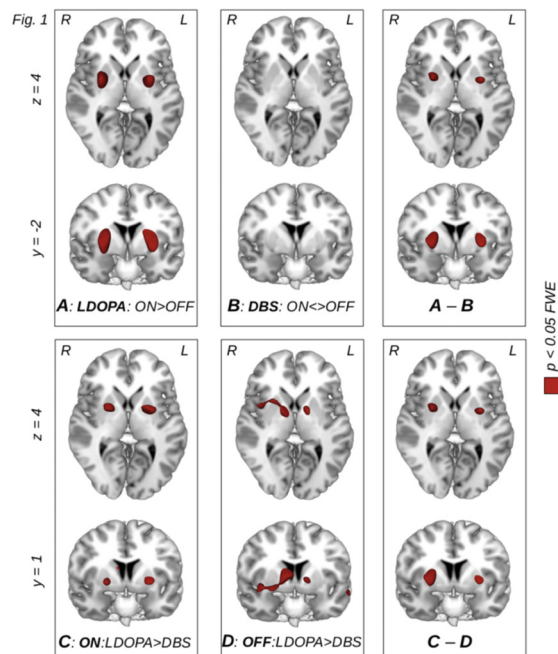


Figure 1

Conclusion: This represents an aberrant activity pattern probably indicating derangement of basal ganglia network activity due to lack of dopaminergic input. Levodopa but not STN-DBS reverted this pattern, so that the putaminal activity during finger tapping was higher than during rest, as previously described in healthy controls (Figure 2). This study shows for the 1st time the fundamentally different aspects of motor network functioning during motion and rest considering differential modulatory effects of levodopa and STN-DBS. Supported by the Czech Ministry of Health AZV NV19-04-00233

Fig 2. Contrast estimates from left and right putamen and motor cortex reflecting a different pattern of brain activity change with levodopa treatment and STN-DBS in Parkinson's disease.

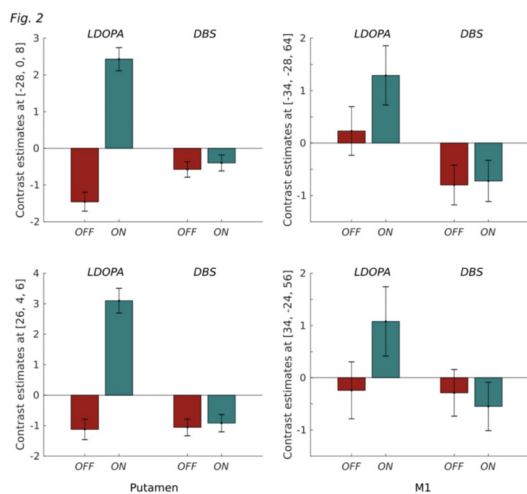


Figure 2

Disclosure: Supported by the Czech Ministry of Health AZV NV19-04-00233

EPO2209

Comparison of dystonic and essential tremor: clinical and quantitative assessment

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Background and aims: Despite being one of the most common neurological disorders, distinguishing different type of tremor is sometimes clinically challenging leading to misdiagnosis. The aim of this study was to assess clinical and electrophysiological features of patients with essential tremor (ET) and dystonic tremor (DT), as well as to test new tools for their differentiating.

Methods: This study included 173 patients with head tremor. Patients were assessed for presence, type and characteristics of tremor. Tremor measurement was done by using inertial sensors. It included frequencies, amplitude and other composed features such as tremor stability index (TSI) and signal power concentration ratio (SPCR).

Results: Of 173 patients, 96 had DT while 77 had ET. Comparison revealed that patients with ET were older at the beginning of disease ($p=0.001$) and had more frequently positive family history ($p=0.006$). Writing tremor, as well as bilateral postural, kinetic and rest tremor of arms were more frequent in ET ($p<0.001$). A further comparison of electrophysiological features of head tremor showed that ET had a higher amplitude ($p=0.02$) and magnitude ($p=0.02$). Also TSI and SPCR were significantly different in these groups ($p<0.001$). Regression analyze single out age and SPCR as statistically significant predictors of type of tremor ($p<0.001$).

Conclusion: Patients with ET are older, more frequently they also had a tremor of other body parts and positive family history than patients with DT. Furthermore, ET had a significantly higher amplitude, magnitude, TSI and SPCR in comparison to DT. Among these, age and SPCR are statistically significant predictors of type of tremor.

Disclosure: Nothing to disclose

EPO2210

Kufor-Rakeb Syndrome due to a new ATP13A2 mutation – Case report

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Background and aims: Kufor-Rakeb Syndrome (KRS) is rare autosomal recessive disorder with diverse phenotypic features. Fewer than 50 affected individuals have been reported in literature. The hallmark clinical manifestations are young onset parkinsonism, pyramidal signs, dysarthria, dysphagia, cognitive impairment. KRS is part of the neurodegeneration with brain iron accumulation (NBIA) disease spectrum. Brain imaging usually demonstrates cerebral, cerebellar atrophy, and sometimes iron accumulation in basal ganglia. Only symptomatic treatment is available, early levodopa administration can be beneficial in terms of motor symptoms.

Mutations in ATP13A2 (formerly termed PARK9) in KRS has initially been described and previous studies uncovered the molecular mechanisms of ATP13A2/PARK9 function in disease pathogenesis : impaired Mn²⁺ and Zn²⁺ metabolism, disturbed mitochondrial homeostasis, and lysosomal dysfunction, whereas its physiological function remains unclear. Preceding papers suggest that there is clinical heterogeneity and variability in ATP13A2-related disorders and that the mutation type can influence clinical phenotype.

Methods: We report on the short-term follow-up of a young woman with adolescent-onset parkinsonism, showing therapeutic response to dopaminergic treatment, objectively measured by UDPRS, UDysRS, BFMDRS scales. Whole exome sequencing previously performed in other institute confirmed a novel mutation of ATP13A2 gene.

Results: We report on the short-term follow-up of a young woman with adolescent-onset parkinsonism, showing therapeutic response to dopaminergic treatment, objectively measured by UDPRS, UDysRS, BFMDRS scales. Whole exome sequencing previously performed in other institute confirmed a novel mutation of ATP13A2 gene.

Conclusion: This is the first reported Hungarian KRS case. Our aim is to highlight clinical variability.

Disclosure: Nothing to disclose

EPO2211

Abnormal thermal sensation thresholds in Parkinson's disease and their relationship to CSF 5-Hydroxyindoleacetic acid

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Background and aims: Little is known about the abnormal temperature sensation in Parkinson's disease (PD). Although abnormal pain thresholds respond to dopamine administration, thermal thresholds do not seem to be related to the dopaminergic deficit. In our study we measured warm and cold sensation thresholds in PD patients and correlated them with CSF 5-Hydroxyindoleacetic acid (5-HIAA), main metabolite of serotonin.

Methods: 28 patients with PD and 15 controls underwent quantitative sensory testing, 10 patients with PD had also CSF examination with 5-HIAA measurement. Conduction studies excluded polyneuropathy in all subjects.

Results: PD patients showed significantly higher thermal thresholds on the more affected side (cold p=0.015, warm p=0.045). There was a significant negative correlation between the CSF 5-HIAA and warm detection threshold on the affected side (p=0.001).

Conclusion: This study may help to better understand the pathophysiology of abnormal temperature sensation in PD. Serotonergic pathology may play a role in these abnormalities.

Disclosure: This study was supported by the grant project from the Ministry of Health of the Czech Republic - AZV NV18-04-00346, by European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868) and by Institutional Support MZ CR – RVO FNOL 2020.

EPO2212

Cancer and Parkinson's disease: is there dependency?

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Background and aims: To determine association between concomitant diseases and Parkinson's disease (PD) forms in early-staged patients.

Methods: Prospective cohort study was performed in 2011-2014 on the base of Republican Center for Movement Disorders, Kazan, Russia. All observed PD patients with 1-2 stages (according to Hoehn&Yahr) without previous specific treatment and age-matching controls (without any signs of neurological impairment) were included. Shaking (SF) or rigid (RF) forms were identified according Unified PD Rating Scale. History taking regarding concomitant diseases and medical events in last 5 years was performed.

Results: 130 patients with PD (mean age 61.04±8.48) and 56 controls (mean age 58.84±12.25) were included. Among PD patients stage 1 was assigned in 76.9% cases and stage 2 – in 23.1%. SF was established in 56.9% cases, RF in 43.1%. The mean age of medical attendance in the Center between SF and RF significantly differed: 63.72±7.19 vs 57.63±8.96 ($p<0.05$). Concomitant diseases were identified in 100% both PD and control groups. The most common concomitant diseases for SF and RF were cardiovascular (55.4% and 57.1%) and gastrointestinal disorders (39.2% and 42.9%), as well as in controls (41.0% vs 48.2%). There were no statistically significant differences in incidence of any concomitant conditions between SF, RF and control groups, except cancer. The incidence of any cancer was 4.1% in SF, 25.0% - in RF and 0% - in controls. Statistically significant difference was determined between RF and both SF and controls ($p<0.0001$).

Conclusion: These results allow to suggest etiopathogenic interrelation between the development of rigid form of PD and cancer.

Disclosure: Nothing to disclose

EPO2213

Reliable diagnosis of spinocerebellar ataxia type 2 using dopamine transporter scan combined with nerve conduction studyT. Kosaka, T. Amano, Y. Tsuda, M. Tsuda, Y. Kouzaki
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Background and aims: Spinocerebellar ataxia type 2 (SCA2) is an autosomal dominant neurodegenerative disorder caused by an increased number of CAG repeats in the SCA2 gene (ATXN2). The diverse phenotypes of SCA2 sometimes make its diagnosis difficult.

Methods: We searched the medical records of 3 Japanese male cases of SCA2 including one example of autopsied twins. In addition to routine histology, immunohistochemical examinations were performed using anti-phosphorylated TDP-43 (pTDP-43) and anti-1C2 antibody recognizing expanded polyglutamine stretches.

Results: Genetic analysis demonstrated an expanded allele with 45, 45 and 36 CAG repeats in ATXN2, respectively. Immunostaining for pTDP-43 and 1C2 revealed many widely distributed positive neuronal inclusions in the CNS including the cerebral cortices, striatum and spinal horn. The pathology of frontotemporal lobar degeneration (FTLD) corresponded to FTLD-TDP type B. The remaining patient was a Japanese male who had developed an unsteady gait at the age of 52 years. Although no parkinsonism or loss of deep tendon reflex was evident, loss of uptake was demonstrated in a dopamine transporter (DAT) scan of the striatum and a nerve conduction study (NCS) revealed sensory axonal neuropathy.

Conclusion: In comparison to other SCA types, degeneration of the striatum and spinal horn cells are unique characters of SCA2, and therefore, DAT scan combined with NCS in addition to routine examinations might be useful for early diagnosis.

Disclosure: Nothing to disclose

EPO2214

VR Environment Can Reliably Trigger Freezing of Gait in Patients with Parkinson's disease

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Background and aims: Freezing behaviour (FoG) can occur in the course of Parkinson's disease (PD) and it significantly impairs the quality of life. Due to its episodic features, it might be challenging to trigger and study FoG in clinical settings. The aim of the current study was to assess the feasibility of a specific VR paradigm using VR first experience fully immersive headset to trigger freezing behaviour in a replicable manner.

Methods: The inclusion criteria were the diagnosis of PD with implanted STN-DBS since at least one year, on stable medication. All patients had to self-report FoG based on the question „Do you have the feeling of feet glued to the floor?“. VR environment consisted of imitation of airport security check including gait through airport security whole-body scanners (for illustration, see Fig.1). Standard spatiotemporal gait parameters were collected using 4 Microsoft Kinect sensors. All patients were measured during OFF stage (OFF medication and OFF stimulation) and ON stage (ON medication and ON stimulation). Freezing behaviour was verified by an experienced clinician blinded to the motor condition.

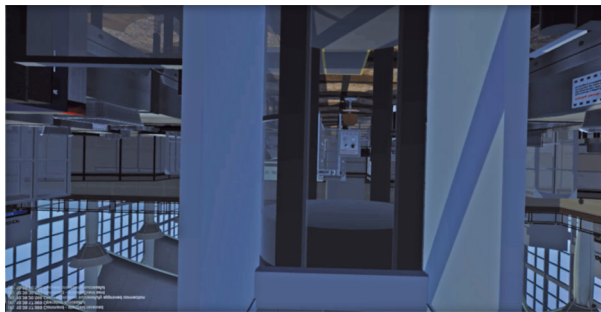


Fig. 1 Example of VR environment used in triggering freezing behaviour

Results: We recruited 8 patients meeting the inclusion criteria and self-reported OFF-FoG (mean PD duration=11y; mean DBS duration=2.6y; mean FoG-Q score=10.5). With VR paradigm, we managed to repeatedly trigger FoG in all 8 patients when being OFF. Two patients had FoG when being ON.

Conclusion: VR simulated environment using VR fully immersive headset can reliably trigger FoG in patients with PD. This suggests a great potential for further use of VR paradigms in studying episodic gait phenomena.

Disclosure: This study was supported by Grant of Ministry of Health, Slovak Republic nr. 2018/32-LFUK-6

EPO2215

Randomised Double-blind Comparison of the Acute Affective and Cognitive Effects of Oral and Intrajejunal Levodopa in Parkinson's disease

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Background and aims: Chronic levodopa treatment in Parkinson's disease (PD) may promote undesirable motor and non-motor fluctuations coinciding with the rise and fall of levodopa levels. To explore differences in the profile of plasmatic levodopa concentrations and associated measures of affect and cognition patients were challenged with an intermittent immediate-release formulation of carbidopa/levodopa (LC-IR) and with continuous infusion of levodopa/carbidopa intestinal gel (LCIG).

Methods: We performed a randomized, double-blind, double-dummy, crossover, acute exploratory study in advanced, non-demented PD. All patients underwent 2 experimental sessions separated by a 2-week interval. They arrived in "off" condition and were allocated to receive every 2 hours first, either their usual dose of LCIG infusion and 3 separate oral doses of over-encapsulated placebo of LC-IR, or an infusion of placebo LCIG plus 3 separate oral doses of over-encapsulated LC-IR. We monitored plasmatic levels of levodopa, motor status, mood, anxiety, and frontal functions at baseline and hourly after each levodopa challenge.

Results: At +1 hour, levodopa concentrations had increased notably and similarly in both groups, but in LC-IR levodopa concentrations fluctuated significantly at subsequent time-points. No significant treatment interactions were seen in MDS-UPDRS-III. Compared to LC-IR, LCIG showed a higher and more sustained improvement in anxiety scores which was associated with the percentage of change in levodopa plasmatic concentrations. In the LCIG group mood and verbal fluency improved significantly at three hours.

Conclusion: The better pharmacokinetics of LCIG is associated with a more favorable profile of acute affective and cognitive fluctuations. The long-term consequences of these differences should be addressed.

Disclosure: Partially supported by FIS Grant PI15/00962; Rio Hortega CM17/00209 and CIBERNED (Instituto de Salud Carlos III, Spain); La Marató de TV3, Expedient 20142910, 2014/U/477, and an unrestrictive research grant from Abbvie.

EPO2216

Risk factors for freezing of gait and related non-motor symptoms in Parkinson's disease

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Background and aims: To identify possible risk factors and the anamnestic association of gait freezing (FOG) in patients with Parkinson's disease (PD).

Methods: 84 patients with PD were evaluated on the basis of a sample on the following scales: MDS-UPDRS scale, modified Hoehn and Yahr (HY) Stage, MMSE and Clinical Dementia Rating scale. MDS-UPDRS was used to evaluate and determine PIGD, as well as for the Balance-Gait (PIGD minus FOG) score, non-motor symptoms (nM-EDL) and motor complications (MC). To clarify the clinical signs and their relationship with FOG, 1-way tests were followed up with subsequent nominal logistic regression (Log Regr).

Results: 36% of patients had FOG, these cases were associated with stage HY ($p=0.05$), 70% of patients had PIGD. Patients with FOG + more often had MC and a higher equivalent dose of levodopa (LED) ($p=0.04$) compared with PIGD/FOG patients, PIGD/FOG + patients had a longer duration of PD duration during the disease, a higher score of Bal -Gait, a higher indicator of LED, a higher frequency of psychosis, they are more likely to have dyskinesia, a higher rate of impact on motor vibrations and a general deviation from the norm and problems with urination, while differences in cognitive status were not significant.

Conclusion: In PD the obvious factors for the development of FOG are PIGD, MC/LED and Cog Imp. Their nature may be additive in its effect. Also, for patients with FOG, more pronounced motor dysfunctions, in particular Bal-Gait disorder are more characteristic.

Disclosure: Nothing to disclose

EPO2217

Effect of dopamine on the level of DNMT1 and DNA SNCA-intron1 methylation status in Parkinson's diseaseA. Lavrinova¹, N. Melnikova², A. Dmitriev²,I. Miliukhina¹, E. Litusova¹, P. Gagarina¹, O. Berkovich³, S. Pchelina¹, A. Emelyanov¹

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Background and aims: Alpha-synuclein (SNCA) oligomers are believed to be the major neurotoxic agents in neurodegenerative process in Parkinson's disease (PD). DNMT1 is predominantly involved in the maintenance of DNA methylation during cell division. SNCA gene expression has been shown to be regulated by DNA SNCA-intron1 methylation status. We examined alterations in DNMT1 levels in cytosolic (CP) and nuclear protein (NP) fractions and the methylation status of the SNCA-intron1 at peripheral blood lymphocytes (PBLs) in patients with sporadic PD.

Methods: Here we examined alterations in DNMT1 levels in CP and NP fractions of cultivated PBLs derived from 10 drug-naïve patients (mean age 63.8 ± 6.46 years) with sporadic PD and 11 controls (mean age 61.82 ± 8.19 years) as well as DNA methylation status of the SNCA-intron1 in presence of dopamine hydrochloride ($100 \mu\text{M}$) (DH). CP and NP fractions were isolated from PBLs using the EpiQuik nuclear extraction kit. The level of DNMT1 in these fractions was estimated by ELISA method (DNMT1 Assay Kit). The assessment of SNCA-intron1 methylation status was performed using Next-Generation bisulphite sequencing on MiSeq. Bisulfite-mediated conversion of the genomic DNA (500 ng) was performed with EZ DNA Methylation-Gold Kit.

Results: The level of DNMT1 in CP and NP fractions of PBLs was decreased in PD patients compared to control both in presence and without DH in cell medium. No differences in the methylation of the SNCA-intron1 region between PD patients and controls were found.

Conclusion: Our data suggest the involvement of DNMT1 in the pathogenesis of PD.

Disclosure: This research has been supported by RFBR grant 16-04-01187.

EPO2218

Reliability and validity of passively collected step frequency variability as a measure of real-life walking impairment in patients with Huntington's disease (HD)

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Background and aims: Remote patient monitoring enables the frequent assessment of HD signs and symptoms in daily life. A previous report on the reliability and validity of active smartphone-based tests showed that step frequency variability in the 2-Minute Walk Test (2MWT) and U-Turn Test were associated with HD clinical scales. Passive, continuous monitoring of motor function using sensor data from mobile devices can circumvent the need for motor tests which rely upon active patient engagement. This analysis aimed to assess the reliability and validity of step frequency variability during passive monitoring of individuals with HD.

Methods: Active and passive data were collected from 184 individuals with HD from the Digital-HD Study, HD Natural History Study (NCT03664804) and open-label extension of the RG6042 Phase I/IIa study (NCT03342053). Passive data were analysed to detect gait bouts and step frequency variability per bout. Values of all bouts during the 2 weeks post-screening were aggregated and correlated with standard clinical tests at screening of motor impairment, with the same feature extracted from the 2MWT and U-Turn Test.

Results: Test-retest reliability for the passive feature was high across studies. Analyses showed significant correlations of passive step frequency variability with the Unified HD Rating Scale, Total Motor Score and gait-specific items, in line with previously reported correlations of the same feature from active gait tests. Passive and active data correlated significantly across studies.

Conclusion: Individuals with HD experience walking difficulties. These data support the validity and reliability of using passive monitoring to measure gait abnormalities, yielding similar results to active tests.

Disclosure: Initial sponsorship for the open-label extension study by Ionis Pharmaceuticals transferred to F. Hoffmann-La Roche Ltd; HD Natural History Study sponsored by F. Hoffmann-La Roche Ltd; Digital-HD study sponsored by University College London and supported by F. Hoffmann-La Roche Ltd; the authors thank Shuang Song, of Meditech Media, for providing editorial support for this abstract.

Movement disorders 6

EPO2219

Oculomasticatory miorhythmia as a key finding in topographic and etiological diagnosis in patients with rhombencephalitis. Videographic record of a case.

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Background and aims: Oculomasticatory miorhythmia (OMM) is a hyperkinetic movement disorder, consisting of synchronous contraction of ocular and oromandibular muscles. This infrequent disorder is of great value for topographic (mesencephalic involvement) and etiological diagnosis (highly specific for Whipple's disease).

Methods: Clinical-radiological description of a patient in whom OMM was key in the diagnosis.

Results: A 60-year-old male is admitted in our Neurology plant due to dysarthria and ophthalmoparesis, experiencing progressive worsening (decreased level of consciousness, tetraparesis and Holmes Tremor). A year prior to admission, he had presented weight loss and polyarthralgias. Later on, a continuous, rhythmic lingual protrusion movements, as well as synchronous palpebral occlusion-opening movements and convergent nystagmus, were added to previous symptoms. These findings were suggestive of OMM (video available) Brain MRI showed T2-FLAIR hyperintensity in rhombencephalon (Figure-1) and corpus callosum (Figure-2), with homogeneous contrast uptake. CSF study shows 28 leukocytes (78% PMN), PCR studies, onconeuronal and anti-MOG antibodies were negative. Upon observation of OMM, T. Whipplei PCR in CSF is requested, which resulted positive; leading to the diagnosis of NeuroWhipple. Given the diagnosis, treatment with IV ampicillin was started (for 3 weeks) achieving progressive clinical improvement (currently able to walk), highlighting OMM resolution.

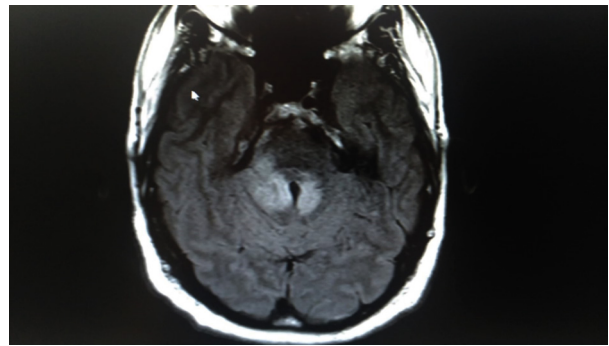


Figure 1

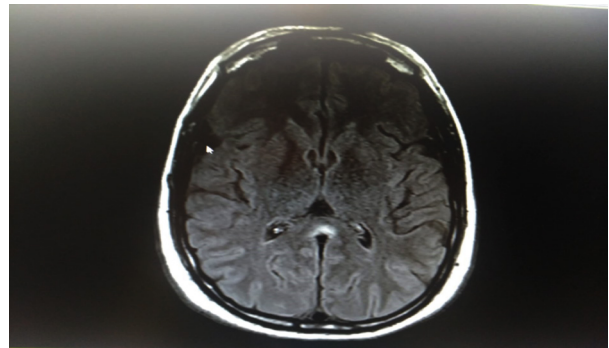


Figure 2

Conclusion: Whipple's disease is an uncommon illness, caused by *Tropheryma whipplei*, typically with digestive and neurological clinic. Exclusive neurological involvement is seen in only 5% of cases, which makes it a challenging diagnosis. In case of OMM finding, neurowhipple should be taken into account, as a potentially curable cause of encephalitis with a fatal course in the absence of treatment.

Disclosure: Nothing to disclose

EPO2220

Influence of peripheral immune system on non motor symptoms in Parkinson's disease

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Background and aims: Recent papers highlight the emerging role of peripheral immune system in the pathophysiology of Parkinson's disease (PD). How the immune system may influence motor and non motor symptoms in PD patients is not yet fully understood. The aim of this study is to describe the suitable role of peripheral immune system on non motor symptoms in PD patients.

Methods: Patients were recruited at the Movement Disorders Center of Novara. All subjects underwent a neurological assessment using specific motor (UPDRS III and H&Y) and non motor scales: Zung score (total and percentage), Epworth, BDI II, Questionnaire for Impulsive-Compulsive Disorders, the REM Sleep Behavior Disorder Screening Questionnaire, Non-Motor Symptom (NMS) assessment scale, Compass 31. Lymphocytes subpopulations (Th1, Th2, Th17) were evaluated with flow cytometry.

Results: 42 PD patients were enrolled (12 female). Mean age was 68.9±8.4. Mean Zung, BDI-II and Epworth total score were respectively 34.8±7.04; 11.08±9.7 and 5.17±4.07. QUIP-RS total score was 13.6±14.9, with the highest sub-score in hobby with a total of 4.11±5.58. Total score NMS score was 31.5±21.7. A significant positive correlation was detected between NMS urinary sub-score and Th2 total number ($p=0.04$; $r^2=0.12$) and between NMS cardiovascular sub-score and Th1 total number ($p=0.004$; $r^2=0.23$). Mean RBD score was 4.8±2.9; a positive correlation was found for RBD total score and Th2 total number ($p=0.003$; $r^2=0.24$).

Conclusion: In this study we point out a possible role of peripheral immune system in the development of non motor symptoms in a cohort of PD patients.

Disclosure: Nothing to disclose

EPO2221

Primary Familial Brain Calcification, a cohort study from Padua

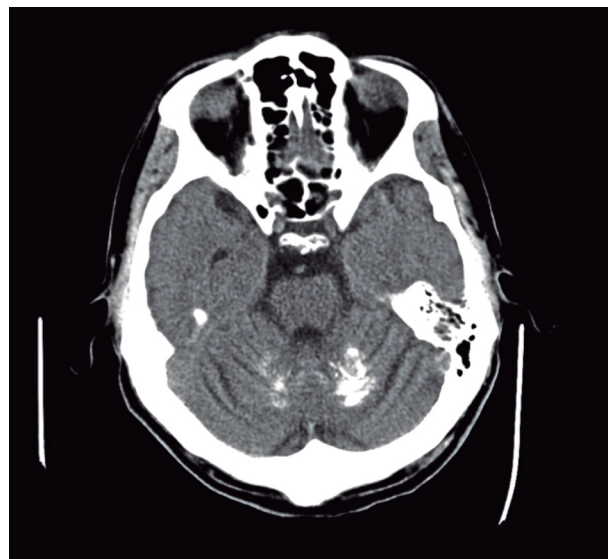
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Background and aims: Primary familial brain calcification (PFBC) is a rare genetic disorder manifesting with bilateral calcification in different parts of the brain. The disease can present with variable symptoms. Related genes are SCL20A2, PDGFRB, PDGFB, XPR1 and MYORG. We investigated the clinical, genetic, neuroradiological and neuropsychiatric characteristics of a cohort of patients.



calcifications in basal ganglia



calcifications in dentate nuclei

Methods: 14 patients (4 F, 10M) with evidence of bilateral brain calcifications on CT scan were enrolled at the

department of Neurology of Padua University. Exact localization of calcification (subcortical white matter, dentate nuclei, cerebral cortex, basal ganglia, brainstem) was detected on CT scan. Genetic testing was performed by NGS with a customized gene panel including all PFBC-related genes; segregation analysis was performed in available relatives. A cognitive evaluation was performed including Mini Mental State Evaluation and Montreal Cognitive Assessment test.

Results: Mean age at onset was 38,4 years; mean age at last examination was 62 years with a mean disease duration of 23 years. 9 patients presented with a movement disorder; 2 had neuropsychiatric symptoms (depression, anxiety and obsessive-compulsive disorder), 4 were asymptomatic. A positive family history was reported in 2 cases. 2 patients carried mutations in SLC20A2, 4 (from 2 different families) in MYORG gene, 2 tested negative for pathogenic variants; genetic analysis is under way in 3 cases. We performed a cognitive evaluation in 7 patients, that found an MCI phenotype in 6 patients.

Conclusion: PFBC represents an important differential diagnosis of Parkinsonism. Patients from our cohort showed heterogeneous clinical presentations, in particular mild parkinsonism, dysarthria and neuropsychiatric symptoms.

Disclosure: Nothing to disclose

EPO2222

Patient Reported Outcomes (PROs) predicting outcome in Parkinson's disease: a Systematic Review

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Background and aims: Patient-reported outcomes (PROs) are easy and cheap to administer but have not been associated with clinically significant outcomes. We recently found a PRO can predict mortality in multiple sclerosis. The United Kingdom Parkinson's disease (PD) tissue bank plan to evaluate their own donor questionnaire, the Imperial College London Disease Questionnaire (ICLDQ), to test if this tool can be used to predict outcome in patients with PD. We conducted a systematic search in order to find out if PROs have been used to assess for outcome in PD, evaluate their structure and compare them to the ICLDQ.

Methods: We conducted a systematic search across 3 databases: MEDLINE, PubMed and Embase looking for cohort studies that matched our aims. Key search terms included 'Parkinson Disease' and 'patient-reported outcome'.

Results: A search yielded 4263 papers however after de-duplication, 6 studies matched our criteria. 5 PROs were used to assess outcome in PD, the 16-item and 6-item Activities-specific Balance Confidence Scale, Short Form Health Survey Questionnaire, Falls Efficacy Scale – International and the Barratt Impulsiveness Scale–11. The only outcome assessed was falling, with all PROs demonstrating a significant ability to predict risk of future falls. Many of these PROs showed overlap with questions found in the ICLDQ.

Conclusion: 6 studies tested PROs to predict prognosis in PD. Falls were the only outcome tested. Research on the predictive capabilities of PROs in PD is still in its infancy and further work is needed.

Disclosure: R Nicholas is funded by the Imperial Biomedical Research Centre (BRC) and Multiple Sclerosis Trials Collaboration (MSTC).

EPO2223

Acquired hepatocerebral degeneration: Experience at a Tertiary Center

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Background and aims: Acquired hepatocerebral degeneration (AHD) is a rare neurological disorder observed in patients with chronic liver disease (CLD) associated with portosystemic hypertension (PH).

To characterize AHD in a cohort of patients with CLD.

Methods: This retrospective study included patients with AHD, defined as neurological manifestations, CLD and globus pallidus T1 hyperintensity on brain MRI. It focused on the clinical, laboratorial, imagiological, and neuropsychological results at first neurological observation. Hepatic encephalopathy (HE) was defined as transient altered level of consciousness.

Results: The clinical records of 76 patients were reviewed (68% males; average age= 56.5±10.8 years). The majority presented mild to moderate hepatic dysfunction (Child-Pugh score A-B). Patients were classified in 2 diagnostic groups: AHD and HE (82.9%) and AHD (17.1%). The most frequent neurological manifestations were: neuropsychiatric disorders (93.4%), tremor (60.5%), gait impairment (55.2%) and parkinsonism (44.7%). On neuropsychological tests, 32 of the 61 evaluated (52%) were in the dementia spectrum (total Dementia Rating Scale-II, percentile<5). The most common neuroradiological abnormalities were subcortical (64.3%) and cortical (49.3%) atrophy and, subcortical T2 hyperintensities (47.1%). In comparison to AHD, the group AHD and EH had higher median ammonia values and had more frequently dementia and cortical hyperintensities. Nineteen patients underwent liver transplantation, with a statistically significant improvement in survival (number of deaths 3 vs 29, p=0.006).

Conclusion: In this study, AHD was clinically heterogeneous. The ammonia levels in plasma and cortical hyperintensity helped identify the coexistence of HE, which was very frequent in our cohort. Liver transplantation significantly modified the survival curve.

Disclosure: Nothing to disclose

EPO2224

Parkinsonism associated with Systemic Lupus Erythematosus: a case report.

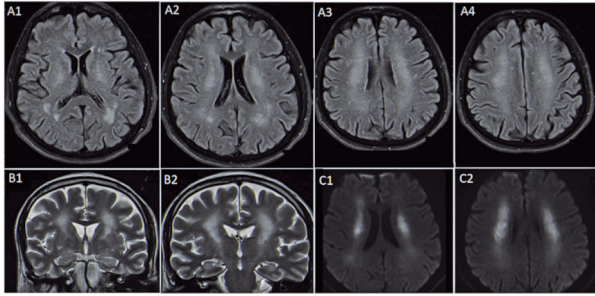
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Background and aims: The involvement of Central Nervous System (CNS) involvement in Systemic Lupus Erythematosus (SLE) usually includes Neuropsychiatric manifestations; Movement Disorders (MD) are barely described, being chorea being the one most frequently reported. SLE is an infrequent cause of Parkinsonism. We report a man with SLE and Parkinsonism

Methods: A 53-year-old man with a 2-years history of SLE and antiphospholipid syndrome, anticoagulated with acenocumarol, presented a 4-months history of cognitive impairment, depression, hypophonia, bradyphasia and bradyphasia, gait disturbances and slowness of movements. Neurological examination revealed hypomimia, overactivity of the frontalis, weak and soft speech, upper limbs paratonic rigidity and bradykinesia, and a short-step gait with a lack of accessory right arm movement. Inexhaustible glabellar and bilateral palmomental reflexes were also noted.

Results: ANAs and lupus anticoagulant were positive. CSF analyses disclosed a mild protein elevation. Electroencephalography (EEG) and DATscan were normal. Brain MRI showed white matter diffuse and symmetrical high-intensity signal in semioval centres, periventricular region and corticospinal tracts on T2/FLAIR weighted sequences. Basal ganglia stroke was not found. Renal biopsy concluded to a lupic nephropathy class III. He was treated with 1g iv/day of methylprednisolone (5 pulses) and mycophenolate mofetil 1g/12h, followed by oral prednisone descending dose during 6 months. After 3 days, he showed an improvement of parkinsonism, particularly of gait and rigidity.

Conclusion: In our case, an inflammatory rather than ischemic cause of parkinsonism was suspected since the patient was under treatment with anticoagulants, and also because of the results of MRI and the good response to corticosteroid treatment.



Brain contrast MRI scan: FLAIR (A1-A4) and T2 (B1-B2) sequence reveals high-intensity signal of white matter near to both posterior horns and bilateral and symmetric at semioval centres, periventricular region and both corticospinal tracts. DWI (C1-C2) shows diffusion restriction.

Disclosure: Nothing to disclose

EPO2225

Plasma NfL correlates with widespread extrastriatal monoaminergic deficits in early Parkinson's disease

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Background and aims: Plasma neurofilament light chain (NfL) has been related to clinical progression in Parkinson's disease (PD). The aim of this study was to investigate the relationship between striatal and extrastriatal 123I-FP-CIT SPECT monoaminergic projections and NfL in patients with recent diagnosis of PD.

Methods: Consecutive patients with suspected PD underwent 123I-FP-CIT SPECT imaging, motor and cognitive assessment and blood sampling. Plasma NfL levels were quantified by Single molecule array (Simoa; Quanterix). 123I-FP-CIT SPECT binding in nigrostriatal and extrastriatal regions of interest (ROI) was calculated in each patient from spatially normalized images. The relationship between NfL plasma levels and 123I-FP-CIT was evaluated by ROI analyses and whole-brain linear regression model adjusting for the effects of age of onset, sex, disease duration and motor functions (UPDRS). A covariance analysis provided the correlates of local and long-distance regions related to higher peripheral NfL levels.

Results: 42 patients with suspected parkinsonism entered the study and 28 patients with established PD at follow-up underwent imaging analyses. Higher NfL plasma levels correlated with lower 123I-FP-CIT SPECT binding in several extrastriatal regions, especially anterior cingulate and temporal lobe ($p < 0.001$) without significant nigrostriatal binding differences. Covariance patterns revealed a widespread monoaminergic depletion in PD patients with high NfL levels, including frontal and parietal lobes.

Conclusion: Our data showed for the first time that serum NfL is associated with widespread extrastriatal monoaminergic deficits in PD patients. This suggests a strong relationship between NfL and cortical function and pathology in PD, pointing out NfL's role as early marker of motor and cognitive progression.

Disclosure: Nothing to disclose

EPO2226

Dystonia is a common feature of adults and adolescents with AS

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Background and aims: Angelman Syndrome (AS) is an inherited, neurodevelopmental disorder mainly characterized by severe cognitive disability, speech impairment, hyperactivity, and seizures. The presence of dystonia in AS subjects has never been studied in detail. The purpose of this study was to evaluate the prevalence, distribution and severity of dystonia in adolescents and adults with AS.

Methods: video-polygraphic recordings of 40 patients with AS genetically confirmed were evaluated. Subjects older than 14 were included. We assessed the presence, distribution and severity of dystonia using the "Barry-Albright Dystonia Scale (BAD).

Results: 26 subjects (aged 14-48 years, median 24) were evaluated. Dystonia was present in 24/26 (92.3%) of the subjects. In all, dystonia involved upper limbs. 7/24 subjects had dystonia involving mouth, 3/24 (12.5%) involving neck, 1/24 (4%) involving trunk. The severity of dystonia ranged from "mild" to "moderate. There was no difference in terms of severity of dystonia among genetic subgroups either for upper limbs ($p=0.86$) or mouth ($p=0.80$).

Conclusion: dystonia is a common feature of adults and adolescents with AS

Disclosure: Nothing to disclose

EPO2227

Effect of tolcapone on peripheral neuropathy in patients with Parkinson's disease treated with levodopa/carbidopa intestinal gel

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Background and aims: Patients with Parkinson's disease (PD) treated with levodopa/carbidopa intestinal gel (LCIG) are at higher risk of peripheral neuropathy. Metabolites of levodopa degradation play important role in its pathophysiology. The aim of study was to assess possible role of catechol-O-methyl transferase inhibitor (COMT) tolcapone on levels of vitamin B12, homocysteine (HCY) and electromyographic (EMG) findings in patients on LCIG.

Methods: We examined 10 patients with advanced PD on stable dose of LCIG for at least 3 months, and after 6 months intervention – either with tolcapone add-on therapy and reduction of LCIG dose ($n=6$), or with B12 and folic acid supplementation ($n=4$). Conduction velocity (CV) of tibial nerve (motor) and ulnar nerve (sensory) was assessed.

Results: The levels of homocysteine decreased similarly in group with vitamin supplementation (3 out of 4) as well as in tolcapone group (5 out of 6) (Fig1). The level of vitamin B12 increased in both groups (vitamin B group 3 out of 4, tolcapone 4 out of 6). Motor CVs improved in 5 out of 6 tolcapone treated patients but in none of patients with vitamin B supplementation (Fig2). Sensory CVs worsened in all patients treated with B vitamins, and in 3 out of 6 patients in tolcapone subgroup (Fig3).

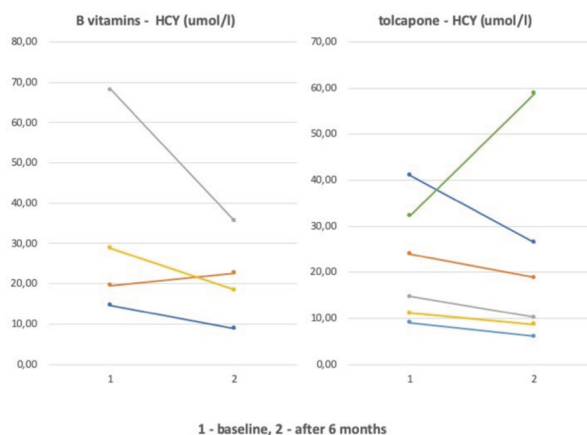


Figure 1

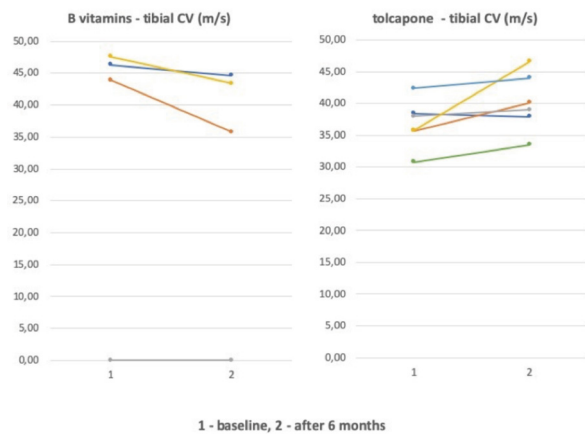


Figure 2

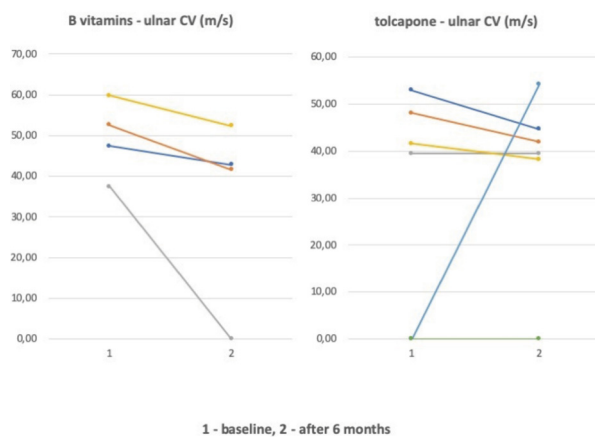


Figure 3

Conclusion: Although tolcapone add-on therapy and vitamin B supplementation decrease HCY and increase vitamin B levels, only patients treated with tolcapone had improved EMG findings – especially improvement in motor CV. This suggests that also other mechanisms connected with COMT function may play role in amelioration of peripheral neuropathy.

Disclosure: Nothing to disclose

EPO2228

Opicapone in Parkinson's Disease – a centre's real-life experience

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Background and aims: Opicapone is a recent treatment for motor fluctuations of patients with Parkinson's disease (PD) under levodopa therapy. This drug has proven efficacy and safety in clinical trials.

Methods: Retrospective study, with evaluation of clinically relevant data from hospital visits of PD patients that initiated opicapone from January 2019 to December 2019. Patients' and clinicians' perception of symptom improvement was objectified by Clinical Global Impression of Change Scale (PGI-C and CGI-C, respectively). Changes in total daily levodopa equivalent dose (LED), adverse events (AEs), dropouts and reasons for discontinuation were also evaluated.

Results: Opicapone was initiated in 35 PD patients (mean age: 71.2±8.9 years; 63% men) and 26 had at least one reevaluation. PGI-C (2.88±1.07 points) and CGI-C (2.86±0.56 points) revealed a perception of improvement of PD symptoms soon after initiation, by both clinicians and patients. The introduction of opicapone led to LED reduction in 13 patients (mean decrease: 226.5±125.6mg). Nineteen patients experienced at least one of the following AEs: dyskinesia (n=12), orthostatic hypotension (n=4), constipation (n=3), dizziness (n=3), hallucinations (n=2), dry mouth (n=1) and confusional state (n=1). Most of the dyskinesia events occurred in patients already experiencing dyskinesia at baseline (n=10;83.3%). Opicapone was discontinued in 6 patients due to AEs. The most common event leading to discontinuation was dyskinesia (n=3;50%).

Conclusion: In this real-life evaluation, in line with data from clinical trials, opicapone was well tolerated and had therapeutic benefits in patients with advanced PD, including LED reduction. Dyskinesia, reflecting greater dopaminergic availability, was the most common side effect and the leading cause of discontinuation.

Disclosure: Nothing to disclose

EPO2229

Apomorphine infusion in the treatment of camptocormia in Parkinson's disease: a 24-months longitudinal open, prospective follow-up study

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Background and aims: Camptocormia in Parkinson's disease (PD) is difficult to affect by therapeutic procedures such as paravertebral botulinum toxin injections, manipulation with oral dopaminergic treatment or deep brain stimulation. The aim of the study was to assess the long-term effect of subcutaneous infusions of apomorphine on this significantly limiting disease manifestation.

Methods: Patients with advanced fluctuating PD who developed camptocormia were treated with apomorphine infusions, based on a positive clinical response and good apomorphine tolerance during apomorphine testing. The daily dose of apomorphine was gradually increased according to clinical effect and tolerance. Patients were monitored regularly, at monthly intervals, over a 24-month follow-up period. The clinical effect of treatment was assessed using the UPDRS-III, UDysRS, and GCI-I scales.

Results: Treatment was initiated in a total of 11 patients. The effective daily doses of apomorphine varied according to clinical effect and tolerance in the range of 40-70mg. Improvement of camptocormia was observed in all patients approximately after four weeks of continuous apomorphine treatment, and this effect remained stable over the whole follow-up period. The treatment was well tolerated by all patients, the side effects were rare and, if present, not serious.

Conclusion: Apomorphine infusion therapy may have a beneficial effect on this very unpleasant manifestation of the disease. This effect can be explained by the sustained stimulation of the ventrolateral striatal D1 receptors, alleviating this type of dystonia.

Disclosure: Supported by: grant from the Ministry of Health, Czech Republic – conceptual development of research organization – MH CZ – DRO (FNOL, 00098892) 2020.

EPO2230

Prevalence of Restless Legs Syndrome in Multiple Sclerosis patients in a tertiary centre – a case-control study

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Background and aims: Previous studies suggested an association between MS and RLS. Data on the influence of DMT are lacking. The aim of this case-control study is to determine the prevalence of RLS in MS patients in an Austrian tertiary centre and to investigate possible associations between the RLS prevalence and disease modifying therapies (DMT) in these patients.

Methods: For this study MS patients seen at the outpatient department and healthy controls aged >18 years were screened between October 2014 and December 2019. RLS was diagnosed based on the criteria of the International Classification of Sleep Disorders, 3rd edition and quantified with the International Restless Legs Syndrome Study Group Rating Scale for Restless Legs Syndrome (IRLSSG).

Results: 302 participants were examined, of which 121 patients (71.9% female) and 120 controls (73.3% female) met the inclusion criteria. The MS group was significantly older than healthy controls (35.4±9.0 vs. 30.8±7.2, p<0.001). In the control group 3.3% (95% CI [0.1%; 6.5%]) had RLS (IRLSSG score >10), in the MS group 21,5% (95% CI [14.2%; 28.8%]). In the subgroup analysis of MS patients 10% had RLS in the “no therapy” group, compared to 23,8% in the therapy groups (detailed percentages see figure 1).

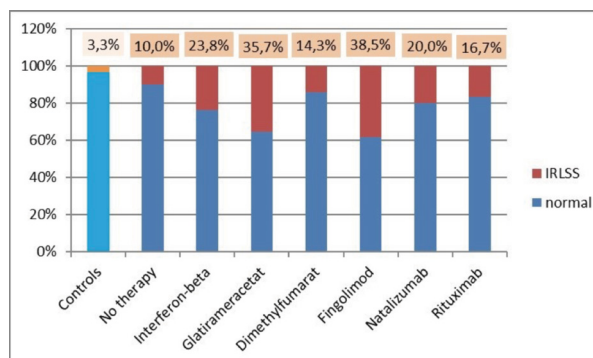


Figure 1: Percentages of RLS in the different therapy groups

Conclusion: Based on our data, a valid association between RLS and MS can be assumed. A higher RLS prevalence in MS Patients with DMT compared to treatment naive patients and healthy controls could be explained by a suspected higher disease activity in these groups.

Disclosure: Nothing to disclose

EPO2231

Series of infrequent cases of Spinocerebellar Ataxias (SCA).

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Background and aims: Spinocerebellar ataxias (SCA) are a heterogeneous group of hereditary diseases, mostly dominant, characterised by a progressive cerebellar syndrome with onset in middle age. They have a great phenotypic variability and they may be associated with eye disorders, pyramidal and extrapyramidal, sensitive or cognitive symptoms.

Methods: The current classification of autosomal-dominant cerebellar ataxias consists of SCA followed by a number, being SCA 3 the most common variety. 3 cases of infrequent variants of genetically confirmed SCA are analysed.

Results: A 38-year-old woman who progressively experiences difficulty walking and lack of coordination in upper limbs. In the following years, she develops abasia, dysphagia, dysarthria and hypophonia, vertical nystagmus, pyramidal symptoms and severe distal hypopalesthesia. Diagnosed with SCA 5 (Holmes or Lincoln ataxia). A 42-year-old man, whose father and brother had similar symptoms, who presents progressive gait disturbance. Over the next few years, he develops scanning speech, nystagmus, slight paraparesis, severe hypopalesthesia and areflexia in lower limbs with pyramidal symptoms. Diagnosed with SCA 11. A woman with a maternal history of gait disturbance who consults at 39 years old due to gait disturbance and dysmetria. In the next 15 years, she develops scanning speech, nystagmus, severe and generalized ataxia and pyramidal symptoms. Diagnosed with SCA 8.

Conclusion: The clinical manifestation of SCA is usually variable and slowly progressive. In its differential diagnosis, acquired ataxias (toxic, metabolic, immunological ...) should be dismissed. After confirming the diagnosis, genetic counselling, neurorehabilitation and symptomatic treatment are important.

Disclosure: Nothing to disclose

EPO2232

Expected and Unexpected Acute Effects on Motility and Balance in De Novo Parkinson's disease Patients due to a Standard Dose of L-dopa. Subclinical Instrumental Evidences.

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Background and aims: Gait impairments are a hallmark of Parkinson's disease (PD). Although patients benefit from L-dopa therapy, its acute effect on gait is poorly understood. This study investigates the acute effects of L-dopa on balance and motility in patients with de novo Parkinson's disease (PD) using an instrumental approach.

Methods: We studied 20 subjects newly diagnosed as clinically probable PD. All patients underwent a standardized acute L-dopa challenge test. Gait assessment was carried out both at baseline and at pharmacologic peak. For each section, subjects performed the Timed Up and Go (TUG) test wearing an inertial sensor. Conventional kinematic parameters processed by the system together with parameters from non-linear multifractal analysis of raw motion data were obtained.

Results: A common trend of improvement on medication was observed for most sensorial parameters. A subgroup of 14 patients was identified based on short-duration response magnitude with a greater clinically detectable motor response. In these patients, L-dopa effect results in unexpected accelerations during postural changes, possibly reflecting instability. Multifractal analysis of motion signals revealed an opposite behavior as expected by the normalization effect of the drug in the rotational tasks.

Conclusion: Balance and motility processes may respond differently to L-dopa in PD, also in an early stage of disease. Patients with a greater acute motor response may present worse postural control when on medication. L-dopa may sub-clinically worsen rotational tasks, requiring an instrumental monitoring for treatment optimization.

Disclosure: Nothing to disclose

EPO2233

Electrophysiological study of eye movements and cognition in Progressive Supranuclear Palsy and Parkinson's disease

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Background and aims: Eye movement abnormalities and cognitive impairment are present to varying degrees in parkinsonian syndromes. They are classic in Progressive Supranuclear Palsy (PSP) and can be seen in Parkinson's disease (PD). Seeing the overlap of neurocognitive and ocular control circuits, the study of eye movements (SEM) could be a tool to assess cognitive functions. Our aim was to compare SEM and study their correlations with cognitive profile in PSP and PD.

Methods: Retrospective study over a period of 16 years (2004-2019) in the Neurology department of Razi University Hospital, including a group of PSP patients (2017MDS-PSP criteria) and a group of PD patients. Clinical, neurocognitive and SEM characteristics of the 2 groups were analyzed. SEM recording studied pursuit, pro-saccades and anti-saccades tasks using video-oculography.

Results: 46 patients were included: 23PSP and 23PD matched in age and sex ($p > 0.05$). Executive dysfunction was the most common cognitive impairment in the PSP group (78.2%). The SEM was uninterpretable in 6 PSP patients and pathological in all the other PSP patients and 30.4% of PD patients. In the PSP group, anti-saccade abnormalities were the most frequent (70%), while in PD group, pro-saccade latencies were abnormal in all patients and pursuit and anti-saccades were affected in 13%. There was no significant correlation between SEM abnormalities and cognitive profile in PSP and PD groups, nor with PSP phenotypes.

Conclusion: SEM anomalies were constant in PSP compared to PD with different profile between the 2 pathologies, which could constitute a differential diagnostic tool. The anti-saccade anomalies in PSP are linked to the more marked frontal dysfunction.

Disclosure: Nothing to disclose

EPO2234

Cerebellar Cognitive affective syndrome scale highly correlates with ataxia score and disease duration in Friedreich Ataxia

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Background and aims: The cerebellum modulates motor and cognitive functions by receiving afferences from cortico-ponto-cerebellar and spinocerebellar tracts and feeds-back through its dentate nuclei (DN) and associated dentato-thalamo-cortical connections. Friedreich ataxia (FRDA) is a genetic disorder characterized by cerebellar and proprioceptive ataxia with progressive atrophy of the DN. FRDA clinical evolution is evaluated by clinical scales that only reflect the motor cerebellar component. Yet, cerebellar cognitive disorders can be assessed by the cerebellar cognitive affective syndrome scale (CCAS).

We looked for a correlation between SARA and CCAS in FRDA that would reflect common pathophysiology through DN impairment.

Methods: 16 FRDA patients were included. CCAS and SARA score were evaluated concomitantly. Pearson rank correlation test was used for correlations between CCAS and SARA, disease duration, age of onset and GAA1.

Patients' characteristics are summarized in table 1.

Female / Male	10/6
Age	27 ± 13
Disease duration (years, mean ± SD)	15 ± 12
Age of onset (years, mean ± SD)	12 ± 6
GAA1 (mean ± SD)	647 ± 179
Point-mutations	2/16
SARA (mean ± SD)	22 ± 10
CCAS (mean ± SD)	
Absolute value (/120)	84 ± 11.4 / 120
Failed items. (/10)	3.3 ± 1.5 / 10

Table 1.

Table legend. SARA: Score on the scale for the assessment and rating of ataxia, CCAS: cerebellar cognitive and affective syndrome scale (2 failed item corresponds to probable cognitive cerebellar disorder while 3 failed items to definite cognitive cerebellar disorder). GAA1: size of GAA1 triplet expansion on the shortest allele.

table 1.

Results: SARA correlated with CCAS absolute score ($r = -0.71$, $p = 0.003$) and failed items score ($r = 0.84$, $p = 0.0007$). Disease duration also correlated with CCAS absolute ($r = -0.53$, $p = 0.04$) and failed items ($r = 0.66$, $p = 0.005$) scores. There was no correlation between GAA1 nor age of onset and CCAS neither for absolute nor failed item scores. (respectively: $r = -0.12$, $p = 0.7$; $r = 0.4$, $p = 0.2$ and $r = 0.21$, $p = 0.43$; $r = -0.2$, $p = 0.43$)

Conclusion: FRDA progressive DN atrophy leads to a cerebellar cognitive impairment that parallels motor ataxic symptoms. CCAS is a reliable tool to study and monitor cognitive function in FRDA patients.

Disclosure: Nothing to disclose

EPO2235

Beyond what the eyes can see, pathology holds the key

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Background and aims: Clinical diagnosis of atypical parkinsonisms may be challenging. The eye-of-tiger sign on MRI, typical of neurodegeneration with brain iron accumulation, has been anecdotally observed in cases clinically diagnosed as atypical parkinsonism.

Methods: Clinico-pathological case.

Results: A 67-year-old-woman presented with progressive painful stiffness and allodynia in her left arm. On examination, she presented hypomimia, bradykinesia, and rigidity with greater involvement of left limbs. 2 years later she developed dystonia, with myoclonic tremor, and hyposthesia involving her left arm, as well as an impairment of balance with falls, in the presence of bilateral but asymmetric parkinsonian signs. She referred constipation, urge incontinence, and restless legs syndrome. Smell was preserved and no pyramidal or cerebellar signs, orthostasis, REM sleep disorder behaviour, cognitive decline, or hallucinations were noted. There was no response to levodopa. She associated a significant axial involvement with disabling rigidity, supranuclear gaze abnormalities, facial dystonia, dysphonia, severe dysphagia, anarthria. Brain SPECT disclosed a presynaptic dopaminergic involvement with postsynaptic preservation, and bifrontal and bitemporal hypoperfusion. T2-weighted brain-MRI revealed a typical eye-of-the-tiger sign. She died 5 years after onset with the clinical diagnosis of progressive supranuclear palsy. Neuropathology disclosed neuronal loss and gliosis, alpha-synuclein-positive cytoplasmic glial and nuclear inclusions, and cytoplasmic neuronal inclusions, typical of MSA, with isolated involvement of nigrostriatal system.

Conclusion: We present the 1st case of neuropathologically confirmed multisystemic atrophy with the eye-of-the-tiger sign on MRI. The presence of gaze abnormalities further complicated a correct clinical diagnosis. Pathological postmortem study remains essential in atypical parkinsonisms.

Disclosure: Nothing to disclose

EPO2236

PRO-PARK study: Is there an association between Professional occupation and Parkinson's disease?

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Background and aims: Some personality features including rigidity, less novelty-seeking, and less creative behaviour have been linked to Parkinson's disease (PD). This may be related to dopaminergic deficit, might influence the preference of professional occupation and substances addiction, even in prodromal/prediagnostic stages.

Methods: On-going case-and-control study in our Movement Disorders Unit. Cases were patients with clinical diagnosis of PD. Controls were patients with different neurological diseases, excluding atypical parkinsonisms, essential tremor, dementia. Professional categories following RIASEC classification and smoke habit were registered.

Results: So far, 330 patients (220 cases, 110 controls), mean age 71.5+9.7 and 64.1+12.5 years-old, respectively ($p<0.001$), have been included. Males predominated among cases (66% vs. 51%, $p=0.006$). Dystonia and migraine were the most common diagnosis among controls.

The most prevalent professions among PD patients were basic works, agriculture and livestock (41.1%), investigative (science and health) (24.7%), administration and finance (15.1%), vs. 31.8%, 20.0%, and 20.0% in controls ($p=0.26$). There was a trend towards an increased frequency of creative professions among controls [teaching (3.6% vs 2.3%), journalism (3.6% vs 0.9%), culture (5.4% vs 3.2%), art (6.4% vs 4.6%)], and lower rate of past/current smoking in PD (36% vs. 46%, $p=0.06$).

Conclusion: Albeit non-significant, we found certain trends suggesting a peculiar professional profile in PD, in line with previous studies. Higher levels of routine and less creative professions might be more appealing for subjects who subsequent develop PD. The relatively small sample size and demographic differences, equally the heterogeneous control group for comparison, may have limited the power of our study to detect significant differences.

Disclosure: Nothing to disclose

EPO2237

Spastic paraplegia as a presentation of oculodentodigital dysplasia with a de novo mutation: case report

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Background and aims: Oculodentodigital dysplasia (ODDD) is an infrequent disorder with craniofacial and limb dysmorphic features due to mutations in the GJA1 gene encoding the protein connexin-43, component of connexon membrane channels.

Methods: Case report.

Results: A 34-year-old man with hypothyroidism and without a relevant family history was referred to our department because of progressive spastic paraplegia. On the examination, apart from generalized hyperreflexia and a spontaneous clonus, dysmorphic features were noted: dorsal kyphosis, scoliosis, flat face, wide forehead, microphthalmia, hypotelorism, narrow nasal bridge, prominent columella, microdontia, misalignment of teeth, low-set ears, camptodactyly, and clinodactyly. He also developed urinary incontinence. His perinatal history was uneventful, just a type 3 syndactyly was observed at birth requiring surgery. Psychomotor milestones were normal. He was able to walk unaided, but he presented frequent falls since early childhood. His gait got worse progressively, being unable to walk unassisted, thereby currently he needs a wheelchair. His parents were not consanguineous. A brain-MRI showed white matter alterations involving both pyramidal tracts, occipital lobes, and a thin corpus callosum. A de novo heterozygous c.443G>A (p.R148Q) mutation was found with damaging impact on connexin-43 structure (absent in his parents). The *Xenopus* oocyte pair system was used to study the functionality of this protein (Neuro2A cell line).

Conclusion: Our patient presents a de novo missense heterozygous mutation in the GJA1 gene leading to a nonfunctional Cx43 of ODDD syndrome. ODDD is uncommon and must be considered in patients with spastic paraplegia. Its recognition is important in terms of genetic counselling and preimplantation diagnosis.

Disclosure: Nothing to disclose

MS and related disorders 3

EPO2238

Anti MOG antibody disease case series: Moroccan experience

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Background and aims: Optic neuritis (ON) is a common clinical manifestation in myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease. Other clinical manifestations include acute demyelinating encephalomyelitis, transverse myelitis and neuromyelitis optica spectrum disorders. MOG Ab disease has recently emerged as a distinct entity carved out of the patient population diagnosed with NMOSD. We aimed to delineate the common features of MOG-IgG-positive ON, and report uncommon presentations.

Methods: In this study, we report 6 cases presenting MOG-IgG-related ON. We collected demographic, clinical, imaging and laboratory data, as well as therapeutic measures and clinical outcome of each patient. The diagnosis was confirmed, according to the 2018's guidelines, by the association of a retrobulbar optic neuritis (RBON) with a high level of anti MOG-Abs in the blood.

Results: ON was described in all our patients with qualifying lesions on brain MRI, except for the 2nd case where imaging was normal. An extensive search for infectious and inflammatory etiology was negative while serum was positive for MOG-Abs tested twice at an interval of 3 months. They showed remarkable clinical resolution with steroids and had remained symptom-free on follow-up. Unusual presentations were identified in 4 patients: intracranial hypertension syndrome, an uveitis, meningitis and epileptic seizures. MOG-Ab-related disorders shared common clinical and prognostic features, but encompass a spectrum wider than recently reported.

Conclusion: Our aim is to increase awareness of the unique findings of MOG-IgG-positive ON, which may initially exhibit uncommon presentations, thereby delaying treatment.

Disclosure: Nothing to disclose

EPO2239

Quality of life (QoL) assessment in multiple sclerosis (MS) patients undergoing autologous hematopoietic stem cell transplantation (AHSCT)

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Background and aims: QoL is an important outcome of MS treatment. We studied QoL changes before and after AHSCT.

Methods: A total of 93 patients with MS. Mean follow-up was 24 months (range 12-53 months), mean age 30.0, range 18-15, male/female -39/54. Relapsing-remitting MS (RRMS) - 49 patients, 44 patients – progressive types of MS (PrMS). All patients were treated by AHSCT. QoL was assessed using generic questionnaire SF-36.

Results: QoL parameters in MS patients at 12 months after AHST improved in comparison to base-line: physical functioning – 66.3 vs 52.6, role-physical functioning - 62.8 vs 43.8, bodily pain - 78.2 vs 76.4, general health - 64.1 vs 56.7, vitality - 62.8 vs 45.4, social functioning - 72.4 vs 57.7, role-emotional functioning - 68.0 vs 55.6, and mental health - 72.1 vs 58.6. With further improvements: Integral QoL Index exhibited 0,50 at long-term follow-up as compared to 0.32 at base-line. QoL improvement was more dramatic in RRMS than in PrMS. We found a significant increase of all 8 SF-36 scales in a year post-transplant as compared with base-line in RRMS patients (p<0.05). In PrMS patients statistically significant improvement was registered for 6 out of eight SF-36 scales (p<0.05). Improved QoL parameters were preserved over the study period in all the patients who did not have disease progression or relapse.

Conclusion: QoL monitoring in MS patients after AHSCT provides clinicians with the unique information regarding the trajectory of changes in QoL parameters. Further studies are needed to examine QoL profile changes in this patient population.

Disclosure: Nothing to disclose

EPO2240

Evaluation of MS diagnostic criteria in a cohort of CIS patients

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Background and aims: Multiple Sclerosis diagnostic criteria, based on Dissemination In Space and Time, have evolved over time leading to earlier diagnosis and simplified process. However, these criterion remained imperfect regarding their accuracy and false positive risk

To analyse the diagnostic performances of 2010 and 2017 McDonald criteria in a cohort of patients since the 1st clinical event

Methods: MS diagnostic criteria were applied to a cohort of CIS patients with baseline brain MRI available and included between 1996 and 2002. We assessed conversion to clinically definite MS, according to Poser criteria clinical definition. The initial MRI was analysed by two neurologists and a neuroradiologist.

Results: 227 patients were included; 136 evolved to a clinically definite MS. At baseline, sensitivities (Se)-Specificities (Sp) for Paty, Barkhof, and Swanton DIS criteria were, respectively: 78.7-52.7%, 61-72.5%, and 81.9-48.2%. Oligoclonal band presence was 71.3% sensitive, and 39.6% specific. DIS according to MacDonald 2017 and 2010 was 82.3% sensitive and 48.2% specific. Se-Sp for DIT according to McDonald 2017 and 2010 were, respectively: 81.8-34.4%, and 55.3-66.7%. Se-Sp for DIT+DIS according to McDonald 2017 were 69.8-52.7%, versus 51.5-72.5% for the 2010 criteria. At 15 years, respective the Sp were: 51.6%, and 68.1% for McDonald 2017 and 2010.

Conclusion: Our results are in accordance with prospective cohorts used to assess MS diagnosis criteria and enforce the need to increase the specificity of MS diagnostic criteria. Some limitations of our study are related to the improvement of MRI technic over time and the absence of sequence dedicated to assess cortical lesion in our MRI material

Disclosure: Nothing to disclose

EPO2241

Unilateral blown pupil as initial presentation of Multiple Sclerosis

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Background and aims: Multiple Sclerosis (MS) diagnosis includes a plethora of MS-related symptoms that prompt evaluation. Since demyelination affects any CNS region, clinical suspicion can be shadowed in the presence of atypical/uncommon symptoms.

Methods: Clinical description of a unilateral fixed dilated pupil as presentation of MS.

Results: A healthy 19-year-old woman presented with complaints of right eye mydriasis and blurred vision. She denied previous medication, drug consumption, contact with plants, ergotamines or head trauma. On examination, a fixed dilated right pupil was striking with slight diminished visual acuity. Pilocarpine test was negative and ophthalmoscopy was unremarkable. Ocular movements were normal. Muscle bulk, tone, strength and reflexes were normal, with flexor plantar responses. All sensitive modalities were preserved. She had no dysmetria nor gait instability. Cerebral CT scan showed multiple white matter subcortical hypodensities. Lumbar puncture revealed positive oligoclonal bands. Erythrocyte sedimentation rate was normal. Drug, infectious and autoimmune testing were negative. Cerebral MRI showed numerous supra- and infratentorial T2 white matter hyperintensities involving periventricular, callosal, and cerebellar areas. 4 months later, she developed left eye optic neuritis, with suboptimal recovery after intravenous methylprednisolone. Last EDSS was 4,5. Natalizumab will be started.

Conclusion: MS suspicion is often challenging given its clinical heterogeneity. A fixed dilated pupil is usually seen with parasympholytics, sympathomimetics, ergotamine exposure or with other signs of III nerve dysfunction. To our knowledge, this is the 1st report of a unilateral fixed mydriasis as the sole presentation of MS. Young age and clinical suspicion were key to prompt diagnostic work-up and start proper treatment.

Disclosure: Nothing to disclose

EPO2242

Haematological abnormalities in a series of patients with multiple sclerosis treated with teriflunomide or dimethyl fumarate

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Background and aims: Teriflunomide (TERI) and dimethyl fumarate (DMF) are oral treatments for relapsing-remitting multiple sclerosis. Both treatments cause lymphopenia by different mechanisms. DMF has been related to the occurrence of progressive multifocal leukoencephalopathy (PML) when lymphopenia is under 500 maintained over time.

Our aim was to assess haematological abnormalities caused by these treatments in our patients.

Methods: All patients in active treatment with TERI (n=55) or DMF (n=44) for at least 12 months were studied. Degree of lymphopenia and neutropenia were established according to Common Terminology Criteria for Adverse Events guidelines. The lowest value of haematological parameters available for each patient was recorded.

Results: TERI group. 1) Leukocyte count: basal vs 12 months (6490±2026 vs 5799±1763, p<0.001); 2) Lymphopenia: 70.9% were normal, 14.5% presented grade 1 (range: 810-970), 12.9% presented grade 2 (530-780), and 1.6% (n=1) presented grade 3. DMF group: 1) Leukocyte count: basal vs 12 months (7171±1912 vs 5746±1756, p<0.001); 2) Lymphopenia: 54.3% were normal, 23.9% presented grade 1 (840-990), 17.4% grade 2 (550-790) and 6.5% (n=3) grade 3. Grade 1-2 neutropenia was presented in 16.7% of TERI group and in 2.4% of DMF group (no increase in infection rate). 6 patients left DMF treatment by lymphopenia (risk of PML).

Conclusion: TERI is a safe treatment and it only caused transient lymphopenia. DMF treatment caused grade 3 lymphopenia in 6.5% of patients and was withdrawn in 13.6% of the patients. Neutropenia is not a serious problem in these patients.

Disclosure: Nothing to disclose

EPO2243

Malignant NMO Rhombencephalitis

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Background and aims: Rhombencephalitis is an inflammatory processes with diverse etiology.

Listeria Monocytogenes, Herpes simplex virus, autoimmune processes such as Behcet's syndrome, and paraneoplastic syndromes are the common causes

Methods: This is a report from 16 years old boy who admitted in our department with a chief complaint of hypersomnia, ophthalmoplegia and blurred vision since 6 months prior to admission.

Results: MRI showed bilateral diencephalic and upper mid brain hyper intense T2 lesion without any enhancement or restriction, which lead us to investigate rhombencephalitis etiologies. Serum and CSF samples evaluated for vasculitis esp. Behcet's disease, autoimmune antibody disorders, bacterial & viral meningoencephalitis and NMO-spectrum disorders.

Based on positive Anti-NMO antibody, plasmapheresis and pulse therapy started and followed with 2 dose of Rituximab (1 gram with 2 weeks interval). Other lab finding showed normal ESR, CRP, and normal serum and CSF analysis for all tested autoimmune and infectious profiles

Conclusion: NMO spectrum disorder is reasonable to consider in patients with autonomic symptoms with drowsiness and thalamic, brainstem lesions in Neuroimaging.

Disclosure: Nothing to disclose

EPO2244

When you have Multiple Sclerosis how bad is it to also have a headache?

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Background and aims: Headache can significantly impact quality of life in patients with multiple sclerosis (MS). Careful distinction between different headache etiologies (disease manifestation, adverse effect of immunomodulatory treatment or associated condition) is essential for establishing the most appropriate therapeutic approach.

Methods: We performed a cross-sectional study including 62 patients with MS; they were asked to complete a questionnaire regarding headache and its characteristics, commonly used therapeutic options, Headache Impact Score (HIT-6 score) and Beck Depression Inventory (BDI-II).

Results: Mean age of the patients was 34.6±9.3 years and 87.1% had relapsing-remitting MS. Median EDSS score was 2 points. 72.6% of the patients had headache: tension-type 46.8%, migraine 16.1%, headache with other characteristics 6.5%, trigeminal neuralgia 3.2%. Headache appeared after MS onset for 36.7% of patients. 24.2% associated depression. Headache had a significant impact on daily life (HIT-6 score >50 points) for 55.1% of patients and was considered by 38.8% a factor that significantly interfered with daily activities. All patients treated with Teriflunomide, subcutaneous Interferon beta1a and beta1b reported headaches. 46% of those treated with Interferon stated that immunomodulatory treatment did not change frequency or severity of preexisting headache, but 36% experienced more frequent and 8% more severe episodes after therapy initiation.

Conclusion: Careful evaluation of headache in patients with MS is of utmost importance as it can have a significant impact on the physical and emotional aspects of daily activity and appropriate treatment can lead to significant improvement of quality of life.

Disclosure: Nothing to disclose

EPO2245

The effect of cladribine tablets in patients with relapsing-remitting multiple sclerosis who had evidence of disease activity in CLARITY

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Background and aims: Less than half of patients with multiple sclerosis (MS) receiving currently approved therapies achieve no evidence of disease activity (NEDA) status over 2 years, and the long-term prognostic value of NEDA is unclear. In the Phase 3 CLARITY study examining the effect of cladribine tablets (CT) 10mg (3.5mg/kg [CT3.5] or 5.25mg/kg cumulative dose over 2 years) in relapsing-remitting MS, 44.3%, 46.0% and 15.8% of patients receiving CT3.5, CT5.25, or placebo, respectively, achieved NEDA status over 96 weeks. Data from CLARITY were used in a post hoc analysis to evaluate CT3.5 treatment benefit in patients who did not achieve NEDA status.

Methods: Treatment benefit was defined as free from qualifying relapse, new magnetic resonance imaging (MRI) activity (new T1 gadolinium-enhancing and active T2 lesions) or 3-month confirmed disability progression (CDP), at Week 96 (Kaplan-Meier). In this exploratory analysis, p-values <0.05 were considered nominally significant.

Results: In CLARITY, 355 patients receiving placebo and 240 patients receiving CT3.5 did not achieve NEDA status, representing 68% of the 2 groups combined. For these patients, baseline characteristics were similar between groups. Compared with placebo, treatment with CT3.5 was associated with a significant treatment benefit, with similar event-free probability of 3- and 6-month CDP between treatment groups (Table 1).

Table 1. Treatment benefit associated with CT3.5 vs placebo in patients who did not achieve NEDA status over 96 weeks

	CT3.5 (N=240)	Placebo (N=355)	P value
Annualised relapse rate (95% CI)	0.26 (0.21–0.31)	0.41 (0.36–0.47)	<0.0001
Number of new T1 Gd+ lesions, mean (SD)	0.5 (1.1)	2.7 (4.7)	<0.0001
Number of active T2 lesions, mean (SD)	1.7 (2.1)	4.4 (5.3)	<0.0001
Event-free probability for risk of 3-month CDP (95% CI)*	0.74 (0.68–0.79)	0.71 (0.66–0.76)	-
Event-free probability for risk of 6-month CDP (95% CI)*	0.83 (0.78–0.87)	0.80 (0.76–0.84)	-

*Kaplan-Meier; CDP, confirmed disability progression; CI, confidence interval; CT3.5, cladribine tablets 3.5mg/kg cumulative dose over 2 years; Gd+, gadolinium enhanced; NEDA, no evidence of disease activity; SD, standard deviation

Table 1

Conclusion: In patients who showed some evidence of disease activity at Week 96, CT treatment still reduced the risk of relapse and active MRI lesions versus placebo with nominal significance.

Disclosure: This study was sponsored by EMD Serono, Inc., a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA, Darmstadt, Germany.

EPO2246

Sensitivity and specificity of 2017 McDonald criteria for multiple sclerosis

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Background and aims: In 2017 McDonald diagnostic criteria for multiple sclerosis (MS) were revised in order to anticipate diagnosis and allow early start of treatment. The aim of the study was to compare sensitivity and specificity of 2010 and 2017 McDonald criteria and to evaluate the risk of MS in patients with an initial demyelinating event (IDE), in a condition in which the time factor has always been decisive.

Methods: We retrospectively analyzed clinical data of 123 patients followed at Verona MS Center with an IDE suggestive of MS in order to demonstrate fulfillment of 2010 and 2017 McDonald criteria. Sensitivity and specificity of both 2010 and 2017 diagnostic criteria were calculated using conversion to clinically definite MS (CDMS) as the gold standard. Survival analysis using Kaplan-Meier curve was also performed.

Results: In the analysis for sensitivity and specificity we included 102 patients with 2 years of follow up [median 70 months (24-185)]. 49 patients (48%) converted to CDMS. 2010McDonald criteria showed 65.3% sensitivity (95% IC: 50.36-78.33%) and 45.28% specificity (95% IC: 31.6-59.5%). 2017McDonald criteria 89.8% sensitivity (95% IC: 77.8-96.6%) and 16.98% specificity (95% IC: 8.0-29.8%). Survival analysis showed that patients with MS diagnosis according to 2010McDonald had higher risk to convert to CDMS with median time to conversion of 1583 days (882.9–2283.1).

2010 McDonald criteria		CD + (n)	CD- (n)		
DIS: can be demonstrated by one or more T2- hyperintense lesions in two or more of four areas of CNS: periventricular, cortical or juxtacortical, infratentorial brain regions and spinal cord. Symptomatic lesions in brainstem or spinal cord are excluded	McD10+ (n)	32	29	61	PPV= 52,5%
	McD10- (n)	17	24	41	NPV=58,5%
	tot	49	53	102	
SENS=65,3% SPEC=45,3%					
2017 McDonald criteria		CD + (n)	CD- (n)		
DIS: can be demonstrated by one or more T2- hyperintense lesions in two or more of four areas of CNS: periventricular, cortical or juxtacortical, infratentorial brain regions and spinal cord. Symptomatic lesions in brainstem or spinal cord are included.	McD17+ (n)	44	44	88	PPV= 50%
	McD17- (n)	5	9	14	NPV=64,3%
	tot	49	53	102	
SENS=89,8% SPEC=17%					

Fig1. Sensitivity and specificity analysis

Fig1. Sensitivity and specificity analysis

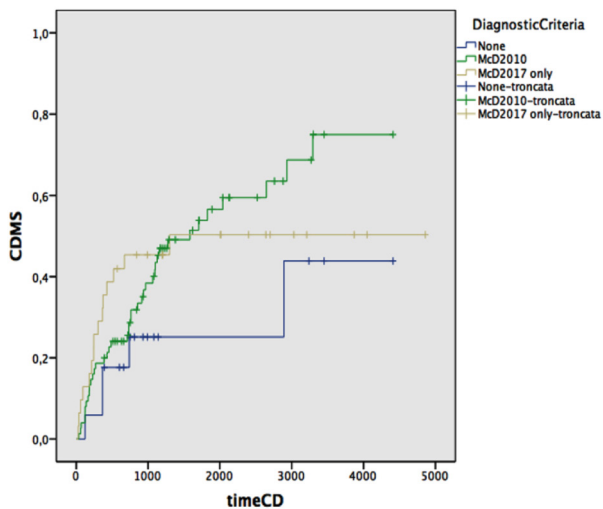


Fig2. Kaplan-Meier curve

Fig2. Kaplan - Meier curve

Conclusion: 2017McDonald criteria enable MS diagnosis in a greater number of patients with IDE compared to 2010McDonald but they seem to underestimate the risk of a second clinical event.

Disclosure: Nothing to disclose

EPO2247

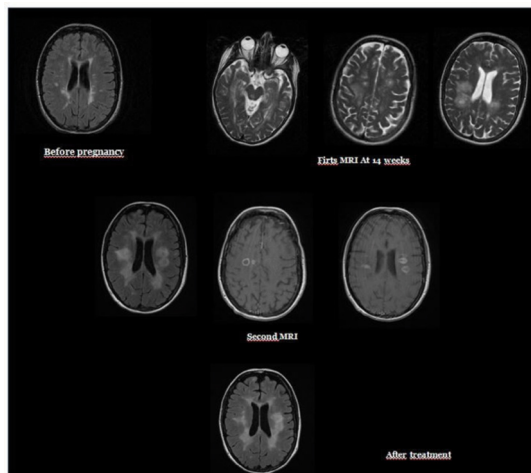
Management of severe rebound of natalizumab during pregnancy

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Background and aims: It is well known that after natalizumab treatment discontinuation there is a risk of catastrophic rebound, specially in highly active multiple sclerosis patients. To manage severe rebound after stopping natalizumab in a pregnant patient.

Methods: A 33-year-old woman with RRMS, treated with natalizumab for the last 5 years. Natalizumab was stopped due to her desire for pregnancy. After a month she got pregnant on purpose.

Results: At 14 weeks pregnant she presented with spastic paralysis of lower limbs and gait ataxia; the EDSS score was 6.5. A brain magnetic resonance imaging (MRI) was performed with increase of the number of T2 lesions. Intravenous methylprednisolone was given for 5 days with partial recovery. At 16 weeks pregnant she came again with progressive worsening. On admission, she presented bilateral lower limbs and left arm plegia with an EDSS score of 8. A 2nd MRI showed increase of the number of T2 lesions, some of them with pseudotumoral form and an opening gadolinium enhancement. Methylprednisolone was given for 5 days, followed by 1 therapeutic plasma exchange (TPE) cycle, with no improvement. For this reason, a combination regimen of methylprednisolone 1g/daily plus alternate-day single-volume plasma exchange prior to alternate-day dose of IV immunoglobulin. She progressively improved up to an EDSS score of 6.5. At 18 weeks pregnant natalizumab was restarted with extended interval dosing (every 6 weeks). Later, she presented with preterm premature rupture of membranes at 34 weeks. She gave birth to a healthy child. Natalizumab treatment was administered 1 week after delivery.



Conclusion: MS treatment during pregnancy is controversial and there is a lack of information about how to treat relapses.

Disclosure: Nothing to disclose

EPO2248

Rate of Confirmed Macular Oedema With Ozanimod in Patients With Relapsing Multiple Sclerosis: Results From the Ozanimod RMS Clinical Development Program

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Background and aims: Ozanimod is a sphingosine 1-phosphate (S1P) receptor 1 and 5 modulator. Macular oedema (ME) has been reported with S1P modulators, and is potentially related to effects on vascular endothelial barrier function. We evaluated the incidence of confirmed ME with exposure to ozanimod across all clinical trials of relapsing multiple sclerosis (RMS).

Methods: This analysis included all RMS participants who received ozanimod HCl 0.5 or 1mg/d in phase 1, 2, and 3 clinical trials, and the ongoing open-label extension (OLE) trial of ozanimod HCl 1mg/d. An independent Macular Edema Review Panel (MERP) reviewed treatment-emergent adverse events of ME and related macular terms, cases of increased central foveal thickness >20% of baseline, and any relevant optical coherence tomography abnormalities.

Results: With exposure to ozanimod in any RMS trial (n=2787; data cutoff 31/1/2019; mean [SD] exposure, 37.1 [14.7] months; 8688.3 patient-years on study), there were 7 cases (0.3%) of MERP-confirmed ME. Of these, 4 occurred during controlled phase 3 trials (0.2% of ozanimod-treated phase 3 trial participants) and 3 occurred during the ongoing OLE trial (0.1% of OLE participants). Most cases of ME occurred between 6-12 months of ozanimod exposure. All 7 cases had either pre-existing or confounding factors and all cases resolved or were resolving (Table).

Table. Confirmed Cases of Macular Oedema in All RMS Patients Treated With Ozanimod

Case	Study	Treatment Group	Time of Onset Relative to Treatment Initiation, Months	Pre-existing Risk Factor or Confounding Factor	Action Taken With Study Drug	Status
1	RADIANCE Phase 3 (NCT02047734)	Ozanimod HCl 0.5 mg	-7	History of ME	Ozanimod withdrawn permanently	Resolved
2	SUNBEAM (NCT02294058)	Ozanimod HCl 0.5 mg	-6	ME secondary to ocular trauma	Ozanimod withdrawn permanently	Resolved
3	RADIANCE Phase 3	Ozanimod HCl 0.5 mg	-12	Central serous chorioidopathy	Ozanimod withdrawn permanently	Resolved
4	SUNBEAM	Ozanimod HCl 1 mg	-6	Prior unreported uveitis (intraocular inflammation)	Ozanimod withdrawn permanently	Resolved
5	DAYBREAK (NCT02576717)	Ozanimod HCl 1 mg	-12	Pigment epithelial detachment with possible choroidal neo-vascularization	No action taken	Resolving*
6	DAYBREAK	Ozanimod HCl 1 mg	-0.5	Uveitis	Ozanimod withdrawn permanently	Resolved
7	DAYBREAK	Ozanimod HCl 1 mg	-10	History of retinopathy and optic neuritis	Ozanimod withdrawn permanently	Resolved

*As of 31 January 2019 data cutoff. HCl, hydrochloride; ME, macular oedema; RMS, relapsing multiple sclerosis.

Conclusion: ME was confirmed in 0.3% of ozanimod-treated participants in the ozanimod RMS clinical development program. All confirmed cases had predisposing comorbid conditions, which may increase the risk of ME in subjects on ozanimod.

Disclosure: Study funded by Celgene, a wholly-owned subsidiary of Bristol-Myers Squibb.

EPO2249

Atrophy of different cortical and subcortical compartments contributes to explain clinical disability in patients with MS: a multicenter study

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Background and aims: Multiple sclerosis (MS) affects several cortical and subcortical structures. The multiparametric assessment of cortical, deep grey matter (DGM), cerebellar and cervical cord atrophy is likely to help characterizing MS phenotypes and explaining patients' disability.

Methods: 3T brain and cervical cord T2- and T1-weighted images were acquired from 195 MS patients (137 relapsing-remitting [RR] MS, 58 progressive [P] MS) and 67 healthy controls (HC) at 3 European sites. Brain and cord lesion burden was assessed. Cortical thickness (CTh), DGM volumes, cerebellar volumes and cervical cord cross-sectional area (CSA), calculated using Freesurfer6.0, FSL-FIRST, SPM12-SUIT and the active surface methods, were compared between patients and HC and between phenotypes. Age-, sex- and site-corrected stepwise linear regression models investigated the association of lesions and cortical/subcortical atrophy with clinical disability.

Results: Compared to HC, MS patients had widespread atrophy in all cortical lobes, DGM nuclei and cerebellar lobules, as well as reduced cord CSA. Similar results were observed in PMS vs RRMS patients, with a particular involvement of frontal, sensorimotor, parietal and insular cortices and anterior cerebellar lobules. In MS patients, higher disability was associated with atrophy of cortical and DGM structures, and with reduced cord CSA ($p = \text{range} < 0.00-0.03$). The multivariate model retained phenotype ($\beta = 0.52$, $p < 0.001$), brain lesion volume ($\beta = 0.16$, $p = 0.002$), left postcentral gyrus CTh ($\beta = -0.11$, $p = 0.029$) and cord CSA ($\beta = -0.25$, $p < 0.001$) as significant predictors of clinical disability ($R^2 = 0.642$, $p < 0.001$).

Conclusion: In MS, the multiparametric evaluation of lesion volume and atrophy of different cortical/subcortical structures contribute to explain a large portion of clinical disability.

Disclosure: Nothing to disclose

EPO2250

Clinical predictors of disability in treatment-naive relapsing-remitting multiple sclerosis patients

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Background and aims: Multiple sclerosis is a demyelinating disease of the CNS characterized by progressive accumulation of disability. Investigation of risk factors for disability progression in multiple sclerosis (MS) is a prospective field of research. In the era of disease-modifying therapy (DMT), most such studies involve mixed populations of patients DMT-receiving and DMT-naive patients. Risk factors of disability in the natural course of MS are poorly outlined.

Methods: Clinical data of DMT-naive patients with relapsing-remitting MS (n=70, mean age 38.73±10.34 years) were retrospectively studied. EDSS score 4 was taken as a disability milestone (DM). 2 sets of clinical parameters (1 for symptoms at the MS onset and 1 for other onset-specific features) were studied as the risk factors for reaching the milestone using multivariate Cox regression.

Results: In Cox model, pyramidal symptoms at MS onset (HR 2.4, 95%CI 1.0-5.8, p=0.05), MS onset at >50 years (HR 5.5, 95%CI 1.4-21.1, p=0.013) and BMI <18.5 (HR 4.05, 95%CI 1.2-12.8, p=0.017) were associated with a higher risk, while EDSS 1 to 2.5 at MS onset (HR 0.23, 95%CI 0.098-0.52, p<0.001) was protective against reaching EDSS 4.

Conclusion: The risk factors identified in our study are consistent with other studies conducted in mixed populations suggesting the same trend for predictive factors in the pure population of DMT-naive patients.

Disclosure: Nothing to disclose

EPO2251

The Epstein-Barr antibody paradox in Multiple Sclerosis

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Background and aims: Increased levels of serum and cerebrospinal fluid (CSF) antibodies against morbilli, varicella zoster and rubella, and increased serum antibodies against Epstein-Barr virus (EBV), are common features of MS. Paradoxically, several studies showed that the level of antibodies against the Epstein-Barr nuclear antigen 1 (EBNA1) is low in the CSF, which may be due to immune evasive properties of EBNA1 or to low level of exposure of this antigen in the central nervous system. Our objective is to determine whether low CSF antibody levels against EBNA1 also apply to an immunodominant viral envelope EBV antigen, gp350.

Methods: The level of anti-gp350 IgG was determined in serum and CSF in MS patients (n = 23) and healthy controls (n = 18) by an ELISA using a recombinant gp350 antigen. The antibody index was calculated as adjusted QOD (QOD/total IgG CSF/total IgG serum).

Results: The serum concentration of anti-gp350 IgG was higher in the MS patients. The CSF antibody index (adjusted QOD) for gp350 was significantly lower in the MS patients (0.070) than in the healthy controls (0.142, p<0.001). We obtained similar results if we included EBV seropositive controls only.

Conclusion: Our finding of low CSF gp350 antibody index is consistent with other reports on the EBV antibody paradox in MS, arguing against antigenic exposure of this virus in the central nervous system. Interaction with EBV in MS pathogenesis might be confined to the peripheral immune system.

Disclosure: Nothing to disclose

EPO2252

Real-world Effectiveness and Safety of Fingolimod in Relapse-Remitting Multiple Sclerosis in a Portuguese Tertiary Center

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Background and aims: Fingolimod is a highly effective disease modifying treatment (DMT) for relapsing-remitting multiple sclerosis (RRMS). Nevertheless, considering the changing treatment landscape with newer drugs, it is important to evaluate its real-world effectiveness to adequate it in the decision algorithm.

Methods: Retrospective study, including all RRMS patients treated with fingolimod in our centre. Demographic and clinical data were collected. Annualized relapse rate (ARR) and EDSS progression was evaluated in patients with more than 6 months of treatment.

Results: 278 patients were included, 62.6% female, with mean age of 41.6 years and mean disease duration of 8.69 years when fingolimod was started. Mean treatment duration with fingolimod was 38.5±24 months. Adverse events occurred in 29.9%, mainly lymphopenia. There were 3 cases of in-situ melanoma, 2 life-threatening infections and 1 macular oedema. Fingolimod was discontinued in 27.1%, mostly due to inefficacy and only in 4.2% due to adverse events. In naïve and switching from first-line DMT patients (n=141), there was a significant decrease in mean ARR (1.15 vs. 0.41) and in median EDSS (2.5 vs 2.0). At the end of follow-up, 44.3% patients remained relapse-free and 90% had no disease progression. 95 patients switched from natalizumab, mostly due to PML risk. Those patients showed no differences in mean ARR (0.49 vs. 0.5), however there was a significant increase in median EDSS (2.5 vs. 3). **Conclusion:** Our study highlights that fingolimod remains a safe DMT for RRMS, with consistent effectiveness. However, its use should be weighted in patients switching from natalizumab.

Disclosure: Nothing to disclose

EPO2253

A long-term follow-up study on biochemical markers of response to interferon beta-1b treatment in relapsing-remitting multiple sclerosis

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Background and aims: While interferon β -1b (IFN β -1b) is still commonly used disease-modifying drug in multiple sclerosis (MS), therapeutic possibilities are expanding, and treatment failure should be identified early. Markers to predict response to IFN β -1b, either clinical or biochemical, are therefore urgently needed. Interferon-induced proteins, including viperin, Suppressor of cytokine signalling-3 (SOCS3), Ubiquitin specific peptidase-18 (USP18) and Myxovirus resistance protein A (MxA), are possible markers of IFN β -1b bioavailability and treatment response. The objective of our study was to evaluate viperin, SOCS3, USP18 and MxA as markers of treatment response in Polish IFN β -1b-treated multiple sclerosis patients.

Methods: In 45 IFN β -1b-treated Polish MS patients, serum concentrations of viperin, SOCS3, USP18 and MxA were assessed before and after 24 months of IFN β -1b treatment. The patients were followed clinically and with magnetic resonance imaging for a median of 6,8 years.

Results: Low viperin, USP18 and MxA at baseline and 24 months and high SOCS3 at 24 months correlated with higher disease activity up to the 6th year of observation, but only baseline MxA and USP18 were independently related to outcome, with higher concentrations predicting less disease activity in the first 3 years and after the 1st year, respectively.

Conclusion: We confirm the predictive value of MxA and propose USP18 as a possible new prognostic biomarker in IFN β -1b-treated MS patients.

Disclosure: Nothing to disclose

EPO2254

Real-World Alemtuzumab Efficacy and Safety in a Multiple Sclerosis Patient Population: A Single-Center Cohort Study

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Background and aims: Alemtuzumab (ALZ) is an anti-CD52 humanized monoclonal antibody approved for the treatment of relapsing-remitting multiple sclerosis (RR-MS). We here present our experience from a cohort of MS patients since initiation of ALZ treatment.

Methods: We analyzed prospectively collected demographic, adverse event and clinical outcome data of all patients with RR-MS treated with ALZ in our tertiary referral MS center, for time period 2014-2019. Clinical outcomes of interest were: a) Expanded Disability Status Scale (EDSS) score, and b) the relapse rate.

Results: We included 20 RR-MS patients (9 women); median age 42 years [range 27-59], median disease duration 14.5 [1-23] years. Median EDSS at ALZ treatment initiation was 5.00 [range 2.00-6.00]. 3 patients received only the baseline treatment and not the 1st annual anniversary course. At the end of 2nd year of ALZ treatment, median EDSS was 4.00 [range 2.00-6.00]. 9 of 20 (45%) patients needed a 3rd treatment. 4 of 20 (20%) patients experienced a relapse within 2 years of treatment initiation; 1 (5%) patient experienced a relapse before the 1st annual anniversary dose. 6 of 20 (30%) patients developed mild infusion-associated reactions. No serious adverse events were observed.

Conclusion: In our cohort of RR-MS patients with more severe disability and longer disease duration at treatment onset compared to patients in the pivotal trials, ALZ led to improved clinical outcomes and was not associated with serious adverse events. Extended period of observation in a larger patient population will help further confirm its safety and efficacy.

Disclosure: Nothing to disclose

MS and related disorders 4

EPO2255

Myelin Oligodendrocyte Glycoprotein Antibody-associated Neuromyelitis optica spectrum disorders (NMOSD)

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Background and aims: MOG-antibody associated neuromyelitis optica spectrum disorder (NMOSD) is an emerging demyelinating disorder that is characterized by a broad range of clinical phenotypes and neuroimaging findings with a disease course that is distinct from aquaporin-4 antibody-positive NMOSD and multiple sclerosis (MS). The aim was to study the clinical, radiological profile and treatment outcome in MOG antibody-positive NMOSD.

Methods: The study was carried out at a tertiary care multi-specialty hospital in Western Maharashtra.

The study protocol was approved by the institutional ethics committee. The study design was a prospective observational study with patients recruited over a period of 1 year from December 2018 to November 2019. The 2015 International consensus diagnostic criteria were used for the diagnosis of NMOSD. 15 patients of MOG-antibody associated NMOSD were studied.

Results: Male preponderance was seen. The mean age of onset was 29 years. Isolated optic neuritis (ON) was the most common presentation, bilateral ON and longitudinally extensive ON was also seen. High dose corticosteroid as 1st-line in treatment of acute attack was not sufficient and 46.67% of patients required plasmapheresis for treatment of acute attack. Frequency and interval of relapse in patients not on prophylaxis was variable, with one patient had 3 relapses in 1 year. Rituximab was most effective in the prevention of relapse.

Conclusion: Despite some overlap, MOG-antibody associated NMOSD exhibits different radiological and phenotypic features than both AQP4-IgG-associated NMOSD and typical MS. MOG-antibody should be tested in all patients of seronegative NMOSD and in patients of MS in whom oligoclonal bands are absent.

Disclosure: Nothing to disclose

EPO2256

Sensitivity of EDSS Cerebral Functional System in assessment of cognitive decline in relapsing-remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease that might lead to physical disability, chronic fatigue, depression and cognitive impairment. The Expanded Disability Status Scale (EDSS) is widely used to assess and monitor progression of disability in patients with multiple sclerosis. It is based on functional assessments in 8 systems (FS): pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual and cerebral (mental) functions. The Cerebral Functional System (CSF) assessment was intended to take into account level of depression and euphoria, decrease in mentation and fatigue. We investigated if the CFS score mirrors more extensive and well validated neuropsychological testing.

Methods: We performed neuropsychological examination including: Symbols Digits Modalities Test (SDMT), Paced Auditory Serial Addition Test (PASAT), California Verbal Learning Test (CVLT), Wisconsin Card Sorting Test (WCST), Benton Visual Retention Test (BVRT), Color Trail Test (CTT) and phonemic and semantic verbal fluency tests in 65 Polish-speaking patients with relapsing-remitting MS (RRMS), all receiving IFN-beta. We tested these data for associations with CFS score (Spearman's rank correlation coefficient).

Results: The greater disability measured with CFS score was associated only with decline in SDMT-evaluated information processing speed ($\rho = -0,32$).

Conclusion: This study confirms previous speculations and some findings that interview-based cognitive assessment - CFS is not enough sensitive to detect subtle but clinically relevant cognitive changes in patients with RRMS. There is an urgent need to replace current CSF protocol with more objective examination tools.

Disclosure: Nothing to disclose

EPO2257

Sleep Disorders in Patients with Multiple Sclerosis

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Background and aims: The aim was to assess relationships between sleep disorders (SD), cognitive impairment (CI), anxiety and depression in patients with relapsing-remitting (RR) multiple sclerosis (MS).

Methods: 105 patients with RR MS (80 females and 25 males) aged from 22 to 67 years were included into the study (mean age: 41.8±10.7; EDSS: 3.5±1.6; disease duration (DD): 10.3±8.5 years). All participants completed questionnaires on sleep (the Pittsburgh Sleep Quality Index /PSQI), cognitive functions (the Montreal Cognitive Assessment/MoCA), depression (Beck Depression Inventory/BDI) and anxiety (Hamilton Anxiety Rating Scale /HAM-A).

Results: According to PSQI score the patients were divided into 2 groups: with (n=42) and without SD (n=63). The patients with MS and SD were older (45.36±1.66 vs 39.41±1.27, p=0.005), had higher score on EDSS (3.98±0.26 vs 3.14±0.19, p=0.008), BDI (13.79±1.14 vs 8.96±0.86, p=0.0009) and HAM-A (24.52±1.42 vs 16.56±0.99, p<0.0001) scales compared with patients without SD. The frequency of anxiety (p=0.0034) and depression (p=0.038) was significantly higher in MS patients with SD compared to those without SD. No significant difference was found in gender, level of education, DD and MoCA score. In patients with SD significant negative correlation between MoCA and BDI score (r=-0.42, p<0.005) was found. In the group of patients without SD significant negative correlation between MoCA and EDSS (r=-0.27, p=0.03), MoCA and BDI (r=-0.26, p=0.043), MoCA and HAM-A (r=-0.25, p=0.041) score was detected.

Conclusion: SD was prevalent in MS patients and associated older age, higher EDSS score and presence of anxiety and depression.

Disclosure: Nothing to disclose

EPO2258

Prevalence of pregnancy outcomes after exposure to interferon beta before or during pregnancy stratified by maternal characteristics: A register-based cohort study in Finland and Sweden

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Background and aims: A cohort study in women with multiple sclerosis (WMS) reported no increase in the prevalence of adverse pregnancy outcomes after interferon beta (IFNβ) exposure before or during pregnancy. However, differing prevalence by maternal characteristics is unknown. This study describes the prevalence of serious adverse pregnancy outcomes (SAPO) among pregnant WMS exposed to only IFNβ and those unexposed to any multiple sclerosis (MS) disease modifying drugs (MSDMD), stratified by maternal characteristics.

Methods: Data on pregnant WMS 1) dispensed only IFNβ within 6 months before last menstrual period (LMP) or during pregnancy (IFNβ-exposed, n=718 pregnancies) and 2) without dispensed MSDMD (unexposed, n=1397 pregnancies) was extracted from Finnish and Swedish Registers. Prevalence (%) of SAPO (elective terminations due to foetal anomaly, major congenital anomalies in live birth, and stillbirth) with 95% confidence intervals (CI) was analysed with stratification by maternal characteristics at LMP: Time since MS diagnosis, duration of IFNβ treatment, maternal age, and having chronic diseases.

Results: Prevalence of SAPO appeared similar in IFNβ-exposed versus unexposed WMS when MS was diagnosed ≤2 years, 3-5 years and >5 years before LMP (Table 1). The prevalence was lower among the IFNβ-exposed versus unexposed WMS with ≤2-year and 3-5-year of treatment, but was higher in IFNβ exposed WMS with >5-year treatment. However, differences were nonsignificant (Table 2). The prevalence was similar among the IFNβ-exposed vs unexposed WMS in strata by maternal age and having chronic diseases.

Table 1. Prevalence of SAPO among the IFNβ-exposed versus unexposed in women diagnosed with MS at =2 years, 3-5 years and >5 years before LMP

	Prevalence of SAPO, % (95% CI)	
	IFNβ exposed	IFNβ unexposed
MS diagnosed at =2 years before LMP	0.9 (0.1–3.2)	3.0 (1.6–5.2)
MS diagnosed at 3–5 years before LMP	2.4 (0.9–5.1)	6.0 (4.0–8.6)
MS diagnosed at >5 years before LMP	3.3 (1.4–6.4)	3.0 (1.7–4.8)

CI, confidence interval; IFN, interferon; LMP, last menstrual period; MS, multiple sclerosis; SAPO, serious adverse pregnancy outcomes

Table 1

	Prevalence of SAPO, % (95% CI)	
	IFNβ exposed	IFNβ unexposed
MS diagnosed at =2 years before LMP	0.9 (0.1–3.2)	3.0 (1.6–5.2)
MS diagnosed at 3–5 years before LMP	2.4 (0.9–5.1)	6.0 (4.0–8.6)
MS diagnosed at >5 years before LMP	3.3 (1.4–6.4)	3.0 (1.7–4.8)

CI, confidence interval; IFN, interferon; LMP, last menstrual period; MS, multiple sclerosis; SAPO, serious adverse pregnancy outcomes

Table 2

Conclusion: The descriptive prevalence of SAPO appeared similar with IFNβ-exposure before or during pregnancy, when pregnant WMS were stratified by maternal characteristics.

Disclosure: Funding for the analysis, project management and medical writing was provided by Bayer AG, Biogen, Merck KGaA and Novartis Pharma AG.

EPO2259

The dynamics of clinical, laboratory and neuroimaging parameters in patients with anti-MOG encephalomyelitis who received a course of B-depletion therapy

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Background and aims: Anti-MOG encephalomyelitis is an autoimmune demyelinating disease which damages optic nerves, brain and spinal cord, with the detection of specific antibodies to myelin glycoprotein oligodendrocytes (anti-MOG) in the blood serum. Despite the similarity of the clinical picture with multiple sclerosis (MS), the treatment of anti-MOG encephalomyelitis is different.

Methods: We monitored 6 patients with anti-MOG encephalomyelitis. revealed acute onset with visual impairment, ataxia, transverse myelitis (pyramidal, sensitive and bladder disorders). The level of anti-MOG was more than 15pg/ml (26-92pg/ml) in all patients. The patients received a course of B-depletion therapy with Rituximab (1000mg +1000mg 2 weeks later).

Results: Neurologic status, neuroimaging and laboratory parameters (main subpopulations of B-lymphocytes) were monitored in dynamics. After 6 months, all patients showed a positive trend in sensitive disorders, spasticity, increased walking distance, but none of them had a full recovery of the CD-20 pool of B-lymphocytes. MRI with contrast enhancement 6 months after B-depletion therapy course displayed positive dynamics - a decrease in the signal intensity on T2, the absence of additional focuses in the substance of the brain and spinal cord, in one patient - regression of focuses in the cervical and thoracic spinal cord. There were no signs of repeated exacerbation.

Conclusion: Rituximab therapy was effective and well tolerated in anti-MOG encephalomyelitis. Therefore, at the atypical beginning of MS, an anti-MOG study is shown, since only early B-depletion therapy reduces the risk of disability

Disclosure: Nothing to disclose

EPO2260

Coagulation activation and cerebral hypoperfusion in relapsing-remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is an inflammatory-demyelinating and degenerative disease of the central nervous system. The aim of our study is to evaluate the serum/plasma levels of coagulation/complement factors in relapsing MS patients compared to remitting ones and to healthy controls, and to assess the presence of brain hemodynamic changes of patients in order to correlate their coagulation status with MRI perfusion data.

Methods: We included 57 relapsing-remitting MS patients and 31 age/sex-matched controls. Complement/coagulation factors, endothelial damage markers, blood count have been dosed in all participants. MS patients underwent dynamic susceptibility contrast-enhanced 3.0-T MRI.

Results: 26 relapsing (21F/5M, age 40.7±9.7 years) and 31 remitting (23F/8M, 40.8±8.8 years) patients compared to 31 controls (23F/8M, 40.9±9.1 years) showed: a higher either body-mass-index (23.8±3.5, 24.4±4.1, 21.8±3.3, respectively, p=0.02), fibrinogen (323±82, 322±80, 282±43mg/dl, p=0.04), d-dimer (299.6±156.9, 307.2±203.7, 210.2±99.3, p=0.06) or protein-C (114±20, 111±18, 99±15%, p=0.004), a lower either hematocrit (40.4±3.4, 41.0±3.4, 42.5±3.1%, p=0.05), lymphocyte count (1564±596, 1797±608, 1947±588n/mmc, p=0.05) or protein-S (86±17, 81±22, 92±15%, p=0.05). Relapsing compared to remitting patients had: a higher either EDSS (2.9±1.1, 1.6±1.3); number of relapses either during overall disease (5.2±3.6, 2.7±3), previous one (0.9±0.8, 0.2±0.5) or 2 years (1.4±1.4, 0.2±0.7), (p<0.0001 for all); a lower lymphocyte B count (217.7±92.6, 293.3±160.9n/mmc, p=0.04). Perfusion MRI data are under evaluation.

Conclusion: Our preliminary data indicate coagulation activation in relapsing-remitting MS patients compared to healthy controls suggesting their inflammatory-thrombotic

status with reduced lymphocyte count as well as decreased number of circulating B-lymphocytes during the relapse.

Disclosure: Our research has been granted by Italian Ministry of Health (Project code: PE-2013-02357745)

EPO2261

The use of plasma exchange in NMOSD and MS

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*Rheumo-neurology, Tashkent Medical Academy, Tashkent, Uzbekistan***Background and aims:** To analyze successful cases of plasma exchange in patients with NMOSD.**Methods:** We retrospectively studied 30 NMOSD episodes and 20 MS cases based on the TMA clinic database over the past 5 years. Among them, 24 patients from the NMOSD group (including 20 patients with seropositive NMOSD) and 15 patients from the MS group underwent plasma exchange. The reason for conducting plasma metabolism was low efficacy with intravenous administration of methylprednisolone in high doses. To determine the dynamics of the course and evaluate the effectiveness of the use of plasma metabolism, we also studied the medical records of patients 6 and 12 months after plasma exchange.**Results:** Among the total volume of patients, plasma exchange was 84% of patients, of which 64% had transverse myelitis and 72% optic neuritis (with an average age of 38 years and an average course of the disease of 0.7 years) at the time of plasma exchange. Plasma metabolism in these patients led to a measurable improvement in clinical symptoms in 62% of patients after 6 and in 81% of patients after 12 months ($p=0.05$). Evaluation of the Extended Disability Status Scale (EDSS) ≤ 6 before the attack was associated with significant improvement after 6 months ($p=0.03$)**Conclusion:** Plasma metabolism after therapy with methylprednisolone is effective as a treatment for patients experiencing a severe attack of NMOSD or MS.**Disclosure:** Nothing to disclose

EPO2262

PRO-MSACTIVE Baseline Patient Characteristics: A Phase IV Study Evaluating Ocrelizumab in Active Relapsing Multiple SclerosisD. Laplaud¹, C. Lebrun-Frenay², S. Vukusic³, T. Moreau⁴, J.-M. Grouin⁵, M. Lotz⁶, E. Manchon⁷¹Nantes, France, ²Nice, France, ³Lyons, France, ⁴Burgundy University, Dijon University Hospital, Dijon, France,⁵INSERM 1219 Pharmaco-épidémiologie et évaluation de l'impact des produits de santé sur les populations, Université de Rouen, Rouen, France, ⁶Roche, Boulogne-Billancourt, France, ⁷Neurologie, Centre hospitalier de Gonesse, Gonesse, France**Background and aims:** PRO-MSACTIVE (NCT03589105) is an open-label, single arm, phase IV study designed to evaluate the efficacy, safety and impact of ocrelizumab on patient reported outcomes (PROs) in patients with active relapsing multiple sclerosis (RMS). This analysis presents patient characteristics at baseline.**Methods:** PRO-MSACTIVE is being conducted in France (49 centers) in patients with active RMS (relapsing-remitting RRMS, secondary progressive SPMS), ≥ 18 years old, naïve or pretreated with disease-modifying therapy (DMT). The initial dose of ocrelizumab consists of 2 infusions of 300mg (D1, D15) followed by one infusion (600mg) at week 24 (W24). Efficacy is evaluated at D15-W24-W48, and safety at D15-W24-W48-W72. The study includes a 4-week screening period, 48 weeks of treatment and 24 weeks of safety follow-up.**Results:** PRO-MSACTIVE has enrolled 422 patients: mean age (SD) 39.7 years (10.5), median age [min-max] 39 years (18-71); 311 women (73.7%), 111 men (26.3%); 375 RRMS (88.9%) and 47 SPMS (11.1%); 106 naïve patients (25.1%) and 316 (74.9%) pretreated with at least one DMT. Mean EDSS score was 2.80 (2.04), median EDSS score was 2.5 [0.0-8.0]; 68.8% of patients had an EDSS <4 . 213 patients (50.6%) were enrolled due to clinical activity (relapse within 6 months prior to screening), 109 (25.9%) to imaging activity, and 99 (23.5%) to both.**Conclusion:** The study population is consistent with some characteristics of the OFSEP cohort (71.1% women, 88.7% RRMS – Vukusic et al. 2018). The forthcoming main analysis will assess the impact of ocrelizumab on disease activity after 1 year of treatment.**Disclosure:** The PRO-MSACTIVE study is funded by Roche SAS

EPO2263

Short-term safety and efficacy of switching from alemtuzumab to ocrelizumab in MS patients with disease activity after two alemtuzumab courses: an Italian multicentric, real-life study.

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Background and aims: The management of MS patients who show disease activity after 2 alemtuzumab courses represents an unsolved issue. No real-life data about the switch to ocrelizumab have been reported yet.

Methods: 21 MS patients who switched to ocrelizumab were retro- and prospectively collected from different Italian MS centers (mean age: 35.2 (SD±7.1); female, 39.5%; Relapsing Remitting, (RR): 76.3%, active Secondary progressive, (aSP): 23.7%; mean time interval (days) from II alemtuzumab course: 85.6 (SD±104); cumulative number of relapses: 22; mean number of new T2 and Gd+ lesions: 3.7 (SD±4.5) and 1.4(SD±3.1); median EDSS: 3 (range 1-7).

Results: Mean follow-up (FU): 5.6±5.4 months. Efficacy: one patient relapsed during the interval between the 1st and the 2nd infusion of ocrelizumab. No further relapses occurred. One patient showed a new asymptomatic T2 lesion at 9 month-FU MRI. EDSS was stable except for 1 aSP patient who showed 1-year disability progression. (II) Safety. A) Infusion Associated Reactions (IARs) occurrence was significantly lower with respect to alemtuzumab courses (p<0.05). B) Infections: mild upper airways (n=1) and urinary infections (n=1), appendicectomy (n=1). No patients showed T CD4+ cell count decrease <200cell/mm³ at 3 month-FU; complete B CD19+ cell depletion (<5 cell/mm³) was confirmed at 3 and 6 months-FU. None of the patients developed hypogammaglobulinemia. C) Autoimmunity: no alemtuzumab-related new complications occurred.

Conclusion: short-term follow-up seems to suggest that the switch to ocrelizumab in MS patients who showed disease activity after 2 alemtuzumab courses is characterized by a good safety and efficacy profile. Longer follow-up is warranted and recruitment is still ongoing.

Disclosure: travel grant from Sanofi and Roche

EPO2264

Adolescents with NMOSD achieved similar exposures and favorable safety profile when treated with the adult satralizumab dosing regimen

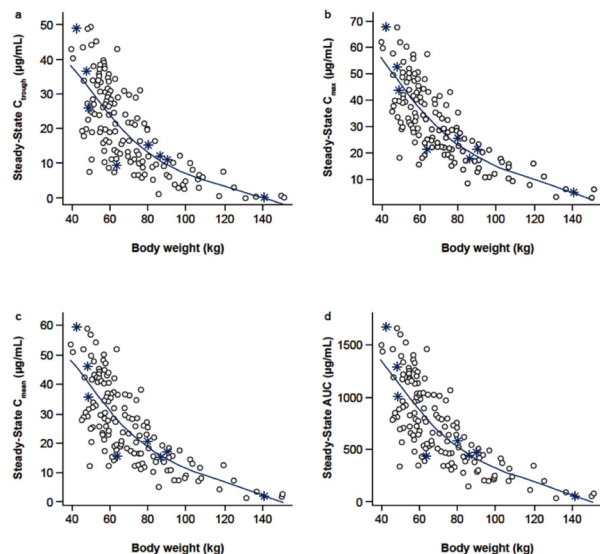
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Background and aims: Interleukin-6 (IL-6) is implicated in neuromyelitis optica spectrum disorder (NMOSD) immunopathology. Satralizumab, a humanized recycling monoclonal antibody that binds to the IL-6 receptor (IL-6R), reduced NMOSD relapse risk in two phase 3 studies: SAKuraSky (in combination with baseline immunosuppressants; NCT02028884) and SAKuraStar (monotherapy; NCT02073279). We describe satralizumab exposure in adolescent NMOSD patients to support dose selection.

Methods: Patients (N=178) received placebo or satralizumab 120 mg at Weeks 0, 2, 4, and every four weeks (Q4W) thereafter. Data on clinical and protocol-defined relapses (PDRs), aquaporin-4 autoantibody (AQP4-IgG) serostatus, safety, pharmacokinetics (PK) and pharmacodynamics (PD) was evaluated in adolescent patients. A popPK model, using data from a Phase I satralizumab trial (healthy volunteers) and both Phase 3 studies, was used to analyse PK data.

Results: Of eight adolescent patients enrolled in SAKuraSky (adolescents were not permitted in SAKuraStar), seven were evaluated for efficacy. Mean age was 15.4 years (13–17); mean weight (79.3kg [47.5–140.4]) was similar to the adult population. Six patients were female; three were AQP4-IgG seropositive. The range of model-predicted exposures was similar to adult patients, correlating inversely with body weight, and not age. There was similar predicted median IL-6R occupancy (>95% maintained over the dose interval) between adults and adolescents. One of four patients receiving satralizumab experienced a relapse (PDR, n=1); all three receiving placebo relapsed (PDR, n=1; clinical relapse, n=2). No new safety signals were identified in adolescents.



Relationship between individual model predicted steady state exposure measures (a) C_{trough}, (b) C_{max}, (c) C_{mean} and (d) AUC and body weight in adolescent patients with NMOSD

Conclusion: Findings support the adult 120 mg loading and Q4W maintenance satralizumab dosing regimen in adolescent NMOSD patients.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.; writing and editorial assistance was provided by ApotheCom, UK.

EPO2265

Characterisation of the PK and PD of satralizumab, a recycling antibody, to support Q4W dosing in patients with NMOSD

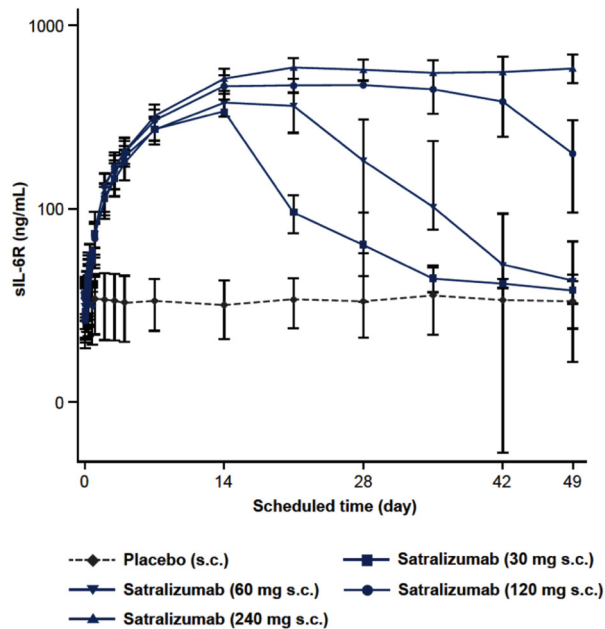
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Background and aims: Interleukin-6 (IL-6) has been implicated in neuromyelitis optica spectrum disorder (NMOSD) immunopathology. Satralizumab, a subcutaneously administered monoclonal antibody, binds to and blocks the IL-6 receptor (IL-6R). Satralizumab is recycled back into the circulation via the neonatal Fc receptor, increasing its serum half-life and prolonging IL-6R inhibition. We aim to define an effective, convenient, long-term satralizumab dosing regimen for NMOSD patients.

Methods: Satralizumab pharmacokinetics (PK) and pharmacodynamics (PD) were assessed in 72 healthy volunteers (HVs; single dose, 30-240mg), 33 rheumatoid arthritis (RA) patients (multiple doses, 30-120mg), and 104 NMOSD patients from 2 phase 3 studies in NMOSD (SAkuraSky [NCT02028884], SAkuraStar [NCT02073279]; 120 mg loading, once every four weeks [Q4W]). A popPK model, based on HV and NMOSD data, was used to derive predictions for individual PK parameters.

Results: Satralizumab significantly inhibited IL-6R signalling for 4 weeks; target engagement resulted in sustained increases in soluble IL-6R levels in HVs, RA and NMOSD patients. In NMOSD, the PK of satralizumab (120mg) was non-linear, with a half-life of approximately 30 days. Median predicted IL-6R occupancy (>95%) was maintained throughout the 4-week dose interval. There was meaningful, comparable efficacy vs placebo in NMOSD patients in both phase 3 studies; hazard ratio (95% CI) for reduction in protocol-defined relapse risk: 0.38 (0.16-0.88), p=0.0184 (SAkuraSky); 0.45 (0.23-0.89), p=0.0184 (SAkuraStar). Satralizumab monotherapy or in combination with baseline immunosuppressants showed a favourable safety profile in NMOSD.



Soluble IL-6R concentration-time profile in healthy volunteers following single s.c. dose of satralizumab (30-240mg) [Figure shows mean±standard deviation. IL-6R, interleukin-6 receptor; s.c. subcutaneous]

Conclusion: The satralizumab 120mg loading and Q4W maintenance regimen is effective, safe and convenient in NMOSD.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.; writing and editorial assistance was provided by ApotheCom, UK.

EPO2266

Effect of teriflunomide on cognitive abilities of patients with multiple sclerosis

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Background and aims: Changes in cognitive function are observed in the early stages of multiple sclerosis (MS), which leads to a decrease in the quality of life.

Objective: to study these changes for patients with relapsing MS who received teriflunomide therapy.

Methods: In this study 91 patients received teriflunomide for 1 year. The majority (84.6%) had previously received first-line injectable immunomodulatory therapy.

To assess the severity of neurological deficits and functional state we used Kurtzke Expanded Disability Status Scale (EDSS), MS Functional Composite test (MSFC), which includes assessment of walking - Timed 25-Foot walk, assessment of upper limb functions - 9-Hole Peg Test (9-HPT), assessment of thinking abilities - Symbol Digit Modalities Test (SDMT) before the start of therapy and after 1 year. We evaluated average frequency of exacerbations, brain neuroimaging data before and after 1 year of therapy. Emotional changes were judged by the results of the Hospital scale of anxiety and depression (HADS).

Results: there was a decrease in the average frequency of exacerbations per year from 0.5 to 0.3. Severity of neurological deficits did not change, but 19 patients maintained negative dynamics during neuroimaging. Frequency of depression decreased by 32%, anxiety by 17% ($p < 0.05$). Performing SDMT 12 patients showed an improvement in the indicator, for 76 - the indicators remained at the same level (about 80-120% of the initial value).

Conclusion: The use of teriflunomide helped to reduce average annual frequency of disease exacerbation, normalize emotional background and led to cognitive function stabilization for patients with MS.

Disclosure: Nothing to disclose

EPO2267

The effects of education in cognitive impairment associated with multiple sclerosis: “classic” neuropsychological domains versus social cognition

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Background and aims: Recent data suggest that education modulates cognitive performance in multiple sclerosis (MS) patients, attenuating the negative effect of brain damage. However, the role of education in social cognition is still unclear. Our aim was to determine if education level moderates the association of grey matter (GM) atrophy with cognitive impairment (CI) in MS patients, on classic neuropsychological domains and on social cognition measures.

Methods: 60 consecutive MS patients were enrolled and underwent a comprehensive neuropsychological assessment, Theory of Mind (ToM) testing (Eyes Test, Videos Test) and 3 Tesla brain MRI. Using Freesurfer software, total GM volume was calculated.

Results: 40 patients (66.7%) were female. 50 patients (83.3%) were classified as relapsing-remitting and 10 (16.7%) as secondary progressive. Mean age was 37.2±7.5 years, with 13.2±4.0 years of education and disease duration of 10.6±6.6 years. Median EDSS score was 2.0 (range, 1-7.5). In the multivariate analysis, controlling for age and sex, the interaction between education and GM volume was retained as the single significant predictor of CI in MS patients (OR:0.575; 95%CI: 0.360-0.917; p=0.020) with higher education moderating/attenuating the negative impact of GM atrophy on cognitive status. Regarding social cognition performance, neither education or interaction of education with the GM volume were significant predictors.

Conclusion: More years of education seem to protect against the negative effect of GM atrophy on neuropsychological performance in classic cognitive domains. On the other hand, interestingly, our study suggests that social cognition does not seem to be modulated by education level, in MS patients.

Disclosure: Nothing to disclose

EPO2268

PRO-MSACTIVE Baseline Patient Reported Outcomes (PROs): A Phase IV Study Evaluating Ocrelizumab in Active Relapsing Multiple Sclerosis

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Background and aims: PRO-MSACTIVE (NCT03589105) is an open-label, single-arm, phase IV study designed to evaluate the efficacy, safety and impact of ocrelizumab on patient reported outcomes (PROs) in patients with active relapsing multiple sclerosis (RMS). 1 of the secondary objectives of the study is to describe the impact of ocrelizumab on several PROs: MS symptom severity, fatigue, health-related quality of life, work productivity and treatment satisfaction. This analysis presents PROs at baseline.

Methods: Questionnaires are self-administered throughout the study at D1-D15-W24-W48 prior to the administration of ocrelizumab: MS symptom severity scale (SymptoMScreen), Modified Fatigue Impact Scale (MFIS), EuroQol 5-Dimension Questionnaire (EQ-5D-5L with VAS), Work Productivity and Activity Impairment scale (WPAI:SHP), Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL), and Treatment Satisfaction Questionnaire (TSQM-14) from D15.

Results: PRO-MSACTIVE has enrolled 422 patients in France with active RMS, including 375 with active relapsing-remitting (RRMS) and 47 with active secondary progressive (SPMS). Mean (SD) EDSS score was 2.80 (2.04). 213 patients (50.6%) were enrolled due to clinical activity (relapse within 6 months prior to screening), 109 (25.9%) to imaging activity, and 99 (23.5%) to both. Of the questionnaires collected at baseline, 416 patients (98.6%) answered to SymptoMScreen and MFIS, 414 (98.1%) to EQ-5D-5L and WPAI:SHP, and 415 (98.3%) to MusiQoL. Baseline data will be reported.

Conclusion: PROs are of increasing use in clinical practice since they provide qualitative information about patients' perspectives of their quality of life and healthcare experiences. This study will provide new data on the impact of ocrelizumab on PROs.

Disclosure: The PRO-MSACTIVE study is funded by Roche SAS

EPO2269

Understanding the economic burden of secondary progressive multiple sclerosis in PortugalM. José Sá¹, G. Kobelt²¹Neurology, Centro Hospitalar de S. João, Porto, Portugal,²European Health Economics, Mulhouse, France

Background and aims: Information on the economic burden of Secondary Progressive Multiple Sclerosis (SPMS) in Portugal is limited. We aimed to estimate costs of Portuguese patients with SPMS by level of disability from the societal perspective.

Methods: This analysis was performed considering the Portuguese subgroup of patients with SPMS included in a cross-sectional retrospective Multiple Sclerosis European study. Vast majority of patients were enrolled from a national Patients' Association. Unit costs were taken from public sources (EUR 2015). Descriptive analyses are presented by Expanded Disability Status Scale (EDSS).

Results: 114 SPMS Portuguese patients were included, representing 21% of the Portuguese full study sample (n=535). EDSS levels were merged due to limited sample size (EDSS 4-6.5, n=74; EDSS 7-9, n=40). About 75.7% of EDSS 4-6.5 and 47.5% of EDSS 7-9 patients were on disease modifying treatments (DMT). Among those, 32.1% and 15.8% were on their first DMT treatment, respectively. Mean annual costs per patient were € 28.493 at EDSS 4-6.5 and € 35.215 at EDSS 7-9. Within direct costs, DMTs in EDSS 4-6.5 (50%) and informal care in EDSS 7-9 (32%) were the main cost drivers. Indirect costs represent 64.3% and 66.9% of the overall cost in EDSS 4-6.5 and EDSS 7-9, respectively. Costs by EDSS in the SPMS subgroup were found to be similar for the overall sample (€ 28.700 at EDSS 4-6.5; € 34.400 at EDSS 7-9).

Conclusion: These results are an important contribution to the knowledge of the economic burden of SPMS in Portugal suggesting that costs do not differ by type of disease when stratified by EDSS.

Disclosure: Nothing to disclose

EPO2270

Neuromyelitis optica spectrum disorder: hospital-based dataV. Martinovic¹, J. Ivanović¹, S. Mesaros², M. Andabaka¹, G. Maric¹, T. Pekmezovic¹, J. Drulovic¹¹Belgrade, Serbia, ²Clinic of Neurology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background and aims: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune demyelinating disorder of the central nervous system, whose prevalence increased with the new diagnostic criteria 2015. The aim of our study was to describe a NMOSD cohort of patients, from the Clinic of Neurology, CCS, Belgrade, Serbia.

Methods: Analysis of patients' hospital records, who fulfilled diagnostic criteria for NMOSD 2015, and who were examined and followed at the Clinic of Neurology, Belgrade, until December 2019. We describe their clinical and paraclinical data.

Results: Our study comprise 112 patients. 92 patients were females. The mean age at onset was 37.7 (range 7.1-69.3) years, with average disease duration 8.4 (range 0.2-34.5) years. Anti-AQP4 antibodies were positive in 87 (77.7%) patients, and 3 patients had anti-MOG antibodies. Oligoclonal bands were present in 21 (18.8%) patients. Most frequent clinical presentation at onset was myelitis (58.1%), followed by optic neuritis (40.2%) and brainstem syndrome (22.3%). Relapsing course was present in 67.9 % of patients, and in the remaining was monophasic. Brain MRI demonstrated hyperintense T2-weighted lesions in 73 (65.2%) patients, and spinal cord MRI lesions in 94 (83.9%) patients (9 never performed spinal cord MRI, and 9 were normal). Commonest treatment option was combination of corticosteroids and immunosuppressants, in 66 (58.9%) patients. Therapeutical plasma exchange as adjuvant option was performed in 25 patients, and Rituximab was administered in 2 patients.

Conclusion: Having in mind significant clinical and paraclinical heterogeneity in NMOSD, data from hospital-based registries might be useful if including a large set of variables.

Disclosure: Nothing to disclose

EPO2271

Multiple Sclerosis: Risk of relapse after yellow fever vaccination

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Background and aims: Yellow fever (YF) vaccine is mandatory for travel in YF-endemic areas but is not recommended for multiple sclerosis (MS) patients because of the potential risk of post-vaccine flare-ups.

The aim of the study is to assess the risk of relapse in RR MS within 12 months after YF vaccination.

Methods: In this observational study exposed/non-exposed, each patient vaccinated against YF after the onset of the disease was matched to 3 patients with no history of YF vaccination and identified by the local EDMUS database. The matching criteria were: age, sex and annualized relapse rate before vaccination. Time to 1st relapse of exposed and non-exposed was analyzed by a log-rank test and by Cox models adjusted to estimate Hazard Ratios.

Results: 31 (20 F/11 M) vaccinated patients were included. The mean age at disease onset was 38 years [SD 10] and the mean disease duration before the vaccination was 10.8 years [SD 6.9]. 19.3% of patients experienced at least one relapse one year before the YF vaccination. At the time of YF vaccination, median EDSS was 1 [0-3]. The final results will be presented at the conference.

Conclusion: French and US recommendations for immunization in MS concluded that “There is insufficient data in the literature to conclude on the potential risks related to yellow fever vaccine because studies are either lacking or insufficiently powered”. The results of this case/control epidemiological study presented at the congress will provide advice to neurologists and MS patients travelling to endemic areas for professional or personal reasons.

Disclosure: Nothing to disclose

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EPO2272

Economic burden of multiple sclerosis (MS) in Bosnia and Herzegovina (BiH)E. Suljic¹, T. Catic², A. Mehicevic¹, N. Mahmutbegović¹¹Department of Neurology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, ²Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina

Background and aims: Many costs of illness (COI) studies have been published around the world, providing valuable input source for health policy and medicines reimbursement decisions. According to our best knowledge no similar pharmaco-economic study has been conducted in BiH previously. Therefore, our aim was to analyze the direct and indirect costs of patients with MS in BiH, and compare it to other Western European populations.

Methods: We applied the same methodology already used in the study conducted across nine European countries with necessary adaptation to local specificities of healthcare system. Questionnaire for cost collection was adopted to specificities of local healthcare system.

Results: Our study enrolled 62 patient, mean age 39.8±10.9 with average duration of the disease 8,33±5,96. Patients were categorized according to treatment; 53.2% of them were treated with disease-modifying drugs (DMD), 32.3% with high doses of corticosteroids (HCD) and 14.5% did not receive any treatment for MS (NT). We observed a significant difference in total direct costs between the groups: DMD (40,884.20 (38,397.60-45,318.70) BAM; HCD 15,768.00 (11,058.00-20,448.00 BAM; p=0.0001. On average, the indirect cost per patient per year based on these bases was BAM 29,093.82 including the costs of 3rd-party assistance, loss of productivity, illness and early retirement.

Conclusion: Our results indicate that in BiH, we record the higher costs of hospitalization in relation to other EU countries, while we do not have recorded the costs of rehabilitation and home care, which is not the case in any of the EU countries.

Disclosure: Nothing to disclose

EPO2273

Interferon-beta for the treatment of multiple sclerosis in the Campania Region of Italy: a retrospective analysis based on routinely collected healthcare data

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Background and aims: The extent to which different Interferon-beta formulations are used in the clinical practice of multiple sclerosis (MS), is currently unknown.

Methods: This is a retrospective analysis of routinely collected healthcare data, recorded from 2015 to 2017, on MS patients living in the Campania Region (Italy), and receiving Interferon-beta. Study variables were treatment features (adherence, discontinuation), healthcare resource utilization (inpatient and outpatient admissions, reasons for admission), and costs. We used mixed-effect regression models to evaluate differences in study variables between Interferon-beta formulations; covariates were age, sex and treatment duration.

Results: Subcutaneous Interferon-beta1a was the most commonly prescribed formulation in the Campania Region (Rebif[®] 22µg and 44µg; 784 patients), followed by intramuscular Interferon-beta1a (Avonex[®]; 618 patients), Interferon-beta1b (Betaferon[®] and Extavia[®]; 417 patients), and pegylated Interferon-beta1a (Plegridy[®]; 259 patients). Rebif was more commonly prescribed to younger patients (<30 years and 30-45 years), when compared with other Interferon-beta formulations (>45 years). Adherence rates ranged between 84% and 96% between different Interferon-beta formulations, without any statistical difference. Over 3 years, 84.8% patients discontinued Interferon-beta, without any statistical difference between different formulations. Patients treated with Betaferon[®] presented with higher risk of MS-related admissions (OR=11.7; 95%CI=3.9, 34.6; p<0.01), and subsequent costs (Coeff=11.94; 95%CI=0.81, 23.07; p<0.01), when compared with Rebif[®].

Conclusion: From 2015 to 2017, Interferon-beta formulations, and especially Rebif[®], were largely used in the management of MS in the Campania Region of Italy. Rebif[®] was specifically prescribed in younger and possibly more active patients, and was associated with lower MS-related complications and costs, suggesting an overall better disease control.

Disclosure: Marcello Moccia has received research grants from MAGNIMS-ECTRIMS, United Kingdom and Northern Ireland MS Society, and Merck; and honoraria from Biogen, Sanofi-Genzyme, and Merck.

EPO2274

Long-term prognosis 15 years after a first demyelinating

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Background and aims: Long-term prognosis in multiple sclerosis (MS) remain partially known in the disease modified treatment area. Observational study with a long-term follow-up are needed to address this question. To assess the long-term prognosis 15 years after a 1st demyelinating event and associated factors

Methods: We analyzed a cohort of patients followed after the first demyelinating event and included between 1996 and 2002. The main evaluation criteria were: 1) MS conversion according to clinical definition and McDonald 2010 criteria. 2) Time to EDSS 3 or EDSS 6. 3) Time to conversion in secondary progressive MS. A descriptive analysis of the population and univariate and multivariate survival analysis of the evaluation criteria were conducted.

Results: The median duration of follow-up since the 1st event was 13.5 years [6.5-19.9] at the time of analysis. 203 patients were included, 120 presented a 2nd clinical event converting to MS, 136 meet the 2010 MacDonal criteria. The predictors for this conversion were: 1) age of onset <25 years, 2) Oligoclonal band. 3) Spatial dispersion of the lesions on the initial MRI. The transition to EDSS 3 (n=32) and 6 (n=10) were associated with early and late inflammatory activity as well as conversion to SP-MS. Oligoclonal band plays a role only in the evolution towards EDSS 3

Conclusion: The analysis of the long-term monitoring data allows us to highlight the pejorative action of inflammation that occurs along the disease and the progressive phase independently.

Disclosure: Nothing to disclose

EPO2275

The Effects of Core Stability Exercises and Transcranial Direct-Current Stimulation of brain on balance, walking capacity and quality of life in women with Multiple Sclerosis

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Background and aims: Multiple sclerosis (MS) is a progressive neurological disorder autoimmune disease that affects the brain and spinal cord. Due to MS, loss of balance and ability to walk in the lower extremities is appeared. In this study the effect of core stability exercises, transcranial direct-current stimulation (tdcs) of the brain on balance, walking capacity and quality of life in MS patients was investigated.

Methods: 39 female with EDSS less than 4.5 with mean age of 37.44±7.891 years were selected purposefully and randomly divided into 4 groups of core stability exercises, tdcs, control and sham. Balance, walking capacity and quality of life were measured and recorded as pretest. The core stability training group participated in a course of core stability exercises in addition to their usual drug therapy for 6 weeks, and the tdcs group received a 5-session course of tdcs. After finishing protocols, posttest was taken from each group.

Results: A significant improvement from pre-test to post-test in core stability training group on balance and walking ability and in tdcs group a significant improvement in balance, ability (walking) and quality of life was observed. The comparison between groups showed that although the tdcs group performed better on quality of life, there was no significant difference between the effects of the 2 training protocols in this index ($p \geq 0.05$) but on balance and Walking Capacity ($p \leq 0.05$).

Conclusion: significant difference was observed between the effectiveness of the 2 training protocols, indicating the superiority of the tdcs group over the core stability group.

Disclosure: Nothing to disclose

EPO2276

Is there relationship between sexual dysfunction and body image of women with multiple sclerosis? A cross sectional study

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Background and aims: Sexual dysfunction is prevalent in women with multiple sclerosis. Men and women who experience greater body image dissatisfaction believe that their physical appearance influences on their sexual function. This study was conducted to determine the relationship between body image and sexual dysfunction in women with multiple sclerosis.

Methods: This study was done in 87,18 to 45 years, married women with MS and sexual dysfunction who referred to Neurology Clinic in Tehran. Patients who met the inclusion criteria (Defined sexual dysfunction by a score of 4 or 5 on any MSISQ-19 item, At least 1 year has passed since diagnosis of MS, EDSS score less than 4.5, no taking any drugs that affect sexual function, no Chronic disease other than MS, and no pregnancy or lactation) completed the Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 and Fisher Body Image test. Data were analyzed using descriptive statistics and SPSS software 16.

Results: Table 1 shows the demographic information. The mean of total sexual dysfunction was 57.41±12.16; including 16.95±3.25 (85%) in primary sexual dysfunction, 21.57±6.14 (60%) in secondary sexual dysfunction and 16.16±2.97 (80%) in tertiary sexual dysfunction. Also the mean score of body image was 135.31±18.98. There was a significant reverse correlation between body image and primary (p=0.001), secondary (p=0.001), tertiary (p=0.041) and total sexual dysfunction (p=0.001).

Table 1: demographic information and their relationship with main variables

variable	Mean ± SD		Relationship with					
			PSD*	SSD*	TSD*	SD*	Body image	
Women age	32.75±6.15		-	-	-	-	-	
Spouse age	37.86±6.75		-	-	-	-	-	
Marriage age	22.78±3.74		-	0.035	0.011	-	-	
Disease duration	4.52±2.91		-0.001	-0.001	-0.001	-0.001	-	
onset of the disease	25.55±6.98		-	-	-	-	0.004	
Child number	2.27±1.41		-	-	0.019	0.018	-	
Women Occupation status	Housewife (N%)	Employed (N%)	-	-	-	-	-	
	48 (55.2)	39 (44.8)	-	-	-	-	-	
Spouse occupation status	Self-employed	Employee	manual worker	Unemployed	-	-	-	-
	39(44.8)	42(48.3)	1(1.1)	5(5.7)	-	-	-	
	elementary School	guidance school	High school	Academic	-	0.009	0.026	0.047
	8	19(11.9)	28 (32.2)	49(56.3)	-	-	-	-
Spouse education	elementary School	guidance school	High school	Academic	0.046	<0.001	0.001	0.002
	8 (8.3)	8 (8.3)	29(44.8)	36(61.4)	-	-	-	-
	PPMS	SPMS	PPMS	PPMS	0.007	0.001	0.001	0.002
	52%	-	8%	-	-	-	-	-
Economic status	Undesirable	Relatively desirable	desirable	-	0.045	-	-	-
	35(67.2)	54(62.8)	18 (20.7)	-	-	-	-	
	-	-	-	-	-	-	-	

*PSD: primary sexual dysfunction/ SSD: secondary sexual dysfunction/ TSD: tertiary sexual dysfunction/ SD: total sexual dysfunction

Table 1: demographic information and their relationship with main variables

Table 2: relationship between sexual dysfunction and body image

variable	Mean ± SD	Relationship with body image
primary sexual dysfunction scoring range: 5-25	16.95±3.25	P=0.001
secondary sexual dysfunction scoring range: 9-45	21.57±6.14	P=0.001
tertiary sexual dysfunction scoring range: 5-25	16.16±2.97	P=0.041
total sexual dysfunction scoring range: 19-95	57.41±12.16	P=0.001
Body image scoring range: 46-230	135.31±18.98	-

Table 2: relationship between sexual dysfunction and body image

Conclusion: Sexual dysfunction is common in women with MS, and body image can be impaired at all levels (primary, secondary, and tertiary) of sexual dysfunction.

Disclosure: Nothing to disclose

EPO2277

Improvement of sexual satisfaction in multiple sclerosis; a systematic review

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Background and aims: Individuals with Multiple sclerosis face sexual dysfunction and they also report lower levels of sexual satisfaction. The purpose of this study was to identify the beneficial interventions for sexual satisfaction.

Methods: The search was performed over electronic databases including PubMed, Scopus, Cochrane, Medline, PsycINFO, EMBASE, CINAHL, and Google Scholar. The interventional studies (in English or Persian) on the sexual satisfaction in patients with multiple sclerosis were included in this review. The search was performed from 1990 to December 2019.

Results: 528 articles were imported to EndnoteX7, after removing duplicate articles 336 studies remained. While reviewing, 313 studies could not provide required information and excluded, Thus 23 studies entered. 10 papers were quasi experimental, 11 were randomized control trials, 2 of them were cohort non-randomized control trial.

990 men and women patients were entered which 575 people were in intervention group and 415 people were in control group. Sexual satisfaction was measured by Marital Satisfaction Inventory (MSI) (N=1) and extracted from the subscale of MSQOL-54 (N=22).

Interventions were divided into 3 categories: educational-counseling interventions (N=14), exercise interventions (N=5) and medical interventions (N=4). Only 8 interventions were effective that 6 were educational-counseling interventions. The courses duration were verifying from 2 to 12 sessions of 40 to 90 minutes. The 2 other remaining effective interventions were an exercise and a medical interventions (table 1 shows effective interventions by details).

Categories	design	questionnaire	interventions
educational-counseling	quasi-experimental	Marital Satisfaction Inventory (MSI)	12 one-hour educational/ counseling sessions with the study psychologist.
	Randomized control trial	MSQOL-54	Eight 45-minute training sessions over a 3-month period were conducted based on patients' educational needs and based on the Orem model.
	longitudinal cohort study	MSQOL-54	The five-day residential retreat (educational and experiential)
	quasi-experimental	MSQOL-54	The experimental group was treated in 8 sessions of group mindfulness-based stress reduction program [one session in a week for 90 minutes each session]
	quasi-experimental	MSQOL-54	12 weekly sessions of sexual therapy
exercise	quasi-experimental	MSQOL-54	2-4 sessions of 40 minutes of training program, based on the extracted needs of the patients in the
	Randomized control trial	MSQOL-54	Yoga exercises for 3 months, which consisted of 8 sessions per month for 60 to 90 minutes at each session.
medical	Randomized control trial	MSQOL-54	The intervention group received 5mg of folic acid daily for two month and 3 doses of 1mg vitamin B12

Table 1: effective interventions on sexual satisfaction

Table 1: effective interventions on sexual satisfaction

Conclusion: educational-counseling interventions had a greater impact on sexual satisfaction. Further studies are recommended to investigate the impact of interventions on sexual satisfaction in patients with multiple sclerosis specifically.

Disclosure: Nothing to disclose

EPO2278

The relationship between quality of life and sexual dysfunction in women with multiple sclerosis; a cross sectional study

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Background and aims: Multiple sclerosis may lead to a wide range of problems related to physical and mental health such as Sexual dysfunction or a reduction in quality of life. We performed a cross-sectional study to assess the relationship between quality of life and sexual dysfunction in women with MS.

Methods: 87 married women with MS and sexual dysfunction were referred to one of the Neurology Clinic of Tehran in 2019. The inclusion criteria were: Defined sexual dysfunction by a score of 4-5 on any MSISQ-19 item, At least 1 year has passed since diagnosis of MS, EDSS score less than 4.5, no taking any drugs that affect sexual function, no Chronic disease other than MS, and no pregnancy or lactation. The assessment tools were MSISQ-19 and MSQOL-54. The collected data was analyzed by Pearson correlation and regression analyses in SPSS 16.

Results: demographic data reported in table 1. The mean score of total sexual dysfunction was 57.41±12.16; including 16.95±3.25 in primary sexual dysfunction, 21.57±6.14 in secondary sexual dysfunction and 16.16±2.97 in tertiary sexual dysfunction. According to our results the overall quality of life score was 56.74±11.31, and mean score of 2 main quality of life subscales including physical health and mental health were 46.16±9.37 and 45.80±13.25 respectively.

Table 1: demographic information and their relationship with main variables

variable	Mean ± SD				Relationship with										
					PSD*	SSD*	TSD*	SD*	PHI*	MH*	QOL*				
Women age	32.72±6.15				-	-	-	-	-	-	-				
Spouse age	37.26±6.25				-	-	-	-	-	-	-				
Marriage age	22.78±3.74				-	0.036	0.011	-	-	-	0.032				
Drug use duration onset of the disease	4.95±3.61				<0.001	<0.001	<0.001	<0.001	0.050	-	<0.001				
Child number	2.37±1.41				-	-	0.019	0.018	-	-	-				
Women Occupation status	Housewife 8(%)		Employed 8(%)		-	-	-	-	-	-	0.032				
Spouse occupation status	Self-employed 48 (55.2)		Employee 39 (44.8)		-	-	-	-	-	-	-				
	manual worker	Unemployed		-	-	-	-	-	-	-	-				
Women education	23(44.9)		42(48.3)		11(1.5)		5(5.7)		-	0.009	0.026	0.047	-	-	0.002
	elementary School	guidance school		High school		Academic		-	-	-	-	-	-	-	-
Spouse education	0		10(11.5)		28 (32.2)		49(56.3)		0.046	<0.001	0.001	0.002	-	-	0.046
	elementary School	guidance school		High school		Academic		-	-	-	-	-	-	-	-
Disease process	RRMS 92%		SPMS 8%		PPMS		PRMS		0.007	0.001	0.001	0.002	-	-	-
	Undesirable 15(17.2)		Relatively desirable 54(62.1)		desirable 18 (20.7)		-	-	0.045	-	-	-	-	-	-

*PSD: primary sexual dysfunction/ SSD: secondary sexual dysfunction/ TSD: tertiary sexual dysfunction/ SD: total sexual dysfunction/ PHI: physical health/ MH: mental health/ QOL: Overall quality of life

Table 1: demographic information and their relationship with main variables

Table 2: relationship between sexual dysfunction and quality of life

variable	Mean ± SD	Relationship with		
		physical health	mental health	Overall quality of life.
primary sexual dysfunction scoring range: 5-25	16.95±3.25	0.038	-	-
secondary sexual dysfunction scoring range: 9-45	21.57±6.14	-	-	0.019
tertiary sexual dysfunction scoring range: 5-25	16.16±2.97	0.003	-	0.001
Total sexual dysfunction scoring range: 19-95	57.41±12.16	0.029	-	0.014
physical health	46.16±9.37	-	-	-
mental health	45.80±13.25	-	-	-
Overall quality of life	56.74±11.31	-	-	-

Table 2: relationship between sexual dysfunction and quality of life

Conclusion: In general, primary, tertiary and total sexual dysfunction had a significant reverse correlation with physical health. Besides, there is a significant correlation between secondary, tertiary and total sexual dysfunction with overall quality of life.

Disclosure: Nothing to disclose

EPO2279

Acute onset psychosis and cognitive impairment as primary manifestation in Relapsing Remitting Multiple Sclerosis.

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Background and aim: Multiple Sclerosis (MS) is a demyelinating disorder of the central nervous system. Neuro-psychiatric symptoms have previously been reported as a rare manifestation of MS, yet onset of MS with psychosis is rarely encountered especially with Relapsing Remitting type of Multiple sclerosis (RRMS). Untreated psychosis in patients with MS can adversely impact on MS medication, levels of disability, and quality of life.

Method: A 23-year-old Caucasian male was admitted due to sudden onset of cognitive deficit, agitation, aggressive self-harming behavior and neurological symptoms with paresis of the right upper extremity along with ataxic gait. His clinical, radiological and laboratorial examinations initially lead to the suspicion of ADEM, eventually diagnosed with RRMS (Fig.).

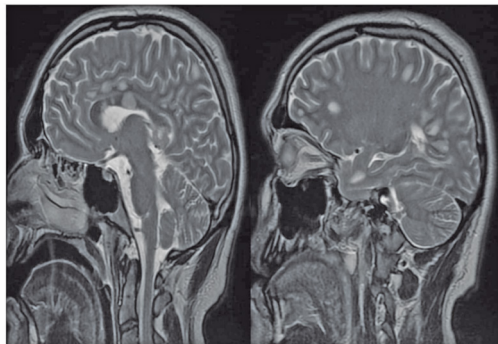


Figure 2: Control SAGITAL T2 FLAIR sequences after 5 weeks (on the right) from the first scan (on the left) showed partial regression of the lesion load with significant reduction of contrast enhancement

Result: Acute onset of neuro-psychotic symptoms with MRI brain verified fulminant contrast enhancing ovoid lesions, both nodular and ring-enhancing involving both cerebral hemispheres (Fig.), response to high dose of steroids and plasma exchange, with a relatively short interval between psychiatric and neurological signs indicate a high likelihood that acute psychosis in our patient could be a manifestation of underlying MS.

Conclusion: Acute onset psychosis and cognitive impairment is a significant problem in RRMS. Particularly in RRMS, the incidence of psychosis and CI is approximately 40%, involving complex attention, processing speed and memory and executive dysfunction, agitation and self harming behavior. As RRMS in relatively young age group, shown worsening of cognitive dysfunction with psychosis, our case report underscores the importance of early recognition of acute psychosis and cognitive impairment, which could impose diagnostic challenge in multiple sclerosis.

Disclosure: Nothing to disclose

EPO2280

Sexual dysfunction in Greek patients with multiple sclerosis.

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Background and aims: Sexual dysfunction is common in both men and women with multiple sclerosis but is often under-estimated. This study was conducted to assess the prevalence of sexual dysfunction (SD) in Greek MS patients and to determine disease-related and psychological risk factors.

Methods: A sample of 218 patients recruited from the MS Center, AHEPA University Hospital of Thessaloniki. They filled out the Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ19) along with demographic data. Psychological status was assessed with Depression Anxiety Stress Scales (DASS), Beck Depression Inventory (BDI) questionnaire and the neurological impairment using the Expanded Disability Status Scale (EDSS). Between group comparisons were made by using Pearson's chi-square test and Mann-Whitney U test. The data were analyzed with SPSS v22.0.

Results: Sexual dysfunction was identified in 98 (45%) out of 218 patients. There was not significant difference with respect to gender in the 2 groups. SD patients were older (44.3 ± 11.4 vs. 34.4 ± 10.7 , $p < 0.001$), had longer disease duration (12 ± 8.6 vs. 8.2 ± 7.4 , $p < 0.001$) and suffered significantly larger disability (4.1 ± 2.0 vs. 2.6 ± 1.7 , $p < 0.001$). Finally, SD patients sustained more depressive symptoms (5.7 ± 3.6 vs. 2.6 ± 2.9 , $p < 0.001$) and more psychological distress in general (20.6 ± 12.9 vs. 10.3 ± 9.8 , $p < 0.001$).

Conclusion: Sexual dysfunction is a common symptom in MS and affects both sexes. Aging, the duration and severity of the disease in addition to depression and psychological distress are significant factors that contribute to sexual dysfunction.

Disclosure: Nothing to disclose

EPO2281

Co-occurrence of Cerebral Toxoplasmosis and Multiple Sclerosis – case presentation

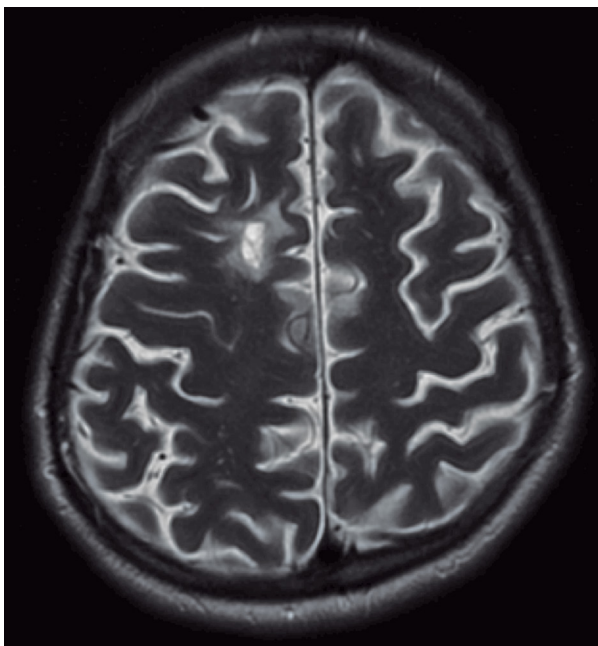
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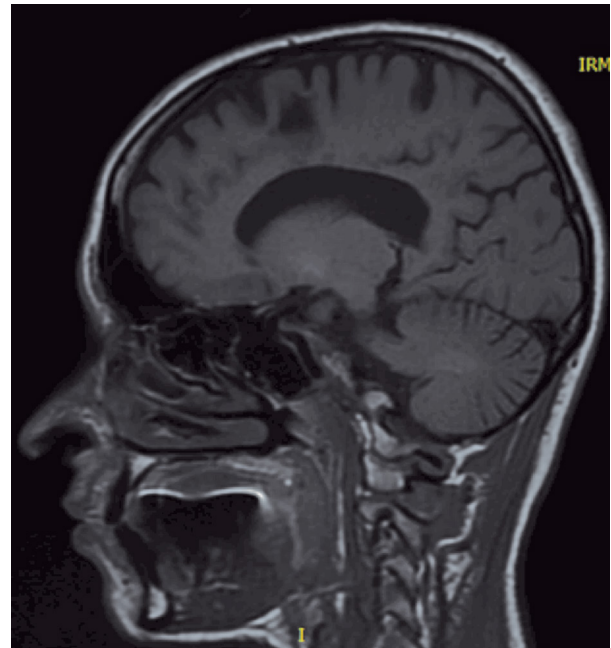
Background and aims: Toxoplasmosis is an ubiquitous infection most frequently encountered in HIV infected patients. The presence of anti-Toxoplasma IgG antibodies in multiple sclerosis (MS) patients is quite common, although the relation between multiple sclerosis and Toxoplasma gondii infection seems controversial. Our objective was to describe the occurrence of toxoplasmosis in an immunocompetent patient with multiple sclerosis.

Methods: Case report. Cerebral MRI with gadolinium enhancement and serology testing.

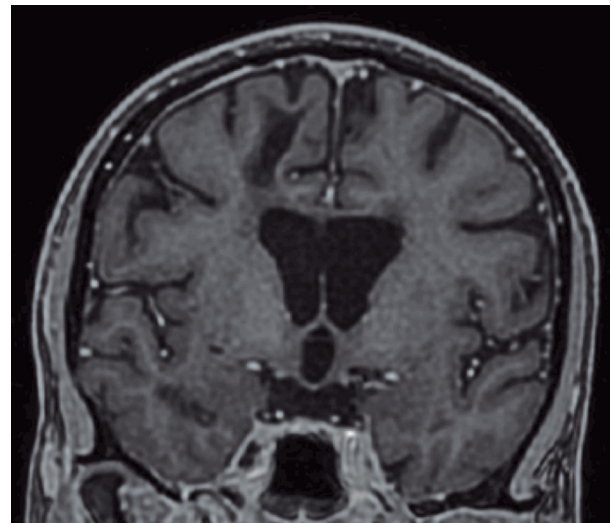
Results: We present the case of an immunocompetent 37-year-old woman, known with relapsing-remitting multiple sclerosis since 2006, who underwent treatment with Glatiramer acetate from 2007 to 2012. In 2008, on annual MRI, there were revealed numerous supratentorial ring-enhancing lesions, with a hypointense core and crenelated outline. Serologic tests for Toxoplasma gondii confirmed the diagnosis of toxoplasmosis and she underwent etiologic treatment. Patient discontinued treatment for RRMS between 2012-2015, due to a personal decision, thus undergoing serious deterioration of her neurological condition. Afterwards, on repeated cerebral imaging there remained a lesion of about 2cm in diameter with peripheral hyperintensity and a hypointense core on T2 and FLAIR, located paraventricular in the right frontal lobe. She undergoes treatment with Natalizumab since 2015.



Axial T2 – hyperintense oval lesion in the right frontal lobe



T1 sagittal – extensive hypointense paraventricular lesion in the right frontal lobe



Contrast-enhanced T1 Coronal sequence

Conclusion: The peculiarity of the case relies in the fact that cerebral toxoplasmosis was accounted in an immunocompetent patient with multiple sclerosis under immunomodulatory treatment with Glatiramer acetate, who remained with a residual cystic lesion on MRI, which could also be encountered in chronic multiple sclerosis lesions. Toxoplasmosis should not be missed out in such cases, as it requires etiologic treatment.

Disclosure: Nothing to disclose

EPO2282

A rare disease in the differential diagnosis of ms: granulomatosis with polyangitis (gpa)

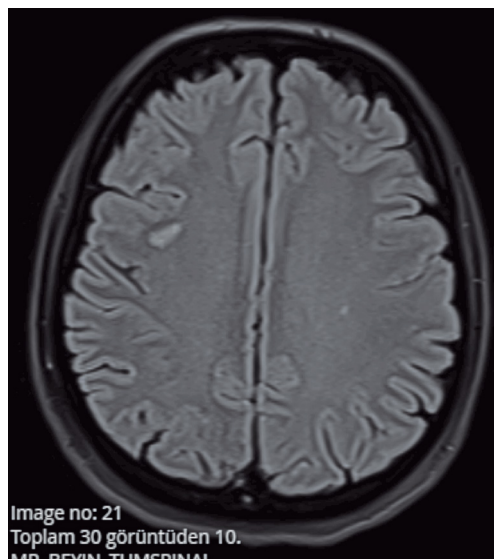
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Background and aims: Granulomatosis with polyangitis (GPA), is a systemic inflammatory disease of unknown etiology, with small and medium arteries involvement, characterized by necrotizing granulomatosis. In this article, we present a patient who was referred to our MS outpatient clinic due to the result of MR scans suspicion of MS, however was diagnosed as GPA with the central nervous systems involvement as a result of the examination.

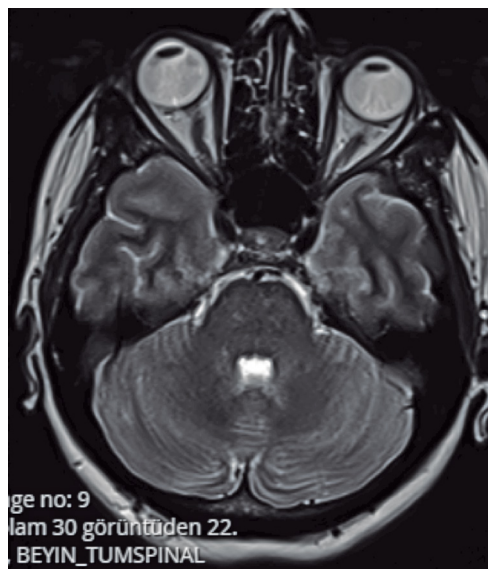
Methods: 39-year-old female, her complaints were visual impairment, hearing loss, and weakness in her right arm and leg. In her history, she had shortness of breath and complaints of painful urination and bloody urine. Her visual acuity was both 0.4. In the muscle strength examination right upper extremity was 3/5 and right lower extremity was 2/5. There was hypoesthesia in the right extremity. Biochemistry values were normal. She had diffuse purpuritic lesions of the lower extremity (Figure 1). On Cranial MRI, non-specific T2-FLAIR sequences hyperintense foci settled in white matter. The right optic nerve was evaluated as having a slight kink (Figure 2-3).



purpuritic lesions of the lower extremity



non-specific T2-FLAIR sequences hyperintense foci settled in white matter



The right optic nerve was evaluated as having a slight kink

Results: Multiple Sclerosis (MS) is an autoimmune central nervous system (CNS) disease characterized with inflammation, demyelination and axon damage. MS is diagnosed according to McDonald's Criteria which was revised in 2017. A lot of disease are in the differential diagnosis of MS. GPA may affect peripheral and central nervous systems in varying proportions (10-45%).

Conclusion: Although Granulomatosis with Polyangitis is with atypical onset and especially involvement of central nervous system is rarely seen, it takes part in the differential diagnosis of MS.

Disclosure: Nothing to disclose

EPO2283

Atypical haemolytic uremic syndrome as rare adverse event of Interferon beta treatment in Multiple Sclerosis: which is the most suitable therapeutic approach?

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Background and aims: Interferon beta (IFNβ) is a consolidated 1st-line therapy for Relapsing-Remitting Multiple Sclerosis (RRMS) patients. We hereby present a case of a young MS patient, who experienced atypical haemolytic uremic syndrome (aHUS) during IFNβ therapy. **Methods:** A 39-year-old Caucasian man was diagnosed with MS in 1997 and since 1999 he assumed IFNβ-1a 44mcg, with good tolerability and optimal treatment-response. In July 2018 he came to our attention for sudden bilateral visual loss, after an episode of severe asthenia and fever, for which he had suspended IFN therapy. Laboratory tests were remarkable for anemia and positive hemolysis indices, thrombocytopenia and acute kidney injury. He underwent a brain magnetic resonance (MRI), and atypical posterior reversible encephalopathy syndrome (PRES) was detected, so he started an aggressive antihypertensive therapy. Clinical and radiological features progressively improved. Finally aHUS was diagnosed. After the failure of plasma exchange, he underwent Eculizumab 900mg (monoclonal antibody against C5 protein), with improvement of glomerular filtration rate and without new signs of MS activity. However, 3rd stage kidney impairment persisted. The patient is currently undergoing neurological follow-up and recently started Dimethyl-fumarate.

Results: In demyelinating diseases there is a possible involvement of the complement pathways. Therefore, Eculizumab, approved to treat HUS, may also have some beneficial effects on neuroinflammation, as proven by its recent approval for NMOSD-treatment in USA.

Conclusion: In this case, a clinical challenge can be the pharmacological decision to start a safe drug in a mild-disease activity, considering the impossibility to discontinue Eculizumab.

Disclosure: Nothing to disclose

EPO2284

Emotional impact on relapsing remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a chronic degenerative disease of the central nervous system that involves the functionality of the brain and spinal cord. Relapsing Remitting Multiple Sclerosis (RRMS) is the most common disease course and is characterized by cognitive deficits and clearly defined attacks of new or increasing neurological symptoms. The goal of our study was to investigate the psychological impact of RRMS (Multiple Sclerosis Relapsing Remitting) in terms of depression, anxiety and stress and to explore the role of metacognitions in relation to emotional variables

Methods: A cross-sectional study was conducted on sample composed of 102 RRMS patients aged 19-50 years (mean 36.3±8sd). The sample consist of 88 women (86.27%) and 14 men (13.73%). The patients were divided into 2 groups: a group consisting of patients diagnosed for more than 10 years and a group consisting of patients diagnosed for less than 10 years. The Expanded Disability Status Scale (EDSS) ranges from 3 to 8 (mean=3.34). Emotional variables have been measured through 2 self-report questionnaire: 1) Depression, Anxiety and Stress Scale (DASS-21), 2) Metacognition Questionnaire (MCQ-30).

Results: The analysis of variance showed significant differences between groups based on the time elapsed since the diagnosis. Data showed inverse correlations between emotional variables, such as depression and anxiety and the role of metacognitions, such as negative beliefs.

Conclusion: These results suggest that a metacognitive approach in psychological care can play an important role in preventing psychological distress in MS patients.

Disclosure: Nothing to disclose

EPO2285

Rate of Nonmelanoma Skin Cancer in Patients Diagnosed With Multiple Sclerosis

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Background and aims: To describe rates of nonmelanoma skin cancers (NMSC) in patients after multiple sclerosis (MS) diagnosis and compare them to matched non-MS patients.

Methods: Using UK Clinical Practice Research Datalink GOLD, each MS patient diagnosed from 2001-2015 with ≥1 year of pre-diagnosis history was matched with non-MS patients of comparable age, sex, and record history length. Patients with history of NMSC were excluded. We identified incident NMSCs recorded after cohort entry (MS diagnosis date or matched date in non-MS patients). We calculated incidence rates (IRs) and incidence rate ratios (IRRs) with confidence intervals (CIs).

Results: In total, 6,846 MS patients were identified and compared with 67,800 non-MS patients (female, 70%; median age, 43 years). During median follow-up of 5 years, IRs of any NMSC diagnosis were 17.5 (95% CI 13.7-22.1) per 10000 person-years (PY) for MS patients and 19.1 (17.8-20.5) per 10,000 PY for non-MS patients. IRs of NMSC with supporting codes (e.g. biopsy) were 10.4 (7.6-14.1) per 10000 PY for MS patients and 11.7 (10.6-12.8) per 10,000 PY for non-MS patients. Rates were similar between MS and non-MS patients among older patients and when stratified by sex. Among patients <45 years old, rates of NMSC were more than 2-fold higher among MS patients compared with non-MS patients; however, numbers were small and uncontrolled bias, such as surveillance bias, may have affected the estimates.

Table 1. Incidence rates and incidence rate ratios of non-melanoma skin cancer (NMSC) by sex and age in MS and non-MS patients.

	MS patients			Non-MS patients			IRR (95% CI)
	# events	Person-years	IR (95% CI), per 10,000 person-years	# events	Person-years	IR (95% CI), per 10,000 person-years	
Any NMSC	67	38219	17.5 (13.7-22.1)	734	383816	19.1 (17.8-20.5)	0.9 (0.7-1.2)
Sex							
Female	41	27251	15.0 (11.0-20.2)	450	274473	16.4 (14.9-18.0)	0.9 (0.7-1.2)
Male	26	10968	23.7 (15.9-34.2)	284	109342	26.0 (23.1-29.1)	0.9 (0.6-1.3)
Age							
<45 years	13	16399	7.9 (4.4-13.2)	60	162344	3.7 (2.8-4.7)	2.1 (1.1-3.8)
45-59 years	19	15021	12.6 (7.9-19.3)	272	150546	18.1 (16.0-20.3)	0.7 (0.4-1.1)
60+ years	35	6799	51.5 (36.5-70.7)	402	70926	56.7 (51.3-62.4)	0.9 (0.6-1.3)
NMSC with supporting codes*	40	38314	10.4 (7.6-14.1)	449	385179	11.7 (10.6-12.8)	0.9 (0.3-1.2)
Sex							
Female	21	27322	7.7 (4.9-11.5)	271	275359	9.8 (8.7-11.1)	0.8 (0.5-1.2)
Male	19	10992	17.3 (10.8-26.4)	178	109820	16.2 (14.0-18.7)	1.1 (0.6-1.7)
Age							
<45 years	10	16411	6.1 (3.1-10.8)	35	162431	2.2 (1.5-3.0)	2.8 (1.3-5.5)
45-59 years	8	15045	5.3 (2.5-10.0)	153	151035	10.1 (8.6-11.8)	0.5 (0.2-1.0)
60+ years	22	6858	32.1 (20.7-47.7)	261	71714	36.4 (32.2-41.0)	0.9 (0.5-1.3)

* Dermatology visit or referral, biopsy, excision, skin operation within 30 days before or after NMSC diagnosis or receipt of consultant or discharge letter on the day of NMSC diagnosis.
 CI, confidence interval; IR, incidence rate; IRR, incidence rate ratio; MS, multiple sclerosis

Conclusion: MS patients have a similar risk of NMSC as non-MS patients, with the possible exception of an increased risk among MS patients age <45 years.

Disclosure: Sponsorship: Celgene Corporation

EPO2286

OCT measures are associated with disease burden and inflammatory activity in newly diagnosed MS and clinically isolated syndromes

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Background and aims: Features of asymptomatic involvement of optic nerve and retina in early multiple sclerosis (MS) and clinically isolated syndromes (CIS) are still unclear. Growing evidences support the use of retinal layers as candidate markers of neurodegeneration (ganglion cell-inner plexiform: GCIPL) and inflammation (inner nuclear layer: INL) occurring throughout the CNS.

Methods: After a clinical episode suggestive of MS, 150 consecutive patients underwent OCT, lumbar puncture, visual, somatosensory, and motor evoked potentials (VEP, SSEP-MEP), brain MRI, visual acuity, and EDSS. The 51.3% reached the McDonald 2010 MS criteria, the 21.3% were clinically defined MS.

Results: 1) evidence of prior subclinical ON was detected using VEP or OCT in the 19.2% and 17.8% of CIS patients, respectively. Asymptomatic VEP involvement was associated with greater disease-burden: brain T2 lesion load (p=0.01), MEP-SSEP score (p=0.002), oligoclonal bands (p=0.005), disease duration (p=0.02).

2) GCIPL thinning was associated with a disease-burden independently of prior clinical or subclinical ON (R2 0.2; p<0.001).

3) INL was thicker in the post-acute phase after a relapse (1.1 to 3.7 months). This phenomenon was reduced by concomitant steroid treatment. No correlation was found with markers of acute inflammation: presence of gadolinium enhancing lesions, Link Index, serum neurofilaments.

Conclusion: Asymptomatic optic nerve involvement, revealed by OCT and VEP, is frequent in CIS and associated with greater disease-burden. While ganglion cells thinning reveals diffuse disease burden in early MS, the INL thickening might reveal a reactive response of Muller cells to neuronal injury.

Disclosure: Nothing to disclose

EPO2287

A case-control study of environmental risk factors in an Italian cohort of Multiple Sclerosis patients

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Background and aims: Multiple sclerosis (MS) is a demyelinating inflammatory disease of the central nervous system due to the interaction between genetic and environmental risk factors. Cigarette smoking, low serum vitamin D levels and obesity at young age are known environmental risk factors. The aim of this work is to analyse the role of environmental factors in an Italian cohort of consecutive MS patients, through the administration of an Italian translation of an environmental questionnaire.

Methods: The questionnaire has been developed by the Karolinska Institute, and it explores the role of different environmental risk factors including smoking habits, sun exposure, physical activity, diet, alcohol intake, working habits and questions specific for women. It has been administered to 136 consecutive MS patients and 136 age- and sex-matched healthy matched controls. Statistical analyses and Odds Ratios (ORs) have been calculated using SPSS software (version 25).

Results: Despite the reduced sample size, we found that smokers had an ORs of disease of 1.87 ($p=0.01$) with a significant dose-effect measured with pack-year index ($p=0.03$). A greater sun exposure before 30 years, a mixed diet at 20 years of age and a lower BMI were protective factors, while a higher vitamin D intake in cases were due to reverse causality.

Conclusion: Despite limitations, this study confirms the role of known environmental risk factors for MS like cigarette smoking and reduced sun exposure at young age, further supporting the importance to discuss lifestyle habits with persons at risk of MS. Further studies are needed to obtain more meaningful data.

Disclosure: Nothing to disclose

EPO2288

Expert opinion consensus on recommendations for treating relapsing multiple sclerosis with cladribine tablets in daily clinical practice

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⁹Center for Clinical Neuroplasticity, Medical Park Loipl and University of Erlangen, Erlangen, Germany

Background and aims: Disease-modifying agents, such as cladribine tablets, are changing the management of patients with active relapsing multiple sclerosis (MS). In the EU, however, product labels tend not to provide specific or detailed information for real-life usage, meaning physicians can have many unanswered practical questions. Therefore, the aim of this consensus-based programme is to provide physicians with practical guidance for using cladribine tablets in clinical practice based on expert recommendations.

Methods: A modified Delphi consensus methodology was used by a steering committee of nine international MS experts to develop the clinical recommendations. Practical clinical questions regarding the use of cladribine tablets were identified and 11 key questions to be answered were selected through a prioritisation exercise. Evidence from a comprehensive literature search, a review of available evidence and the experience and perspectives of the MS experts was used to develop statements for each question. These questions were also extended to 33 faculty members to be answered via an online platform. The 9 MS experts used the consolidated answers to devise the clinical recommendations. For each recommendation, consensus was achieved when $\geq 75\%$ of the respondents conveyed an agreement score of 7 to 9, on a 9-point scale.

Results: Table 1 provides an overview of the consensus achieved based on six individual topics. Consensus was achieved for 46 out of 47 clinical recommendations with only one failing to achieve consensus.

Table 1: Consensus achievement in clinical recommendations by topic

Topic	Consensus achieved for clinical recommendations	Consensus range achieved for clinical recommendations	Strength range
Defining highly active disease	2 of 2	2 at 80–90%	8
Patterns of treatment response in patients treated with cladribine tablets	3 of 3	2 at 90–100% 1 at 80–90%	8–9
Managing patients with evidence of disease activity while being treated with cladribine tablets	6 of 7	5 at 90–100% 1 at 80–90% 1 at <75%	7–9
Infection risk and immune function in patients being treated with cladribine tablets	14 of 14	8 at 90–100% 4 at 80–90% 2 at 75–80%	8–9
Pregnancy planning management and malignancy risk in patients being treated with cladribine tablets	8 of 8	7 at 90–100% 1 at 80–90%	8–9
Treatment switching to and from cladribine tablets and monitoring considerations	13 of 13	12 at 90–100% 1 at 80–90%	8–9
Total	46 of 47	34 at 90–100% 10 at 80–90% 2 at 75–80% 1 at <75%	7–9

Table 1

Conclusion: This expert consensus-based programme provides physicians with practical recommendations on the use of cladribine tablets for managing MS in clinical practice.

Disclosure: This work was supported by Merck KGaA, who provided funding for the project but had no influence on the development of the questions or recommendations.

Muscle and neuromuscular junction disease 2

EPO2289

Time-course of respiratory decline in type 1 myotonic dystrophy (DM1): longitudinal 19-year experience from a Neuromuscular clinic

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Background and aims: Restrictive ventilatory pattern is common in DM1. There is no clear relationship between trinucleotide repeat length and time-course of respiratory decline. Furthermore, role of central respiratory drive dysfunction is not established

Methods: The study included 33 DM1 with abnormal CTG expansion of DMPK gene seen between 2000 and 2018. Trinucleotide repeat year scores reflecting disease duration and mutation severity were determined. Participants were assessed with Muscular Impairment Rating Scale (MIRS). Respiratory evaluations included pulmonary function tests (PFTs) i.e. forced vital capacity (FVC), forced expiratory volume in 1 sec, FEV₁/FVC. Non invasive ventilation (NIV) either positive airway pressure, continuous or bilevel was planned by pneumologist in presence of respiratory symptoms worsening and/or PFT abnormalities. Impact of PFTs on MIRS worsening and NIV requirement as outcomes were assessed at baseline, during follow up and at last evaluation

Results: NIV was started in 12 cases (36%). Median age at NIV was 50 years (range 33-54). Median time to NIV was 195 months. Basal FVC values were significantly lower in subjects who underwent NIV (p<0.001). FVC showed worsening (p=0.003) between baseline and last follow up. Linear regression suggested cumulative effect of trinucleotide repeat year scores on FVC at baseline and at last follow up. FVC was linked to progression of neurological impairment assessed with MIRS at Wilcoxon (p=0.038) and logistic regression (p=0.02). MIRS scores related with NIV need.

Conclusion: Size of repeat, duration of exposure to specific repeat size and FVC are independent predictors of respiratory outcome in DM1.

Disclosure: Nothing to disclose

EPO2290

Duchenne Muscle dystrophy due to a novel silent p.Ser443= mutation in the DMD gene

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Background and aims: Duchenne muscular dystrophy (DMD) is the most common and 1 of the most severe progressive, hereditary muscle diseases affecting boys. This X-linked inherited disease is predominantly caused by out-of-frame mutations in DMD gene leading to absence of dystrophin protein. Here, we report a 14-year-old Mongolian boy presented with proximal muscle weakness, pseudohypertrophic deltoid and gastrocnemius muscles since early childhood. Gower's sign and myopathic pattern were reported on EMG. Lactate dehydrogenase was increased 1.3-fold and creatine kinase (CK) was elevated 13-fold. The boy is the only child of a healthy mother with no family history of muscle disorders.

Methods: Mutation analysis including MLPA and sequencing of the DMD gene was performed. cDNA analysis was performed to assess exon splicing pattern of exon 11.

Results: A hemizygous silent variant, c.1329C>T (p.Ser443=) in exon 11 was identified. This silent mutation, listed in the SNP database, was described as a variant of unknown significance (VUS) in ClinVar database. cDNA analysis demonstrated partial skipping of exon 11 due to this mutation.

Conclusion: Present data shows that silent mutations in DMD are perhaps not very rare. So far, only one pathogenic DMD silent point mutation p.Leu2256= (c.6766C>T) has been listed in UMD-TREAT database. Published data and further details on this mutation are not available. Although silent mutations are usually considered non-pathogenic, our case emphasizes that silent mutations can be potentially pathogenic. Hence, if silent variants are not annotated in database or not known to be benign, they should be analysed further at cDNA level.

Disclosure: Nothing to disclose

EPO2291

Oligoclonal bands in the cerebrospinal fluid of patients with Guillain-Barre syndrome

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Background: Finding of increased cerebrospinal fluid (CSF) proteins and absence of cells is a diagnostic criterion for Guillain-Barre syndrome (GBS). Data on presence of oligoclonal bands in CSF of GBS patients are scarce.

Aim: To analyze presence of oligoclonal bands in CSF and serum from a large cohort of GBS patients and to assess their significance.

Methods: Overall 344 patients were diagnosed with GBS at our hospital from 2009-2018, among whom 213 (62%) had analysis of oligoclonal bands. Severity of GBS was graded using GBS disability scale (GDS).

Results: Eighteen (8%) GBS patients had CSF oligoclonal bands: 2 only CSF bands, one CSF bands and a smaller number of bands in serum, and 15 patients had parallel bands both in CSF and serum. Patients with and without CSF oligoclonal bands did not differ regarding clinical and sociodemographic features ($p > 0.05$), except for GDS at nadir (3.8 ± 0.8 in patients with bands vs. 3.4 ± 1.1 in patients without bands, $p < 0.05$). Among patients with CSF bands only, one developed CIDP and other 1 connective tissue disease (CTD). The patient with CSF bands and a smaller number of bands in serum was diagnosed with Lyme disease. Among 15 patients with parallel bands, 2 had CTD, 2 system vasculitis, 1 Hodgkin, 1 monoclonal gammopathy of undetermined significance, and 1 Lyme disease. Among 195 patients without oligoclonal bands, 2 later developed CIDP and one Hodgkin.

Conclusion: CSF oligoclonal bands are rare in GBS and when present, further analysis should be performed to seek for other diseases.

Disclosure: Nothing to disclose

EPO2292

Longer-term Experience with Nusinersen in Teenagers and Young Adults with Spinal Muscular Atrophy: Phosphorylated Neurofilament Heavy Chain (pNF-H) and Efficacy Results From the CS2-12/SHINE Studies

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Background and aims: Nusinersen has demonstrated clinically meaningful efficacy in presymptomatic and symptomatic infants/children with SMA.

Methods: 5 teenagers aged 14–15 years initiated nusinersen (3mg, n=3; 6mg, n=1; 9mg, n=1) in CS2 (Phase 1b/2a), received intrathecal nusinersen 12mg in the CS12 extension, transitioned to the SHINE (NCT02594124) long-term extension, and were 19–21 years as of 15 October 2018. Assessments included: plasma pNF-H levels and HFMSE (all participants); ULM (non-ambulatory); 6MWT (ambulatory).

Results: Participant 1 had SMA Type II; all others had SMA Type III. At CS2 baseline, Participants 2–4 (female) were ambulatory, Participants 1 and 5 (male) non-ambulatory. CS2 baseline plasma pNF-H levels were 317 pg/ml in Participant 1, and 146, 421, 1170, and 693pg/ml in Participants 2–5, respectively. At the end of CS12 plasma pNF-H levels had declined and were 263, 110, 293, 659, and 512pg/ml, respectively. From CS2 baseline to SHINE last visit (median time: 1952 [range: 1860–2121] days), HFMSE scores changed by +5 (Participant 1), +4 (Participant 2), -3 (Participant 3), 0 (Participant 4), and -2 (Participant 5) points. ULM scores were stable in Participants 1, 2, and 5 (0-point change) and 6MWT distance increased in Participants 2 (+69m), 3 (+81m), and 4 (+24m). New 2019 interim analysis data will be reported, including pNF-H analyses.

Conclusion: Plasma pNF-H levels were lower at the end of CS12 than CS2 baseline. Teenagers with SMA Type II/III treated with nusinersen demonstrated stable/improved

motor function, in contrast to the expected slow decline based on SMA natural history.

Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Horsham, UK): funding was provided by Biogen.

EPO2293

Clinical characterization of familial hyperkalemic periodic paralysis with a SCN4A Met1592Val mutation

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Background and aims: Hyperkalemic periodic paralysis (HyperPP) is characterized by episodic flaccid paralysis of skeletal muscles that is exacerbated by the consumption of potassium-containing foods, fasting, or rest following exercise. We describe the clinical and electromyographic characteristics in familial HyperPP with the Met1592Val mutation in the SCN4A gene.

Methods: 30 patients from 7 families were assessed by interviews and clinical examinations. Standardized protocols comprising short and long exercise tests were applied to 15 unaffected control subjects and the 30 patients with familial HyperPP. To identify comorbidities in patients, we surveyed subjects for common medical conditions.

Results: All patients experienced clinical myotonia at the eyelids or lips. Attack duration varied from less than 1 hour to greater than 3 weeks. The mean age of onset was 7.3 years (range 1-14 years), attacks beginning before 10 years in 86.3% of patients studied. Exercise of short duration induced an immediate increase in the amplitude of the compound motor action potential (CMAP) in the patients, and this was significantly larger and lasted longer than that observed in controls within 50 seconds ($p < 0.05$). A long exercise test induced a large increase in the CMAP amplitude in patients immediately after exercise completion, which decreased to normal values with 1 minute. In contrast, controls showed a decreased CMAP amplitude immediately after exercise, which subsequently also returned to the normal value.

Conclusion: Affected members were phenotypically heterogeneous and showed similar response in exercise test. The exercise tests may be helpful in confirming abnormal excitability of muscle membrane in HyperPP patients.

Disclosure: Nothing to disclose

EPO2294

The epidemiology of hereditary pediatric neuromuscular disorders in the Republic of Belarus

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Background and aims: Most hereditary neuromuscular disorders (NMD) are life-long, life-limiting, disabling conditions. Understanding the epidemiology of NMD at prevalence exist is important to understand the effect on the healthcare system and standard of living of patients. In 2019, the first Belarusian register for children with NMD started.

Methods: We collected data about all patients with NMD using health administrative databases to determine the prevalence for children from 0 to 18 years old. Information was received on 417 pediatric patients, 246 male and 171 female.

Results: NMDs showed prevalence rates 4.4 per 100,000 population. The leading position of nosology is occupied by myopathies of 214 (51.3%) cases (2.3 per 100,000 population), of which Duchenne/Becker muscular dystrophy consists of 125 (29.9%) cases (1.3 per 100,000 population, 2.8 per 100,000 male population), group of hereditary polyneuropathy - 74 (17.7%) cases (0.8 per 100,000 population). Also a large group includes patients with spinal muscular atrophy - 76 (18.2%) people (0.8 per 100,000 population). 53 (12.7%) patients had an unspecified diagnosis of NMD. The prevalence of NMD among boys was higher than among girls due to high prevalence of Duchenne/Becker muscular dystrophy. The largest number of patients with NMD lives in Minsk - 79 (18.9%), the lowest level in Grodno - 43 (10.3%).

Conclusion: Data were obtained about patients who will be used to prepare the NMDs registry. Myopathy is the most common NMD in children, of which Duchenne/Becker muscular dystrophy dominates.

Disclosure: Nothing to disclose

EPO2295

GNE Myopathy in the Bulgarian Roma population: clinical course and 24-month follow-up study

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Background and aims: GNE myopathy is a rare autosomal recessive neuromuscular disorder. The aim is to describe the clinical presentation and to follow up the progression of the disease over a period of 2 years.

Methods: Genetic testing, neurological examination, spirometry, echocardiography, serum CK levels and motor functions were tested at baseline, after 6, 12 and 24 months. Patients were divided into 4 groups, depending on the period of progression (I-1 to 10yr.,II-11 to 20yr.,III-21 to 30yr.,IV>30yr.).

Results: 42 patients were homozygous (p.I618T) while 2 were compound heterozygous (p.I618T/p.R277W, p.I618T/M60V). Mean age at onset was 23±6yr. The most common initial symptom was foot drop (70%). 11/22 patients had impaired cardiac fraction. 10/19 patients had restrictive respiratory weakness. Significant difference (p=0.014) was detected in serum CK levels at baseline between the groups and did not continue to be observed during follow-up period. Patients from III and IV groups had significantly lower motor activity scores than I group and their results did not change during follow-up period. In I and II groups a decline in the motor activity was observed. Significant difference (p<0.05) between the results in I and II, III and IV groups were detected at baseline for all the motor tasks.

Conclusion: GNE myopathy is a slowly progressive disease. The motor activity is relatively preserved in the first 10 years of the clinical course. Serum CK levels can be used as a biomarker of the progression rate. Even in the advanced stages of the disease restrictive respiratory failure was not observed.

Disclosure: Nothing to disclose

EPO2296

Determinants of quality of life in myasthenia gravis patients

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Background and aims: Approximately half of myasthenia gravis (MG) patients achieve remission, the remaining have a chronic disease. Understanding factors affecting Quality of Life (QoL) in MG is needed to optimize treatment.

Methods: We performed a cross-sectional study in 339 MG adults (64.9 % women). SF-36 and a structured questionnaire was administered.

Results: Mean disease duration was 7.5+9.3 years, current age 51.6+18.3 years, 55% had Early-Onset (>50 years) MG. There were no significant differences in mean SF-36 subscores between women and men. Worse MGFA class was related to lower QoL in physical (PCS) and mental (MCS) subscore (p=0.000). Patients with MGFA I-II class had significantly better QoL in physical and mental subscores than patients with more severe MG (p<0.005). Late-onset MG patients had worse QoL than EOMG in PCS (p=0.049). Overweight and obese patients had lower PCS (p=0.002) and MCS (p=0.038) than patients with normal BMI. Depression adversely affected vitality score (p<0.02). University education was related to statistically higher PCS (p=0.015) and MCS (p=0.006). QoL in currently employed was better in PCS and MCS (p=0.000), white collar workers reported higher PCS (p=0.049) than the remaining group. Patients living with family evaluated their MCS (p=0.015) better. Moderate physical activity (2x week) improved PCS (p=0.045).

Conclusion: Our data support the need to address not only severity of MG but comorbidities, such as obesity or depression as well, to improve QoL. Family support, employment and moderate physical activity are important as well.

Disclosure: Nothing to disclose

EPO2297

Camptocormia as a novel phenotype in a heterozygous POLG2 mutation

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Background and aims: Mitochondrial dysfunction is known to play a key role in the pathophysiological pathway of neurodegenerative disorders. Nuclear-encoded proteins are involved in mtDNA replication, including DNA polymerase gamma, which is the only known replicative mtDNA polymerase, encoded by nuclear genes Polymerase gamma 1 (POLG1/POLG) and Polymerase gamma 2 (POLG2). POLG1 mutations are well-known as a frequent cause of mitochondrial myopathies of nuclear origin. However, only rare descriptions of POLG2 mutations leading to mitochondriopathies exist.

Methods: Here we describe a 68-year-old woman presenting with a 20- year history of camptocormia, mild proximal weakness and moderate CK increase.

Results: Muscle histology showed COX-negative fibres. Genetic analysis by next-generation-sequencing revealed an already reported heterozygous c1192-8_1207dup24 mutation in the POLG2 gene.

Conclusion: This is the 1st report on a POLG2 mutation leading to camptocormia as the main clinical phenotype, extending the phenotypic spectrum of POLG2-associated diseases. This underlines the broad phenotypic spectrum found in mitochondrial diseases, especially in mitochondrial disorders from nuclear origin.

Disclosure: Nothing to disclose

EPO2298

Comparison of recent pivotal recommendations for the diagnosis and treatment of late onset Pompe disease using diagnostic nodes

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Background and aims: Pompe disease is a rare autosomal-recessive disorder characterised by limb girdle myopathy and respiratory weakness in the late onset form (LOPD) and cardiomyopathy only in the early onset form. Various mutations in the acid alpha-glucosidase gene lead to toxic lysosomal and extra-lysosomal glycogen accumulation in all organs due to ineffective glycogen clearance by the encoded enzyme. Only one randomized trial demonstrated beneficial effects of respiratory function and meters walked in the 6-minute walking test with enzyme replacement therapy (ERT). These results were confirmed in several retrospective and prospective observations and in meta-analyses. Due to a potential life-long therapy, moderate efficacy and high treatment costs time of ERT initiation and cessation is an ongoing matter of debate. So far, several national and international recommendations have been published with different criteria concerning diagnosis, initiation and cessation of ERT in LOPD.

Methods: We therefore formally analysed recent published recommendations and consensus statements of LOPD using diagnostic nodes (DODES) as a special software tool. With DODES, an objective analysis becomes possible if the content of the recommendations is represented as algorithms using cross-compatible elements.

Results: This analysis formally disclosed both, areas of great heterogeneity and concordance for the diagnosis and management of LOPD and paved the way for a Pompe disease burden scale focussing on ERT initiation.

Conclusion: According to this investigation further clinical research should concentrate on ERT in pre-symptomatic and severely affected LOPD patients and on cessation criteria for ERT as these issues are areas of international uncertainty and discordance.

Disclosure: Nothing to disclose

EPO2299

Myasthenia gravis in the elderly: evaluation of an Italian cohort.

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Background and aims: Myasthenia gravis MG is an autoimmune disorder of neuromuscular junction (NMJ); in the last years an unexpected increased incidence of elderly-age MG was found. Very late onset MG can be underdiagnosed because some disturbances can be ascribed to more common chronic diseases. We evaluated the incidence and the features of MG, presenting after the age of 75 years, among our MG population

Methods: 35 patients (17F,18M) with a MG onset >75 years (age-range 75-89) were identified. All the patients were evaluated at onset with clinical examination, QMG score, SFEMG, RNS, thorax CT, routine blood examinations, Ab AChR and Anti MuSK assays.

Results: According to MGFA criteria, the majority of patients at onset showed a type-2 MG (25/35), 7 patients type-1 MG, 2 patients type-3 and only one patient type-4. AChR Ab were positive in (31/35); 4 patients were negative for AChR and MuSK Ab. Thymoma was found in 2 patients. The average time before the diagnosis was 11 months. The most common regimen of therapy was prednisone at low doses (less than 12.5mg/day); Azathioprine (50 to 100mg) was used as steroid sparing agent.

Conclusion: Our findings show that the diagnosis and therapy of MG in the elderly can be difficult. Among our population, there were no patients with MuSK related MG. MG type, comorbidities (hypertension, diabetes, glaucoma, osteoporosis) should be carefully considered for a positive outcome.

Disclosure: Nothing to disclose

EPO2300

Myotonic dystrophy type 2: a single-centre experience

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Background and aims: Myotonic dystrophy type 2 (DM2) is an autosomal dominant muscle disease caused by CCTG-repeat expansion in the 1st intron of CNBP gene. It is an underdiagnosed multisystem disorder characterized by myalgias, muscle weakness, myotonia and cataracts. The aim of this study was to analyse demographic and clinical data of DM2 patients diagnosed at our Neuromuscular Disease Unit.

Methods: Clinical examination and review of medical files of eight patients with genetically confirmed DM2.

Results: 8 patients (50% females) from 6 unrelated families were studied. The actual mean age is 56.9±10.2 years and the mean age of first symptoms was 52.5±10.0 years. The most common 1st symptom was lower limb weakness (n=3), followed by lower limb stiffness (n=2) and frequent falls (n=1). 2 patients were diagnosed after the DM2 diagnosis in a family member, as they were originally pauci-symptomatic. Myalgia was present in 5 patients and clinical myotonia in 3. Cataracts occurred in 5 patients and diabetes mellitus in 2. 1 patient had an history of 2 myocardial infarctions with permanent pacemaker placement by the age of 48. His father, sister and paternal uncle, the latter with genetically confirmed DM2, all suffered sudden cardiac death. 2 patients presented ECG abnormalities: atrial fibrillation and 1st-degree atrioventricular block.

Conclusion: In this cohort, the main demographic and clinical features are similar to what has been previously described. However, regarding cardiac involvement, our results emphasize clinical similarities with myotonic dystrophy type 1. Careful cardiac follow-up is recommended, even in asymptomatic carriers.

Disclosure: Nothing to disclose

EPO2301

Diagnostic yield of an NGS panel of muscle genes in a Reference Unit in Neuromuscular Diseases

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Background and aims: Next generation sequencing (NGS) methods have become a fundamental tool for the diagnosis myopathies. However, its final performance must be evaluated in a global context taking into account clinical aspects and biomarkers, often requiring a multidisciplinary interpretation.

Methods: The objective is to evaluate the diagnostic performance of 2 home design gene panel in muscular diseases. We studied 417 undiagnosed patients at a Reference Center in Valencia County. 1st we sequenced 253 cases by an Ion Torrent PANEL1 composed of 40 genes during 2015-2017 year period. An Illumina PANEL2 harboring of 272 genes was applied to 184 subjects (including PANEL1unsolved cases) during 2017-2019.

Results: PANEL1 gave a diagnostic outcome of 24% confirmed, 32% possible and 44% inconclusive cases; being ANO5, FKRP, DES and MYH7 the most frequent gene mutations. PANEL2 yielded 32% confirmed, 26% possible and 42% inconclusive cases; in this group the most frequent mutations were those related to metabolic myopathies and channelopathies genes. The global performance rate was 28% with definitive molecular diagnosis, 27% of a possible one and 45% remained unsolved.

Conclusion: These results confirm NGS is a very useful tool in the study of neuromuscular diseases, especially when the panel contains a large gene list and hold high coverage. Nevertheless, this procedure provides many raw data that requires experience and sometimes biological analysis in tissues or cells to confirm the pathogenicity of the variants.

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EPO2302

Spanish family with scapulo-peroneal myopathy due to HNRNPDL mutation: the first European family

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Background and aims: LGMD D3 is a rare genetic disease caused by mutations in HNRNPDL. There are only 5 unrelated families described with this inherited condition: 4 South American families with European ancestors, and 1 Chinese family. We describe the 1st European family with HNRNPDL related muscle dystrophy.

Methods: The index patient was a 70-year-old female with a late-onset scapulo-peroneal weakness and scapular winging. Her 67-years-old paternal cousin had a more severe late-onset scapulo-peroneal and distal weakness predominantly affecting flexor muscles of fingers. They had a family history with an autosomal dominant inheritance. They also had 2 relatives with cognitive impairment, 1 of them also affected with myopathy.

Results: CK levels were mildly increased. Electromyography presented myopathic features. Muscle MRI of the index patient showed a involvement of quadriceps, tibialis anterior and medial gastrocnemius with focus of brightness in STIR sequences, while her cousin had a more widespread involvement. Muscle biopsy showed myopathic changes with atrophic angulated fibers and rimmed vacuoles with abundant inclusion bodies. Sanger sequence of VCP and other multisystem proteinopathy genes were normal. A NGS study with a self-custom panel yielded a pathogenic missense mutation in codon 378 of HNRNPDL gene, already described in an Uruguayan family.

Conclusion: We present the 1st European family with HNRNPDL related muscle dystrophy. Our data support a particular phenotypic profile that differentiate HNRNPDL from others dominant hereditary IBM. Further information will be needed to study association between HNRNPDL mutation and cognitive impairment, as already described in other ribonucleoproteinopathies.

Disclosure: Nothing to disclose

Neurogenetics 1

EPO2303

Expanding the genotype and phenotype of filamin-C-related myofibrillar myopathy.

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Background and aims: Filaminopathies are recently identified progressive skeletal myopathies manifesting initially by bilateral weakness in either proximal leg muscles or in distal upper limb muscles spreading to other muscle groups and in some forms eventually resulting in tetraparesis and wheelchair dependence. 3 distinct types of filaminopathy are recognized.

Methods: We investigated 13 patients (3 males and 10 females) from the 3 different families. Needle electromyography and blood test for creatin phosphokinase were done in all patients. 5 patients underwent MRI of the crural muscles of both legs. Genetic examination was done in eight patients.

Results: We revealed moderate myopathic lesions by needle electromyography in all patients. The 1st manifestations were at the age of 25-43 starting from distal muscles of legs and then arms with subsequent involvement of proximal muscles of legs and then arms. The clinical core of this filaminopathy is proximal paresis, distal paresis is in the background. All patients showed a severe, in most cases, total lesion of m. tibialis anterior, m. extensor digitorum longus. Slight increase of creatin phosphokinase and frequent heart pathology are observed in the given form of filaminopathy. The progression of this filaminopathy is either moderate or severe. A genetic examination detected a new, previously undescribed variant in the FLNC gene (Chr7:128498528, NM_001458:c.G8129A:p.Trp2710Ter), which can be considered as the probable cause of the development of the disease. The variant was classified a likely pathogenic according to ACMG criteria.

Conclusion: We revealed a new late autosomal dominant filamin-C-related myofibrillar myopathy with distal-proximal phenotypes.

Disclosure: Nothing to disclose

EPO2304

MicroRNA in mitochondrial patients with mtDNA deletion and ETF dehydrogenase variant

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Background and aims: MicroRNAs are small non-coding RNA that regulate gene at post-transcriptional levels. Changes in circulating microRNAs (miR-34a and miR-29b) play an important role in aging processes such as hearing loss. Mitochondrial dysfunction is associated with the aging process and with the pathogenesis of a variety of disorders such as sensorineural hearing loss (SNHL).

Methods: We investigated 3 patients with a SNHL that were analyzed evaluating the hearing capacity by pure tone auditory test (PTA) and impedance, Auditory Brainstem Response (ABR) test and Distortion Product Otoacoustic Emissions (DPOAE). We also measured serum mitochondrial microRNAs (34a, 29b) that are probably involved in damage and in the mitochondrial metabolism.

Results: The 1st patient was a 76 y/o man affected by a mitochondrial myopathy with multiple mtDNA deletions. He presented limb asthenia and bilateral SNHL on PTA. The other 2 were a 82 y/o female patient that presented hypoacusia, weakness, and scoliosis and her 55 y/o daughter with a lipid storage myopathy. Muscle MRI was done in every patient. We observed an adipose tissue substitution in posterior muscle thigh of patients 1 and 3 while in patient 2 the muscles more compromised were Sartorius and Gracilis. We also found a significative increase of circulating level of miR-34a in all patients compared to the controls while an up-regulation of miR-29b was present only in patient 3. All patients showed altered responses in the DPOAE.

Conclusion: Circulating microRNAs are non-invasive and useful biomarkers that may represent an accessible window to visualize changes in mitochondrial disorders.

Disclosure: Nothing to disclose

EPO2305

Assessment of cryptochrome gene expression in multiple sclerosis patients

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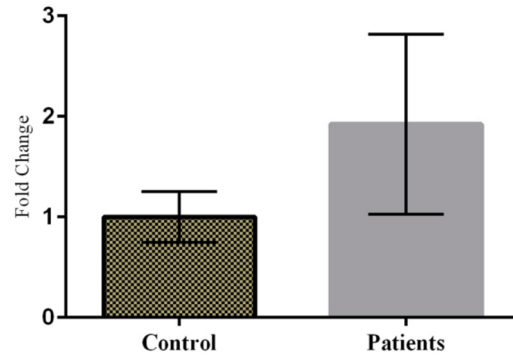
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Background and aims: Multiple Sclerosis and Geomagnetic Disturbances: Investigating a Potentially Important Environmental Risk Factor

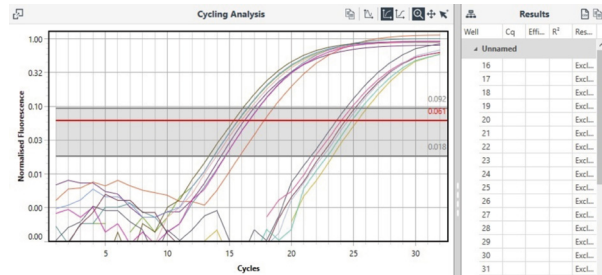
Methods: In this study we examined the expression levels of CRY2 gene in patients with MS and compared with controls has been discussed, RNA was extracted from blood samples of 35 patients with MS and 35 healthy controls. Patient complimentary information form in order to equality of the age status of the disease and patients' examination of migration and change of residence was also completed by patients After Cdna synthesis, gene expression by using Real-Time PCR technique was evaluated.



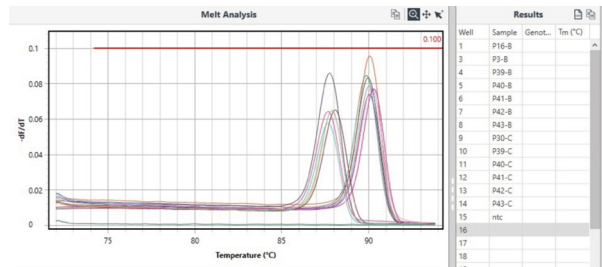
Comparative graph

Conclusion: Our pilot study result didn't show a significant difference in CRY expression among MS and healthy controls. It indicates this gene product is not the basis of MS patient possible sensitivity to geomagnetic field disturbance and other candidate should be considered for future studies.

Disclosure: Nothing to disclose



Duplication curve



Melting curve

Results: The results showed that CRY2 expression levels in patients compared to controls is not significant, since the value of the p (p value) obtained from the statistical analysis is 0.78 which is more than 0.05.

EPO2306

Non-motor features in carriers of intermediate alleles in the huntingtin gene with Parkinson's disease

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Background and aims: Huntington's disease (HD) is a neurodegenerative disorder caused by a mutation in the huntingtin gene (HTT) of 36 or more CAG repeats. Intermediate alleles (IA) of HTT gene are in range 27-35 CAG repeats and have been associated to a normal phenotype. A growing body of evidence has emerged that individuals with IA have clinical symptoms similar to HD. The goal is to carry out research of a prevalence of CAG repeats in the IA range of the HTT gene in patients with Parkinson's disease (PwPD) in Tomsk, Russia.

Methods: We studied 64 unrelated Europeans PwPD (mean age 66.2±8.3, PD duration 7.6±5.6, H&Y stage 2.86±2.64, MDS-UPDRS-III 33.2±16.3). Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Hospital Anxiety and Depression Scale, Apathy Scale, Epworth Sleepiness Scale, QUIP-RS, PDQ-39, C-SSRS. Genomic DNA was extracted from peripheral blood. HTT CAG repeats genotyping was determined by a PCR with 5'-fluorescence labeled primers (Bastepe&Xin, 2015). The number of repeats was determined by capillary electrophoresis using the ABI 3730.

Results: HTT alleles with 13-18 CAG-repeats were the most observed. IA 27 CAG repeats were identified in 2 PwPD with 2 H&Y stage, severe cognitive impairment (15&13 points according to MOCA-test, compared with 24.4±7.8 in 62 PwPD equivalent by sex, age, education, stage) and suicidal thoughts/behavior (it was observed in only 4 PwPD: 100% PwPD with IA and 3.2% PwPD without IA).

Conclusion: The individuals with IA demonstrate non-motor features characteristic of PwHD (more pronounced and early manifesting cognitive and psychotic disorders). This study shows the need for further research of IA and clinical features in PwPD.

Disclosure: This work was supported by Council on grants of the President of the Russian Federation (№ MK-813.2019.7, "Clinical and epidemiological features of neurodegenerative diseases of the Tomsk region").

EPO2307

A biallelic GDAP2 loss-of-function variant in a patient with adult-onset cerebellar ataxia

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Background and aims: Recently, a new autosomal recessive cerebellar ataxia subtype (ARCA27) caused by biallelic mutations in the GDAP2 was described, a gene previously not linked to any diseases. The authors reported 2 unrelated cases with late-onset ataxia, progressive spasticity and dementia. Herein, we report a 3rd patient with a homozygous frameshift variant in GDAP2 and thus confirm the causality of this gene.

Methods: Exome data from a large UCL cohort of patients with ataxia were re-analyzed. This study was approved by the ethics committee of UCL Hospital NHS Foundation Trust (UCLH) and the Eginition Hospital.

Results: We identified a Greek patient carrying an ultra-rare homozygous 1-bp-deletion (NM_017686.4;c.134delC), resulting in a frameshift and premature termination (p. Pro45LeufsTer22) in GDAP2, validated by Sanger sequencing. The patient was a 58-year-old male of Greek origin presenting with a progressive cerebellar syndrome starting at the age of 33 years with mild gait imbalance, ataxia and dysarthria. On examination at the age of 58, severe gait disturbance, dysmetria, dysdiachokinesia and brisk deep tendon reflexes were noted. Brain MRI revealed marked cerebellar atrophy, mild cortical atrophy, midbrain and pons atrophy (hummingbird sign), and thinning of corpus callosum as well as lentiform hemosiderin depositions.

Conclusion: Our patient is in line with the patients previously reported, presenting with a progressive cerebellar syndrome complicated with pyramidal features, dementia and dysexecutive syndrome. Our study provides a novel GDAP2 mutation in this Greek family, expanding the spectrum of causative mutations and further confirming the pathogenicity of GDAP2 mutations in ARCA.

Disclosure: Nothing to disclose

EPO2308

Spastic paraplegia 48 (SPG48): expanding the spectrum of AP5Z1 mutations – a phenotypic, genotypic and functional analysis

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Background and aims: Biallelic mutations in the AP5Z1 gene are known to cause a very rare complex form of hereditary spastic paraplegia (HSP) referred to as SPG48. SPG48 follows an autosomal recessive inheritance pattern. To date, only 4 confirmed pathogenic mutations in the AP5Z1 gene have been reported. The aim of this study was to investigate a Greek HSP cohort for mutations in the AP5Z1 gene.

Methods: We performed whole exome sequencing (WES) in 38 probands with HSP phenotype negative for variants in common HSP genes. Functional studies were conducted on fibroblast cell lines derived from the patient identified.

Results: We identified a Greek patient carrying a novel homozygous frameshift pathogenic variant c.1719delG (p. Gly573fs*) in the AP5Z1 gene (NM_014855.2), confirmed by Sanger sequencing. The patient was a 65-year-old man with known epileptic seizures (generalized tonic-clonic) since he was 30 years old that presented at the age of 48 years with a progressive spastic gait disorder, complicated by peripheral neuropathy. Brain MRI findings included thinning of corpus callosum and ears-of-the-lynx. Functional studies performed on fibroblast cell lines support and expand previous findings from SPG48 cell lines showing defects in endosome/lysosome homeostasis.

Conclusion: Insights from the present report expand the clinical and genetic spectrum of SPG48 and our understanding of the underlying pathomorphological processes. The exact pathomechanism of AP5Z1-associated complicated HSP remains, however, to be elucidated.

Disclosure: Nothing to disclose

EPO2309

Late-onset familial amyloid polyneuropathy (FAP): A Case Report and Literature Review of a rare entity

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Background and aims: Transthyretin (TTR) Val30Met familial amyloid polyneuropathy (FAP ATTR Val30Met) is the most common form of FAP, emerging usually in patients' 3rd or 4th decade. It is characterized by ATTR amyloid deposits in various tissues and organs, like peripheral nerves, heart, gastrointestinal tract, kidneys, and eyes. A late-onset form of TTR-FAP involving both large and small sensory fibers and more severe motor involvement has been recently identified. Here, we report a late-onset case of hereditary ATTR amyloidosis and review the literature of late-onset FAP ATTR Val30Met cases.

Methods: DNA-sequencing of the TTR gene was performed, identifying a Val30Met mutation. Literature searches were conducted on MEDLINE (PubMed), Scopus and clinicaltrials.gov, using several key words and their combinations. Subjects were selected with symptom onset at age ≥ 50 years (late-onset).

Results: We describe a 67-year-old who developed a progressive axonal sensorimotor polyneuropathy with autonomic and gastrointestinal involvement at the age of 64. Family history was initially negative but the origin of the patient was from an endemic FAP area of Sweden. Abdominal fat biopsy showed the presence of amyloid deposits. The patient did not have any renal, ocular, leptomeningeal or cardiac symptoms caused by amyloidosis. An affected 1st cousin of the proband was later identified. He was initiated on treatment with tafamidis.

Conclusion: Late-onset FAP Val30Met is a fatal, progressive disorder with varying penetrance difficult to diagnose, and may occur in cases without family history. Increased characterization of these cases may assist earlier recognition and improve patient therapeutic outcomes.

Disclosure: Nothing to disclose

EPO2310

Deletion in HSPB8 gene leads to dilated cardiomyopathy with impaired autophagy worsened by immunosuppressive drugs: characterization of a new phenotype.

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 University of Campania "Luigi Vanvitelli", Naples, Italy*

Background and aims: Mutations in genes encoding for small heat shock proteins such as HSPB8, are associated to distal hereditary motor neuropathies (dHMN) and distal rimmed vacuoles myopathy. We characterize a new phenotype in a family with a novel mutation in HSPB8 gene and we support the role of peripheral blood smear (PBS) as a simple and effective tool for screening in vacuolar autophagic myopathies (AVMs).

Methods: A 52-year-old man complained about distal muscle weakness, persistent hyperkalemia and severe dilated cardiomyopathy. Familial history revealed one sister with mild cardiomyopathy and his mother deceased for heart failure. A complete neuromuscular protocol was carried out, including whole exome sequencing (WES). 3 months later he received heart transplant and started treatment with cyclosporine.

Results: WES identified a novel heterozygous deletion in HSPB8 (c.266del/p.Pro89HisfsTer12), also detected in his affected sister. PAS-positive vacuoles were evident in lymphocytes such as on muscle samples. Immunofluorescence study conducted using LC3 and P62 antibody confirmed an impaired autophagy on both tissues (Fig.1). After one year follow-up, a severe muscle weakness of axial and proximal districts was noticed.

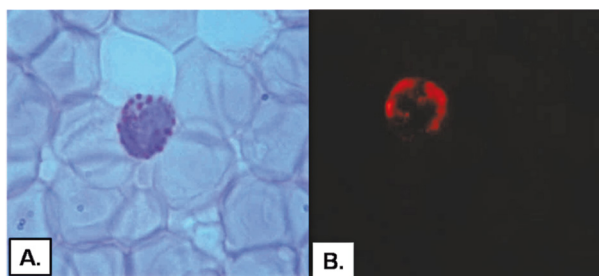


Fig. 1 Peripheral blood smear. a) Lymphocyte with Pas positive granules b) Impaired autophagy demonstrated by LC3 spots on lymphocytes of the patient.

Conclusion: We expanded the phenotypic spectrum of HSPB8 mutations describing for the 1st time a familial dilated cardiomyopathy related to a deletion in this gene. Moreover it is well known that HSPB8 silencing exhibited blocking effects on the autophagosome-lysosome fusion and we suppose that cyclosporine could have worsened muscle weakness due to his effect on autophagic flux. An adequate use of drugs that induces autophagy should be considered in patients with AVMs.

Disclosure: Nothing to disclose

EPO2311

Phenotypic variability in two patients with GLUT1 mutations

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Background and aims: Glut-1 deficiency is a heterogeneous metabolic disorder. Phenotypic presentations range from infantile epilepsy with developmental delay and microcephaly to a myriad of movement disorders.

Methods: case report.

Results: Patient 1: 34-year-old female followed since childhood due to epileptic encephalopathy. Family history was unremarkable. On examination she presented microcephaly, cognitive impairment, face and upper limb dystonia with action myoclonus, and spastic-ataxic gait. She was on levetiracetam 2000mg, zonisamide 200mg, clonazepam 1mg and baclofen 20mg. Brain-MRI showed mild atrophy. EEG showed normal background activity with no epileptic discharges during myoclonus. The spinal tap showed CSF glucose of 39mg/dl. Genetic testing disclosed the c.1097_1100del in the SLC2A1 gene, not previously described. She started ketogenic diet, with clinical improvement. Patient 2: 20-year-old female with idiopathic generalized absence epilepsy from age 6. She also presented painful paroxysmal events of involuntary movements in her legs, usually occurring during exercise, compatible with a possible exercise-induced paroxysmal dyskinesia. A paternal aunt had epilepsy. She was on ethosuximide 250mg. Examination was normal. EEG showed normal background activity with paroxysmal 3-4Hz spike-and-wave activity. Ethosuximide was then increased and clonazepam was introduced. The seizure frequency improved, and complete dyskinesia remission was achieved. Spinal tap showed low glucose of 41mg/dl. Genetic testing revealed c.458G>A variant in SLC1A1.

Conclusion: Glut-1 presents a wide spectrum of phenotypes, often overlapping. Variability might contribute, as in our patients, to delayed diagnosis – depriving patients of timely treatment. Reporting and raising awareness for this variability might help improve diagnosis acuity.

Disclosure: Nothing to disclose

EPO2312

Rare cause of Hypomyelinating Leukodystrophy type 7: “Gly672Glu homozygous variant of the POLR3A gene”

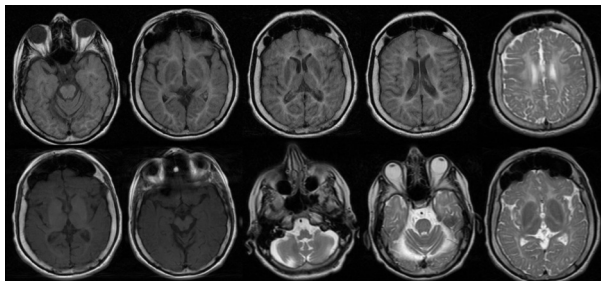
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Background and aims: We present the 1st Spanish patient report with a rare Hypomyelinating Leukodystrophy of autosomal recessive (AR) inheritance by homozygous p.gly672Glu in the POLR3A gene.

Methods: A 34-year-old male patient present progressively since childhood, psychomotor retardation, appendicular and trunk ataxia with negative romberg, accompanied in the last years of a spastic tetraparesis with aquileo clone and Babinski, severe dysarthria, limitation of ocular extrinsic motility and dystonic cephalic movements. Subsequently, the patient develops mild cognitive impairment and dysphagia. On examination, there are objective tooth separation and hypogonadism.

Results: Cerebral MRI visualizing Hyperintensity of white substance, cortico-subcortical and cerebellar atrophy. Metabolic, autoimmune, enzymatic, infectious were normal. Genetic Study: Homozygous pathogenic variant p. GLY672Glu in the POLR3A GEN compatible with type 7 hypomyelinating leukodystrophy with hypogonadotropic hypogonadism of AR inheritance.



Conclusion: Hypomyelinating leukodystrophy 7 described by Wolf is an AR neurodegenerative disorder characterized by the appearance of progressive motor impairment in childhood that manifests as spasticity, ataxia, tremor and cerebellar signs, as well as mild cognitive regression. Other features may include hypodontia or oligodontics and hypogonadotropic hypogonadism. Brain MRI is typical of a hypomyelinating leukoencephalopathy (hyper or isointense appearing white matter on T1 and concomitant hyperintense white matter structures on T2), corticosubcortical and cerebellar atrophy. The protein encoded by the POLR3A gene is the largest subunit of the RNA polymerase III complex, the pathogenic mechanism being the loss of function of this protein. As far as we know, this is also the first report of the missense pathogenic variant p.Gly672Glu in homozygosis in Spain

Disclosure: Nothing to disclose

EPO2313

Amyotrophic Lateral Sclerosis, genetics and ambient risk factors, a cohort epidemiologic study

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a rare and progressive neurodegenerative disease, involving upper and lower motor neurons. The real cause of this motoneuron diseases (MND) remains unknown. More than 100 autosomes genes have already been described, and some factors associated with radiations, heavy metals and repetitive motor neuron trauma, associated with work or sports have been related to ALS.

Methods: An epidemiologic study was conducted, with application of an epidemiologic questionnaire and a genetic exome analysis to 30 ALS patients, with probable or confirmed diagnosis by El Escorial criteria, consecutively enrolled from October 2017 to March 2018.

Results: Of the 30 ALS patients enrolled, 70% (n=21) were males, with a mean age of 65.2±9.8 years. Spinal onset ALS was predominant (60%; n=18), and almost cases were sporadic (1 family ALS). In 6 (20%) patients all risk factors were excluded, and gamma radiation was associated with 8 (26.7%) ALS patients. For these patients, the whole exome sequencing was also performed, and a phenotype-genotype analysis was developed using the GenIO software, and the variants were classified according to the American College of Medical Genetics (ACMG) classification. In this study, Senataxin (SEXT) and Neurofilament heavy polypeptide (NEFH) gene mutations were the most prevalent as dominant mutations. The SEXT mutation was associated with a better prognosis even in bulbar onset ALS patients, and, mainly when the SEXT mutation was the only mutation identified.

Conclusion: SEXT mutation alone interferes positively in ALS disease progression.

Disclosure: Nothing to disclose

EPO2314

A novel variant in DNAJC13 gene associated with Parkinsonism syndrome.A.-G. Corbille¹, P.G. Damier¹, J. Chelly²¹Neurology, *hopital Laennec, Nantes, France*, ²Genetics, *CHU, Strasbourg, France*

Background and aims: Genetic involvement accounts for approximately 5-10% of patients with Parkinson's disease (PD). DNAJC13 p.Asn855Ser mutation was identified in a large Canadian family by exome sequencing and seems to be involved in the pathogenic process. Other rare variants in the gene have also been identified as PD susceptibility factor but their causative role remains to be demonstrated.

Methods: We analyzed a panel of 127 genes involved in Parkinson and related disorders in a patient who has developed a neurological disease with parkinsonism features, and in her two siblings.

Results: The patient is a 65-year-old woman who has progressively developed a cerebellar syndrome associated with choreic movements, intermittent myoclonus with postural tremor, cognitive alteration mostly affecting executive and praxic functions, and hyperreflexia. After 15 years, she developed a severe resting tremor, markedly improved by levodopa. Cerebral MRI showed parietal predominant cortical atrophy. Electrophysiological study of the tremor found a regular 4.5Hz resting tremor.

Conclusion: This observation supports the potential role of p.His1789Arg variant in DNJC13 in parkinsonism syndrome.

Disclosure: Nothing to disclose

EPO2315

Recognition of some genetic diseases in cerebral palsy casesL. Cuznetz^{1,2}, S. Hadjiu^{1,2}, C. Căclii^{1,2}, N. Lupusor^{1,2}, C. Griu¹, L. Feghiu^{1,3}, R. Eremea¹, M. Sprincean^{1,2}, N. Revenco^{1,2}¹State University of Medicine and Pharmaceutics „Nicolae Testemițanu”, *Chisinau, Republic of Moldova*, ²Municipal Scientific and Practical Institute Mother and Child, *Republic of Moldova*, ³National Centre of Epileptology

Background and aims: We set out to conduct a study to analyze children with CP in order to elucidate some distinct phenotypes. To conduct differential diagnosis between CP and some Neurogenetic pathologies by analyzing the phenotype of patients suspected for PC, with the purpose of assessing the prognosis and improving the care of patients.

Methods: A retrospective study was conducted to analyze the history and disease records of children admitted to the neurology sections of the IMSP Institute of Mother and Child of the Republic of Moldova during 2014–2018. All 200 children underwent a complex clinical-paraclinical examination, in addition to performing brain MRI and genetic-molecular examinations.

Results: The following pathologies were confirmed among patients suspected of CP: (1) neuronal ceroid lipofuscinosis (1 case), (2) childhood Krabbe disease (1 case), (3) Dopa-responsive dystonia (1 case), (4) deficiency glucose transport type 1 (1 case), (5) mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS) (1 case), (6) Hereditary spastic paraplegia (1 case), (7) spinal amyotrophy (2 cases), (8) hereditary myopathy (1 case), (9) Gaucher disease (1 case), (10) Rett syndrome (1 case).

Conclusions: Children with CP should be evaluated for some neurogenic disorders, which may mimic a PC. Neuroimaging and molecular-genetic examinations are the ones that help us elucidate the diagnosis. Recognition of the underlying causes of neuro-motor disability will allow improvement in the prognosis, treatment and care of these patients. Specialists in the field should remain cautious in all cases when a PC is suspected, in order to discover the causes of disability.

Disclosure: Nothing to disclose

EPO2316

Ubiquilin 2 gene mutation presenting with adult-onset ataxia and spasticity; report of a novel phenotype case.

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Background and aims: Ubiquitin-positive inclusions are considered a hallmark of ALS pathology. Ubiquilin 2 (UBQLN2) is a member of the ubiquitin-like protein family for which studies have revealed a pathogenic role in X-linked ALS with/without frontotemporal dementia.

Methods: We present a 35-year-old female with unremarkable history that presented with oscillopsia, dizziness and gait instability with subacute onset and gradual progression.

Results: The neurological examination revealed mild cognitive impairment (MCI), diplopia, dysarthria, tendon reflex hyperexcitability, marked limb and gait ataxia. During the first two years the patient evolved dysphagia, incontinence, fasciculations and required bilateral assistance for walking. CSF analysis, blood, autoimmune, metabolic and genetic exams for common modalities causing ataxia and spasticity showed no pathology. Brain and spinal MRI as well as investigation for underlying malignancy were normal. Needle EMG was consistent with mild denervation in the first dorsal interosseous muscle. Immunotherapies were administered with no response. Whole Exome Sequencing revealed a mutation in UBQLN2 gene [c.1019G>T (p.Ser340Ile)]. The patient's parents underwent genetic testing and the same mutation was found in her 65-year old father, who is asymptomatic with the same needle EMG findings. The patient after initial deterioration has a stable course in a 5-year follow-up receiving symptomatic treatment.

Conclusion: UBQLN2 mutations have been associated with ALS with spasticity, muscle weakness, dysphagia and dysarthria. Women tend to manifest milder phenotypes with late onset and decreased penetrance. In our case the predominant clinical features are MCI, motor neuron involvement (mostly upper) along with evident ataxia that is not previously described for UBQLN2 gene mutations.

Disclosure: Nothing to disclose

EPO2317

A14696G HOMOPLASMIC MUTATION IN THE MITOCHONDRIAL tRNAGlu GENE - CASE REPORT

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Background and aims: Mitochondrial diseases have a wide clinical spectrum. After the 1st reporting of pathological mutations in mitochondrial DNA in the late 1980s, many mitochondrial genomic mutations have been identified to date. Herein, we report a case with a mutation in the pseudouridine loop stem of mitochondrial tRNAGlu.

Methods: A 35-year-old male patient presented with bilateral visual loss, speech impairment, and difficulty in walking at the age of 7. Over the past 5 years, he has been complaining of hearing loss and difficulty in swallowing. His mother and his father were cousins and his mother's uncle had a history of progressive vision loss. Neurological examination revealed cognitive impairment, dysarthria, bilateral vision and sensorineural hearing loss, bilateral muscle weakness and spasticity of the lower extremities, increased deep tendon reflexes. Laboratory tests were normal except for high serum lactate levels. Brain MRI showed bilateral T2 hyperintense and T1 hypointense lesions in the putamen. Electromyography demonstrated myogenic involvement in the proximal muscles. The Alexander Practical Intelligence test was consistent with severe mental retardation.

Results: Whole-mitochondrial genome analysis revealed homoplasmic A14696G mutation in the mt-tRNAGlu gene

Conclusion: The mutation A14696G changes the nucleotide 51 of the pseudouridine loop of the canonical tRNA molecule to create a new base pair and reduces wobble. In the A14696G mutation, the phenotype is expressed only in cases with elevated mutant mitochondrial DNA ratio. Interestingly, our case was homoplasmic, although this mutation was reported as only heteroplasmic in the literature.

Disclosure: Nothing to disclose

EPO2318

The study of arteriovenous malformations in the residents of Russia

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Background and aims: Brain arteriovenous malformations (BAVMs) are vascular lesions characterized by a tangle of abnormal arteries and veins that directly shunt blood from the arterial to venous circulation. The combination of some external (smoking, alcohol consumption) and internal (the influence of polymorphic variants of genes) factors can lead to BAVM. In our study we aimed to investigate the influence of SNPs involved in BAVM and their influence on clinical cases: VEGFA, VEGFR2(rs2010963, rs2305949), CDKN2B-2A(rs1333040, rs7865618), TNF-a(rs1800629), IL-1a(rs1800587), IL6(rs1800795) genes, which were associated with BAVMs.

Methods: Clinical trial included 361 patients with BAVMs confirmed with Magnetic Resonance Imaging in clinical centers in Novosibirsk. The control group consisted of 380 individuals without BAVM. Determination of polymorphic variants of genes was performed by Real Time qPCR using TaqMan-competing probes.

Results: For the SNP rs1800795 of IL6 gene is shown the risk of BAVM for patients with genotype GG (OR=1.372, p=0.004) is 2 times higher than for patients with genotype CC and GC. For the SNP rs7865618 of CDKN2A gene the risk of BAVM with genotype GG (OR=1.132, p=0.02) is 2 times higher than for patients with genotypes GA and AA.

Conclusion: Thus, the GG genotype of IL6 gene and GG genotype of CDKN2A gene may be a risk factor for Russian population, result of the clinical course and lead to complications of patients with BAVM. As for the other studied polymorphic loci, any statistically significant differences weren't found in the frequency of alleles and genotypes in the control group and the group of patients.

Disclosure: Nothing to disclose

EPO2319

A retrospective observational study looking at phenotype and genotype in a cohort of HSP patients in a specialist neurology centre

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Background and aims: Hereditary spastic paraplegia (HSP) is a phenotypically diverse condition with at least 60 genes shown to be associated with the condition resulting in difficult genotypic diagnosis and diagnostic uncertainty.

Methods: We conducted a retrospective review of the case notes of patients with a diagnosis of HSP at the Walton Centre focusing on clinical characteristics such as gender; age at onset; simple or complicated; clinical signs and symptoms; genetics and management.

Results: A total of 19 patients were identified, of which 1 had inadequate information available. 15 patients were male and overall 13 were classified as simple HSP (72%). The age of symptom onset was spread evenly between infancy up to 49 years. All patients had a degree of lower limb spasticity, with additional features including dysarthria, cognitive impairment, seizures, upper limb weakness and global development delay. 2 patients had an SPG4 mutation, whilst 1 had an SPG11 mutation and 1 an SPG11 and 15 mutation. 2 patients declined genetic testing and 12 were unknown. 11 (67%) went on to have IT baclofen and 1 underwent elective dorsal rhizotomy.

Conclusion: The relationship between symptoms and genetics is complex as age of symptom onset, disease severity and response to treatment are variable and additional symptoms in complicated HSP are diverse. HSP can pose a diagnostic dilemma due to the heterogenous phenotype and broad genotype.

Disclosure: Nothing to disclose

EPO2320

The Involvement of Humanin in Development of Parkinson's disease

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Background and aims: Humanin (HN) was identified in the brain of a patient diagnosed with Alzheimer's disease (AD). This 24-amino acid peptide was shown to suppress the neuronal cell loss caused by amyloid- β (A β) and by amyloid precursor protein (APP) mutations associated with early onset familial Alzheimer's disease (FAD). Recent studies revealed that HN activity is not confined only to neurons, but it also involves other compartments of the brain as well as extraneural tissues. These results suggest that HNs may influence other neurodegenerative disorders such as Parkinson's disease (PD).

Methods: DNA was isolated from peripheral blood from 214 patients with diagnosed PD and 193 healthy adult individuals. Genotyping was performed on the 3130xl Genetic Analyzer (Applied Biosystems).

Results: We genotyped the not-known polymorphic variants of 13Thr- and 13Ile-HN10b (with threonine or isoleucine in amino acid position 13), encoded by HN gene in PD-diagnosed patients. Genotyping results have not shown any significant association between identified 13Thr- and 13Ile-HN10b polymorphic variants (38C>T) in control as well in PD-diagnosed individuals. However we demonstrated higher frequency of C/T and C/C genotypes in comparison to T/T in patient with dementia (MMSE). Similar relation were observed in patients with severe symptoms of PD progression (basing on Hoehn and Yahr as well as UPDRS rating scale).

Conclusion: Our results suggested that 13Thr- and 13Ile-HN10b polymorphic variants (38C>T) is not associated in development of PD. However we can speculate that T/T genotype could be considered as a protective factor during the development of PD.

Disclosure: The study was financially supported by the Ministry of Science and Higher Education (grant No: K/PBP/000318). i to coś na koniec abstraktu

Neuroimaging 2

EPO2321

Cerebro-cerebellar structural covariance in temporal lobe epilepsy with hippocampal sclerosisV. Marcián¹, R. Mareček², M. Pail³, M. Brázdil³

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Background and aims: To evaluate the relationship between the cerebral and cerebellar morphological changes in temporal lobe epilepsy with hippocampal sclerosis (TLE-HS). We focused on vermis because it is an anatomically well-defined structure and within the majority of its substructures significantly different in patients as compared to controls in which the interconnection with the amygdala and hippocampus were experimentally demonstrated and the effect of stimulation on hippocampal seizures was studied. Structural covariance, as a measure of the degree to which studied gray matter volumes are associated, is considered to reflect both structural and functional connectivity.

Methods: The study cohort included 21 intractable TLE-HS patients (14 left-sided, 7 right-sided) and 38 healthy controls (HC). All patients later underwent anteromedial temporal lobe resection. All subjects were examined using 1.5T MRI. The structural covariance of temporal lobe structures, insula, and thalamus with cerebellar substructures was examined using partial least squares regression.

Results: The structural covariance differed significantly between left and right TLE-HS patients as compared to healthy controls. The analysis revealed significant negative covariance between anterior vermis and the right amygdala-hippocampal complex in the left TLE-HS group. No significance was observed for the right TLE-HS group.

Conclusion: The observed structural covariance between the cerebellum and supratentorial structures in TLE-HS suggests associations beyond the mesial temporal lobe structures and thalamus. Our data confirmed the anterior vermis to be an integral part of this system of interconnected changes.

Disclosure: Nothing to disclose

EPO2322

Painful diplopia: Do not forget Thyroid-Associated Ophthalmopathy.T. Mavridis¹, G. Velonakis², A. Kallergi³, E. Vogiatzi³, E. Zapanti³, V. Zouvelou¹

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Background and aims: Thyroid-Associated Ophthalmopathy (TAO), is part of an autoimmune process caused by antibodies directed against receptors present in thyroid cells, extraocular muscles and soft tissue of the orbit. TAO is generally associated with hyperthyroidism (~90% of the cases). However, ~10% of patients with TAO present with euthyroidism or hypothyroidism. We present a rare case of painful ophthalmoplegia attributed to euthyroid TAO.

Methods: Case Report

Results: A 45-year-old male presented with 3 days history of painful diplopia. Clinical examination revealed right exophthalmos, increased resistance and pain to retro-pulsion, bulbar conjunctival injection with associated lacrimation, eye lid edema and weakness of the right external rectus muscle. MRI of the orbits revealed extensive fusiform enlargement of the right medial rectus, superior rectus and superior oblique muscles with gadolinium enhancement and sparing of their myotendinous junction. The above clinical and radiological presentation suggested a retractive ophthalmopathy with tendon sparing; thus the diagnosis of TAO was made. Endocrinological examination confirmed diagnosis of TAO, in the presence of normal thyroid function tests. Anti-Tg, anti-TPO and TRAbs were within normal range. Interestingly, spontaneous clinical remission was noted a month after the onset. Spontaneous remission of TAO is rare and requires regular monitoring.

Conclusion: TAO is not always associated with hyperthyroidism and in cases where anti-thyroid autoantibodies are also negative, diagnosis is challenging. Clinical and radiological findings remain the best diagnostic tools for painful ophthalmopathy. Exclusion of other causes of orbital muscle swelling (e.g. inflammatory orbitopathy, granulomatous diseases, caroticocavernous fistula, tumors and idiopathic myositis) is mandatory for the diagnosis of TAO.

Disclosure: Nothing to disclose

EPO2323

Idiopathic thoracic spinal cord herniation (ITSCH) with minimal neurological deficit: report of two cases

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Background and aims: ITSCH is a rare but serious pathology causing progressive thoracic myelopathy. Symptoms typically include back pain, progressive spastic paraparesis and sphincter dysfunction. We report 2 cases of ITSCH with minimal neurological symptoms, which were initially misdiagnosed.

Methods: Case 1. A 41-year-old women presented with burning pain in her right leg for the last 6 months. Neurological examination showed impaired pain and temperature sensation in the right leg without any other neurological deficit. Case 2. A 53-year-old man presented with a 2-month history of abdominal pain radiating to the back in left T9-T10 dermatome. His neurologic examination was normal. Patients didn't have the history of spinal surgery, trauma and back pain. They underwent MRI of the thoracic spine.



Fig-1

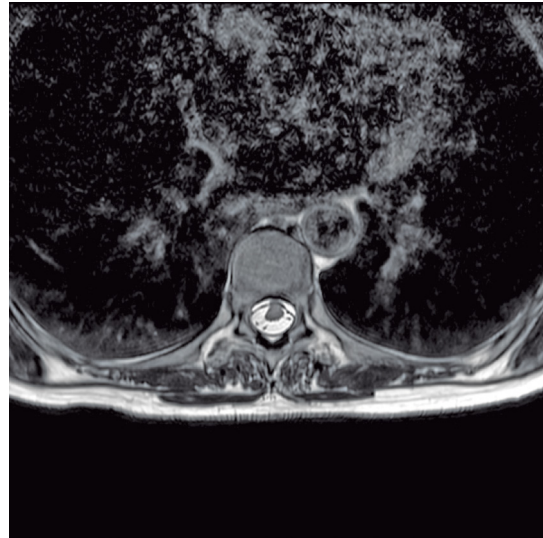


Fig-2

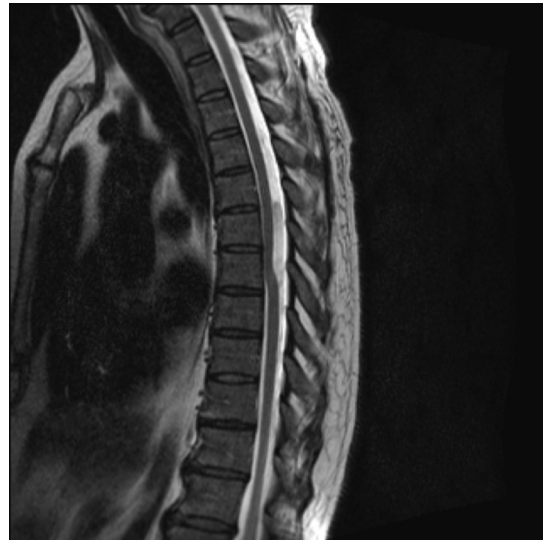


Fig-3

Results: In the 1st case, MRI revealed ventral displacement of the spinal cord with a C-shaped dorsal indentation and small anterior dural defect at the level of the T7-8 disk. Subarachnoid space posterior to the cord was enlarged (Fig-1 Sagittal T2-WI, Fig-2 Axial T2-WI). In the 2nd case, MRI shows focal dorsal indentation and anterior displacement of the thoracic cord at T6-7 with positive "Scalpel Sign", consistent with dorsal thoracic arachnoid web (Fig-3 Sagittal T2-WI). Association of ITSCH with a dorsal arachnoid cyst has been reported. The patients were treated conservatively with clinical improvement and remained neurologically stable during 1-month follow-up.

Conclusion: ITSCH is a frequently misdiagnosed pathology that can manifest with minimal clinical symptoms. MRI is an excellent tool for diagnosing this rare entity.

Disclosure: Nothing to disclose

EPO2324

Application of Diffusion Tensor Imaging (DTI) in Demyelinating White Matter Disease (MS)

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Background and aims: Highlight the clinical utility of qualitative and quantitative DTI parameters in diagnosis, prognosis and follow up of demyelinating white matter disease (MS).

Methods: 40 patients (17 males and 23 females) were included with (mean age 33.6 years, range: 17-49 years and mean disease duration, 35 months). 20 healthy controls (8 males and 12 females), were recruited (mean age: 30.3, range: 18-47 years). All patients underwent routine pulse sequences, including axial fast spin echo T1, T2 and 3D high resolution T2 FLAIR images. Also delayed post-Gadolinium T1 images were obtained in MS cases for assessment of plaque activity. DTI was acquired after the routine sequences using single-shot EPI sequence.

Results: In this study all MS patients have shown significant increase of the MD and to less extent decrease of FA of NAWM compared to NWM of the control group (p-value 0.003 for MD and 0.012 for FA). Also, this study revealed high significant differences of all DTI indices between active and inactive plaques (p-value <0.001). On using cut off value of FA ≤ 0.23 , ADC ≥ 1.31 , AD ≥ 1.63 and RD ≥ 1.05 , we get the highest sensitivity, specificity and accuracy. So, these results suggest the relevance of DTI utility as additional quantitative parameter for assessment of plaque activity.

Conclusion: Diffusion tensor imaging has promising role in addition to conventional MR imaging in early diagnosis, prognosis and follow up of MS cases. Also, characterizes intrinsic damage of each individual major WM tract, and study damage topography among MS patients

Disclosure: Nothing to disclose

EPO2325

Role of Diffusion Tensor Imaging in Patients with Cervical Myelopathy

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Background and aims: Background: Myelopathy is a neurological deficit of the spinal cord, which is usually due to compression of the cord most commonly by osteophyte or herniated disk substance into the spine. Aim of the Work: To highlight the role of DTI in evaluating patients with cervical myelopathy.

Methods: This study included 21 patients who were referred to the radiology department at Dar Al Shifaa hospital. It had a contract with a private radiology center where 15 cases had their studies done, while the remaining 6 cases were referred to the radiology department at Mansoura university hospitals from neurology & neurosurgery departments during years of residency between March 2016 and April 2018, and all cases underwent a protocol of imaging including conventional MR imaging and DTI.

Results: In our study we correlated the FA & ADC values of the cervical cord in normal and pathology with patients' demographic data and degree of cord affection. The mean normal FA in our study was 0.55. We found high statistically significant results correlating the reduction in FA values with the cord affection i.e. the more severe the cord affection, the more reduction in FA values will occur.

Conclusion: DTI parameters can improve the clinical outcome and help in treatment plans.

Disclosure: Nothing to disclose

EPO2326

Different brain activation could explain the success of the bariatric surgery in morbid obesity

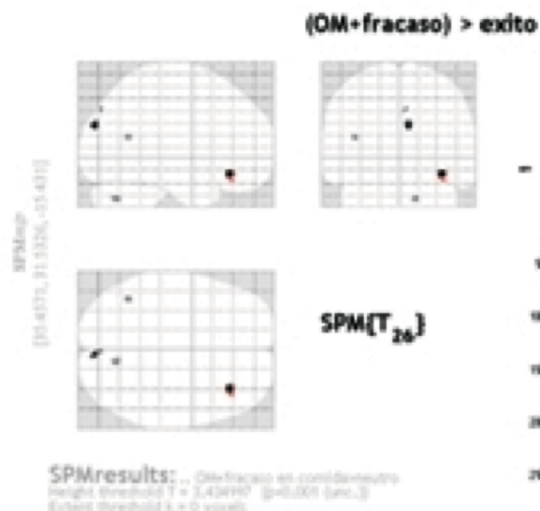
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Background and aims: Morbid obesity has markedly increased in the last years. Despite adequate bariatric surgery (BS) some patients increased the weight after the surgery again. It seems that neuropsychological factors could influence in the success of the surgery.

Aim: To identify brain activation areas to explain the success or failure of the BS in MO patients

Methods: Cross-sectional study. 3 groups of 10 patients each: morbid obese MO patients (A), patients undergoing BS with weight loss success (B), patients undergoing BS with failure (C) 2 years after surgery underwent a fMRI study using a visual block paradigm with different high and low calories food pictures. Data were analyzed with SPM12, threshold $p < 0.001$ was applied in all cases.

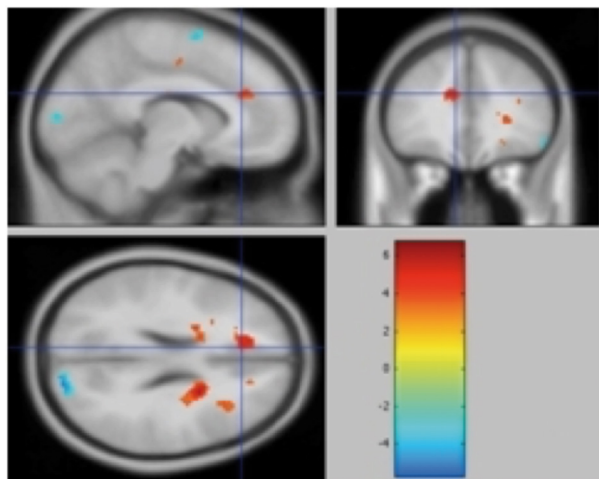
Results: 29 patients (22 women) were studied. High and low calorie pictures were found to show no differences in the BOLD signal. Looking at food pictures was found a significant great activation in cingulate area and insula in Group B as compared to MO patients and in visual areas in MO patients in comparison with group A (Fig.1). Moreover a greater activation in the visual areas and right fronto-parietal areas was shown comparing group C to B (Fig.2).



Group MO + C > B seeing food

Conclusion: Only the “success” group showed activity in the dorsolateral frontal cortex, possibly associated to an appropriate “conflict resolution”. MO and failure group showed a significant increased activity in visual areas seeing food. These findings could help to a better selection of surgery patients and to perform behavioural psychotherapy in some of them.

Disclosure: Nothing to disclose



Red: Group B > OM ; Blue: OM > Group B

Group B versus MO patients seeing food

EPO2327

Transient global amnesia (TGA) radiological assessment of the hippocampus

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Background and aims: Transient global amnesia (TGA) is a rare condition characterized by a sudden deficit of anterograde and retrograde memory that lasts up to 24 hours. The episode is sudden, transient, benign and is not accompanied by any other neurological symptoms. Pathogenesis is unknown and complex. TGA has been correlated with hippocampal abnormalities on Diffusion Weighted Imaging (DWI) sequence but neuroimaging findings in TGA are heterogeneous and most of them report the lack of obvious abnormalities. The aim of this study is to identify and describe the MRI findings in patients with TGA, specifically on DWI sequence and in a control group.

Methods: We evaluated 25 patients (17 women and 8 men, mean age 65 yrs) with a diagnosis of TGA hospitalized at the Department of Neurology in Wrocław between 2017 and 2019. The control group consisted of 25 healthy persons (19 women and 6 men, mean age 66 yrs). The most common risk factor was hypertension (16/25). A brain 1.5-T MRI was performed including conventional sequences: T1, T2-weighted, axial fast fluid attenuated inversion recovery and diffusion-weighted imaging at 24-48 hours after symptom onset. We also assessed hippocampal volumes.

Results: None of the TGA patients showed DWI lesions. There was no significant difference between the TGA patients and the controls in volume of hippocampus.

Conclusion: Conclusion TGA remains a clinical diagnosis without MRI visible abnormalities

Disclosure: Nothing to disclose

EPO2328

Bilateral asymmetric ptosis: when to consider a vascular cause?

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Background and aims: Ptosis is a neurological sign that can be explained through multiple causes: mechanical, aponeurotic, myogenic, neurogenic or neuromuscular junction disease. Only 4% of ptosis are bilateral. Lesions in the central nervous system affecting the oculomotor nerve can lead to bilateral ptosis in case of frontoparietal or midbrain lesions. We report a case of sudden bilateral ptosis in a patient with cardiovascular risk factors.

Methods: A 45-year-old woman with personal history of poorly controlled hypertension and type 2 diabetes, was admitted to hospital for hypertensive crisis and headache episode, followed by gait instability, photophobia and ptosis. Physical examination revealed high blood pressure and an isolated bilateral asymmetric ptosis, more evident on the left side. No pupillary or ocular movement abnormalities were present, neither fatigability.

Results: Brain CT showed a dubious left thalamus-mesencephalic lesion and MRI confirmed diffusion restriction in left paramedian midbrain. Thus, the diagnosis of left lacunar mesencephalic stroke was established. Infectious, metabolic, autoimmune and neurovascular causes were excluded in additional studies. However, hypertensive heart disease was identified on echocardiography. After ptosis' improvement, the patient was discharged with acetylsalicylic acid and adjustment of antihypertensive treatment.

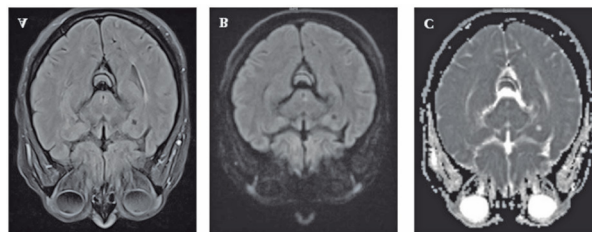


Figure 1. Isolated midbrain signal abnormality. MR scan of brain: (A) axial T2, (B) axial diffusion-weighted B1000 hyperintensity and (C) axial corresponding low signal on ADC. These show an isolated left paramedian midbrain signal abnormality, ventral to the aqueduct.

Conclusion: Midbrain infarctions represent a minority of strokes. Paramedian lesions associated with oculomotor nuclei involvement can cause an incomplete bilateral ptosis due to an infarct on the single central caudal subnucleus, which controls the levator palpebrae superioris muscles. A sudden onset of bilateral ptosis, especially in patients with cardiovascular risk factors and no other oculomotor symptoms, might suggest a vascular cause in this location.

Disclosure: Nothing to disclose

EPO2329

Changes in resting state functional networks of the brain in patients with tension headaches (TH) after osteopathic manipulation

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Background and aims: Resting state functional magnetic resonance imaging (rs-fMRI) is a promising technique for detecting initial changes of the functional connectivity in the brain in patients with TH for diagnosis the cognitive and psychoneurological symptoms and for a more detailed study of the pathogenesis. The effectiveness of osteopathy in the treatment of patients with TH has been proven. Studying the effectiveness of the 1st osteopathic manipulation on the state of functional connections of the brain in patients with TH is relevant.

Methods: Rs-fMRI was performed on 1.5 T MR-scanner on 18 patients (female, age 32±5.6 years) with TH twice (before and immediately after first osteopathic manipulation).

Results: According to the results of an intergroup statistical analysis (2-sample t-test), when comparing the functional connectivity of the brain at rest before and immediately after osteopathic manipulation, a weakening of the negative functional connection of the medial prefrontal cortex with the left upper parietal lobe was revealed ($p < 0.005$).

Conclusion: The results of the study indicate that patients with tension headaches before and after 1st osteopathic manipulation have minimal differences in the functional activity of the brain, this is often correlated with the clinical picture (reduction of headaches often occurs after a series of osteopathic manipulations), so now an analysis of functional connectivity after a full course of osteopathy is being conducted. The obtained can serve as a basis for studying the pathogenetic mechanisms of tension headache, assessing the impact of osteopathic manipulation on the functional connections of the brain.

Disclosure: Nothing to disclose

EPO2330

Resting state functional magnetic resonance imaging in detecting changes of functional connectivity of the brain in patients after radical mastectomy

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Background and aims: Different neurological and psychiatric disorders such as vertebrobasilar insufficiency, chronic pain syndrome, anxiety and depression are observed in more than 90% of patients after total mastectomy. These disorders can cause impaired functional connectivity in the functional brain networks. Resting state functional magnetic resonance imaging (rs-fMRI) is a promising technique for detecting initial changes of the functional connectivity in the brain in these patients.

Methods: Rs-fMRI was performed on 3.0T MR-scanner to 15 patients with neurological disorders in the late postoperative period (>6 months) after radical mastectomy for breast cancer. All patients were pre-examined by neurologist and had complaints of chronic pain, dizziness, headaches, and/or tinnitus. Quality of life in these patients was assessed using the SF-36 scale, anxiety and depression – using STAI and Zung scales.

Results: According to the intergroup statistical analysis, there were differences in functional connectivity of the brain in all 15 patients ($p < 0.01$), with the increased functional connectivity in the default mode network in 12 patients. All 15 patients had the significant decline in quality of life on the SF-36 scale, 7 had high anxiety level, 6 showed depression on the Zung scale.

Conclusion: The use of rs-fMRI in patients after total mastectomy allows us to identify changes of functional connectivity in the brain caused by neurological disorders, which correlated with anxiety, depression and decreased quality of life in these patients.

Disclosure: Nothing to disclose

EPO2331

Why a clinical sign does not always correlate with lesion size?

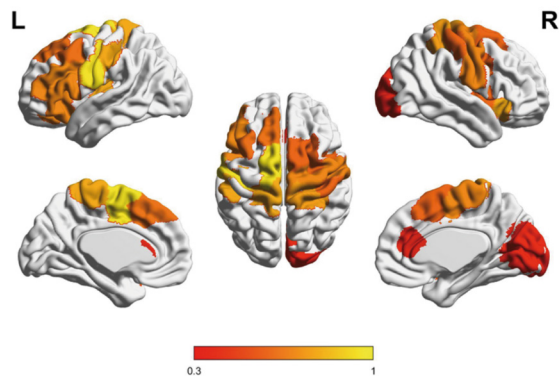
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Background and aims: Very often in routine clinical practice we see some patients with very small lesion having a gross neurological deficit whereas some others with a large lesion have little or no deficits. To explore this, we analysed whole brain connectivity and there topological characteristic in patients without deficits and compared them with a group of clinically matched patients with clinical deficits.

Methods: Resting state functional MRI (rsfMRI) data were recorded for 26 patients with high grade glioma located in the dominant left frontal lobe involving eloquent motor or brocas areas were retrospectively selected for the study. There were 10 patients with deficits (moderate motor and language deficits) (Tumor-D) and 16 patients without deficits (Tumor-WD). The rsMRI data were pre-processed, then brain parcellation to functional brain regions (N=256) were carried out using Shen atlas. Brain connectivity were computed based on phase synchronisation. The brain topological properties were assessed using graph theory measures of brain segregation (clustering coefficient) integration (participation coefficient) and dynamic integration (Ignition-driven mean integration) methods. Between group differences were estimated using '2-sample t-test' with FDR corrected $p < 0.05$.

Results: Tumor-D had diffuse decreased connectivity in several brain regions also involving the sensory motor network in comparison with Tumor-WD and healthy control. Tumor-WD had widespread increased connectivity involving bilateral frontal, motor and motor association cortices. Apart from brain connectivity, increased brain dynamic integrity was noted in Tumor-WD compare to Tumor-D.



Brain region having increased dynamic Integration difference in Tumor-WD compare to Tumor-D

Conclusion: Whole brain synchronicity and dynamic integrity may explain clinical manifestation of a focal deficit apart from the anatomical location.

Disclosure: Nothing to disclose

EPO2332

External Cerebral Artery Stenting – A Good Strategy to Preserve Cerebral Circulation in a Patient with Ipsilateral Internal Carotid Artery Occlusion

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Background and aims: In patients with internal carotid artery (ICA) occlusion the ipsilateral external carotid artery (ECA) may supply the cerebral circulation through collateral vessels.

Although endarterectomy for ECA stenosis has been described in the literature, stenting has rarely been reported. The aim of our paper is to present the case of a patient with ECA stenosis and ipsilateral ICA occlusion in whom stenting of ECA was performed.

Methods: A 73-year-old male was admitted for the 1st time in our Neurology Department 3 years ago for angiographic examination of carotid and vertebral artery stenoses (VAS). The patient had medical history of a right frontal and insular ischemic stroke, arterial hypertension and dyslipidemia. Digital subtraction angiography of the cervical and cerebral arteries (DSA-CCA) revealed the presence of a right ICA occlusion, 60% right ECA stenosis, 80% left ICA stenosis and 90% VAS with intracerebral filling of right middle and anterior cerebral arteries (rMCA, rACA) from left ICA. Left ICA stenting was performed. 1 year later DSA-CCA showed progression of right ECA stenosis under best medical treatment with intracerebral filling of rMCA from right ECA. ECA stenting was decided.

Results: 1 year later the ultrasonographic exam of the cervical arteries showed increased velocities and endothelial proliferation at the ECA stent site and balloon angioplasty was performed.

Conclusion: We chose to present this case in order to highlight the importance of revascularization therapy and follow-up in patients with cervical arteries stenoses this way maintaining the patency of these arteries and preventing further ischemic events and vascular cognitive impairment.

Disclosure: Nothing to disclose

EPO2333

Hypoparathyroidism and Fahr syndrome

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Background and aims: Hypoparathyroidism is an uncommon pathology. It can cause multiple neurological disorders that can be associated with Fahr syndrome.

Methods: It is a cross-sectional study including patients with hypoparathyroidism who were followed in the Military Hospital of Tunis. The patients were assessed by phosphocalcic markers, parathormone and vitamin D assays and a computed tomography (CT) scan of the brain.

Results: 8 patients were included. The average age was 53.9 years old with a male predominance. The hypoparathyroidism was autoimmune in 1 case while it is secondary to the removal of the glands during thyroid surgery in 7 patients. The average duration of hypoparathyroidism was 12.5 years. 4 patients reported paraesthesia. Convulsions were present in 2 patients, tetany in 3 patients, isolated headaches in 7 cases. Depressed mood was detected in 4 patients and 3 cases had memory disorder. A parkinsonian syndrome was found in 3 patients. The lowest corrected calcemia was 1.76mmol/l. Hypovitaminosis D was found in 3 cases and hypomagnesemia in 1 case.

4 patients had calcifications of the basal ganglia on brain scan. The treatment was carbonate of calcium and 1-OH vitamin D, cholecalciferol and magnesium if deficiency.

Conclusion: It is important to detect Fahr syndrome especially if there is a resistant hypoparathyroidism. Treatment based on the vitamin-calcium substitution or even synthetic PTH must be started early to avoid the development of this syndrome.

Disclosure: Nothing to disclose

EPO2334

Clinical and cerebral MRI findings in acute carbon monoxide intoxication

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Background and aims: Carbon monoxide intoxication is a common cause of morbidity and mortality. Several neuropsychiatric features and cerebral magnetic resonance imaging (MRI) findings were found in this patients. The aim of our study was to describe clinical and radiological features of CO intoxication

Methods: A retrospective study of 3 years was performed, including patients who presented an acute carbon monoxide intoxication. Clinical, cerebral magnetic resonance imaging findings were collected and analysed.

Results: 15 patients were included (9 men and 6 women). The average age was 42.4 years old (11-82 years old). All patients presented with mental status change with different severity. Repeated clinical examination revealed cortical visual impairment in 3 patients. 6 patients had memory loss and 3 had extrapyramidal syndrome. Cerebral MRI had shown restricted diffusion of the bilateral globi pallidi in 6 patients. Cerebral cortex, cerebral fronto-parieto-occipital white matter were also involved in 3 patients. 1 patient had bilateral lesions of hippocampi. Occlusion of the cerebral posterior artery with ischemic stroke lesion was observed in another case. 6 patients had normal cerebral MRI.

Conclusion: Several clinical features may be caused by acute CO poisoning. Cerebral MRI with diffusion-weighted imaging (DWI) play an important role to detect the damage caused by acute CO intoxication. Bilateral globi pallidi, cerebral cortical and cerebral white matter with restricted diffusion may be a characteristic MRI feature in this patients.

Disclosure: Nothing to disclose

EPO2335

The role of semi-quantification of 123I-FP-CIT SPECT scans in improving the quality of reporting

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Background and aims: 123I-FP-CIT SPECT is increasingly used to assist the diagnosis of Parkinson's disease (PD). In clinical practice, visual assessment is quite reliable. Semi-quantification of FP-CIT data is more informative; however its use is conventionally used in research. Aiming to improve current care, we designed this audit to value the role of semi-quantification of 123I-FP-CIT SPECT in improving the quality of clinical reporting.

Methods: 44 subjects who had 123I-FP-CIT SPECT twice at Imperial College Healthcare NHS Trust over the past 10 years. Anonymised clinical and imaging data were analysed at Imperial by 2 teams of experienced researchers, who were blinded to each other's results. Firstly, the outcome of each scan report was recorded in a normal/abnormal/inconclusive basis. Following that, semi-quantification was applied on all SPECT data using HERMES BRASS software to generate specific-to-nonspecific binding ratios (SBRs) for striatal regions, with the occipital lobe as the reference region. Regional SBR values were compared to a group of age-matched healthy controls in order to categorise each scan as normal/abnormal. Differences between visual assessments and semi-quantification results were sought for each scan at each time-point.

Results: For 26 out of 44 subjects (total 88 scans), the visual clinical report did not agree with the interpretation based on the SBR values. Of the 88 scans, 8 were inconclusive following the 1st assessment. With quantification, those 8 scans could have been significantly more conclusive.

Conclusion: Semi-quantification combined with visual assessment may remove doubts from inconclusive cases, and significantly improve reporting, thereby reducing the unjustified procedures and incurred costs.

Disclosure: Nothing to disclose

EPO2336

MRI features of patients with autosomal dominant optic atrophy mutation and Multiple Sclerosis

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Background and aims: Co-occurrence of OPA1 mutations (Dominant Optic Atrophy, DOA) and Multiple Sclerosis (MS)-like disease have been described. The nature of this association is a matter of debate. Here we studied 2 patients with concomitant DOA and MS-like disease by conventional and advanced MRI techniques.

Methods: Case presentation:

1) A 26-year-old woman was diagnosed with MS due to the occurrence of facial palsy and hypoesthesia associated with MRI T2-weighted (T2w) hyperintense lesions in the right pons. Spinal cord MRI showed a T2w hyperintense lesion in the C2-C4 tract. Furthermore, the patient showed a progressive visual impairment since 2005, associated with acute episodes of visual acuity worsening. Lack of response to immunomodulatory treatment led to the genetic test with the detection of a mutation in OPA1 gene (c.58C>T/p. His20Tyr).

2) A 27-year-old man was diagnosed with MS due to the onset of right limb hypoesthesia with the detection of multiple T2w lesions on brain MRI associated with central nervous system restricted oligoclonal bands. He had also been suffering from a severe visual impairment since childhood, as his mother. Genetic test revealed OPA1 gene mutation (c.3G>A, p.Met1Ala).

Results: Brain and spinal cord MRI of both patients fulfilled criteria for dissemination in space (DIS) and time (DIT) for MS. Central vein sign (CVS) analysis performed on 2), detected 33% of lesions positive for (CVS), similarly to typical MS.

Conclusion: Pathophysiology of MS concomitant with DOA is unclear. Advanced MRI techniques (i.e.: CVS) may be helpful to shed light on this issue.

Disclosure: Nothing to disclose

EPO2337

Pre- and Post-treatment Diffusion Tensor Imaging and Fiber Tractography in Marchiafava-Bignami Disease

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Background and aims: Marchiafava-Bignami disease (MBD) is a rare alcohol-related disorder that results in progressive demyelination and necrosis of the corpus callosum. Diffusion tensor imaging (DTI) could be employed for studying the clinical correlates of MBD and the recovery process.

Methods: Case report

Results: A 33-year-old male presented with an insidious decrease in consciousness level. He had a history of heavy alcohol intake for 4 years and his nutritional status was very poor. He was unable to perform any daily activities and had been bedridden since 2 months prior to admission. On the day of admission, he was confused and delirious state. He was cachexic. Diffusion-weighted and fluid-attenuated inversion recovery MRI showed high signal intensities in the corpus callosum and bilateral frontotemporal cortical and subcortical areas. He was diagnosed MBD. 4 days after admission, DTI showed normal corticospinal tracts, thinning of corpus callosum on fiber tractography and focal area of decreased anisotropy of the corpus callosum with FA (fractional anisotropy) value of 0.5451. Patient was treated with intravenous vitamin B complex and methylprednisolone. His consciousness level and general condition gradually improved. Follow-up DTI performed 39 days after admission showed thickening of corpus callosum on fiber tractography and increased anisotropy with FA value of 0.5870.

Conclusion: DTI and fiber tractography may be useful in assessing the degree of regional abnormalities and clinical recovery in MBD.

Disclosure: Nothing to disclose

Neuroimmunology 2

EPO2338

Nivolumab induced-encephalitis

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Background and aims: Immune checkpoint inhibitors have emerged as new treatments for numerous types of cancers. However, those patients are at increased risk of life-threatening developing neurological complications such as encephalitis.

Methods: Case report and review of literature.

Results: A 75-year-old woman with metastatic lung cancer developed a nivolumab-induced seronegative encephalitis (presented with seizure and cognitive dysfunction) after 4 weeks of treatment. Brain MRI was normal, CSF showed mild pleocytosis and EEG revealed diffusely slow tracing. She was treated with steroids and nivolumab therapy was discontinued. The patient's neurological status improved after 2 months. We identified more 20 cases of nivolumab induced-encephalitis in the literature (13 men and 7 women) with a median age of 63 years (range 50-78). Median time to onset of symptoms since drug initiation was 64 days (range 4-293). Most frequent clinical manifestations were: decrease in level of consciousness (35%), confusional state (20%), memory dysfunction (15%), aphasia (15%), extrapyramidal symptoms (15%) and memory dysfunction (15%). CSF study showed lymphocytic pleocytosis in 12 patients. 9 patients have positive autoantibodies (Anti-AGNA, -NMAR, -HU, -Ma2 or -GAD 65). 13 patients had T2-weighted hyperintensities in MRI (65%) and 9 had EEG changes (45%). Patients were treated with steroids alone or with other agents. Mortality rate was 30%.

Conclusion: Nivolumab-induced encephalitis presents with diverse symptoms and nonspecific changes on image, CSF and EEG studies. The relation between nivolumab administration and subsequent onset of symptoms is key for diagnosis. Early recognition and prompt treatment are important to prevent significant morbidity and mortality.

Disclosure: Nothing to disclose

EPO2339

ANTI-TUMOUR NECROSIS FACTOR- α RELATED DEMYELINATING DISEASES. CAUSE, TRIGGER OR COINCIDENCE?

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Background and aims: Anti-tumour necrosis factor- α (anti-TNF- α) agents are frequently used in the treatment of gastroenterological and rheumatological autoimmune diseases. Despite its good tolerance, in the last years an increasing number of reports are associating Adalimumab(ADA) with new-onset demyelinating diseases.

Methods: We present 3 cases of anti-TNF- α related demyelinating diseases:

- 29-year-old woman, previous history of pulmonary, ocular and cutaneous sarcoidosis in treatment with ADA since 5 months before. Presented a 6th cranial nerve palsy and numerous lesions on MRI in the medulla, pons, periventricular and subcortical white matter, some of them with gadolinium-enhancement. Normal ACE in blood and CSF and no other evidence of active sarcoidosis.

- 26-year-old woman, previous history of coeliac disease, Hashimoto thyroiditis and psoriatic seronegative spondyloarthritis, for which she had started ADA 36 months before. She presents lower-limb numbness and acute myelitis on MRI, as well as typical periventricular lesions.

- 55-year-old man, family history of Multiple Sclerosis(MS) and previous personal history of recurrent bilateral intermediate uveitis and ADA treatment since 14 months before.

Results: All the patients were treated with ADA from 5 to 36 months (mean time of 18 months). All the patients fulfilled McDonalds criteria of MS. All patients discontinued ADA and were started on Rituximab or Dimethylfumarate.

Conclusion: Anti-TNF- α agents seem to be associated with demyelinating diseases. Their role in the pathogenesis is not clear, but their use as disease-modifying treatment have been proved to worsen disease activity in MS. Physicians should be careful when using them in patients with heavy immunological background or family history of MS.

Disclosure: Nothing to disclose

EPO2340

Immune-reconstitution inflammatory syndrome in multiple sclerosis, are all severe cases associated with a bad prognosis?

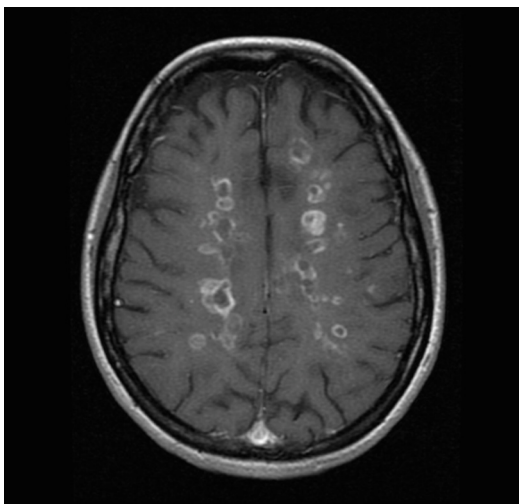
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Background and aims: Immune-Reconstitution Inflammatory Syndrome (IRIS) is a well-known immunological reaction to the withdrawal of an immunosuppressive state. It was described in advanced HIV-patients who started triple-antiretroviral treatment. In neurology it has been associated with Natalizumab, and less frequently Fingolimod, especially if acute withdrawal or plasma-exchange is used in Progressive Multifocal Leucoencephalopathy (LMP). We present a severe case of IRIS and analyze its clinical course, neuroimaging features and prognosis.

Methods: A 35-year-old woman, diagnosed with relapsing-remitting multiple sclerosis (RRMS) at 19 years-old. Her disease was very active despite many disease-modifying therapies, so Natalizumab was started a year before, with a basal Expanded Disability Status Scale (EDSS) of 2.5. She was brought to our Emergency Room due to altered level of consciousness in the last 24h. She had interrupted the treatment by own-decision 2 months before. She was started on intensive steroids and recovered completely after a month, presenting EDSS at discharge of 3.

Results: MRI showed approximately 100 white matter ovoid lesions with open-ring enhancement suggestive of IRIS. In control MRI she presented a total brain volume loss of 3% compared to previous neuroimaging. Between 2012 and 2019 the volume loss was 4.4%.



Multiple white matter ovoid lesions with open-ring enhancement suggestive of IRIS

Conclusion: IRIS has a variable prognosis, usually fatal when associated with advanced LMP but may have a good outcome if not present or early-diagnosis is made. The average brain volume loss in RRMS is estimated to be 0.5-1%, which correlates with our patient. However, IRIS induced in a few months a volume loss 3 to 6 times more than expected in a year.

Disclosure: Nothing to disclose

EPO2341

Anti-NMDA receptor encephalitis: suspicion in clinical practice and mimics.

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Background and aims: Anti-NMDA receptor (anti-NMDAR) encephalitis is currently the most well-characterized autoimmune encephalitis (AIE). Despite the existence of well-established diagnostic criteria, there are diseases capable of mimicking it which require distinct therapeutic approaches. We sought to retrospectively evaluate the reasons for testing and the final diagnosis of patients admitted to the Neurology ward who were tested for anti-NMDAR antibodies in CSF.

Methods: Using the Immunology Department database of our hospital, we identified patients admitted to the Neurology ward who were tested for anti-NMDAR antibodies in CSF between November 2012 and July 2019. The clinical information was then retrospectively reviewed.

Results: 124 patients were identified, of which 39 (31%) met the criteria for possible AIE. Among these we identified 26 mimics (21%), with the predominance of new-onset epilepsies (6), toxic-metabolic encephalopathies (5) and viral meningoencephalitis (5). 85 patients (69%) did not meet the criteria for possible AIE, and the main reasons for antibody testing were isolated or protracted cognitive deterioration (31), isolated or protracted neuropsychiatric condition (21), and new-onset epilepsies (11). 3 patients (2%) had the final diagnosis of definite anti-NMDAR encephalitis - only 1 fulfilled the criteria for possible AIE and none fulfilled the criteria for probable anti-NMDAR encephalitis.

Conclusion: In clinical practice, the threshold for testing anti-NMDAR antibodies was lower than that of the prevailing diagnostic criteria, which allowed for the diagnosis of 2 seropositive patients who did not fulfil those criteria. The proportion of mimics was high, reinforcing the pivotal importance of the search for alternative diagnoses.

Disclosure: Nothing to disclose

EPO2342

Stability of antibody titers to JCV in patients under treatment with natalizumab

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Background and aims: Progressive Multifocal Leukoencephalopathy (PML) associated to Natalizumab has been related to prolonged exposure to this treatment and to high levels of anti-JCV. Furthermore, the variation of anti-JCV index could influence in treatment decisions.

Methods: A retrospective longitudinal study of anti-JCV index measurements, analyzed before starting and after 1 and 2 years of treatment with natalizumab, using STRATIFY, in patients with recurrent relapsing multiple sclerosis (RRMS) attended at our Multiple Sclerosis Unit.

Results: 52 patients (63.5% women). Average age: 39.12 years old (SD 8.67). Time since MS diagnosis: 7.38 years (SD 6.19) and EDSS 2.61 (SD 1.71). An increase of index average has been registered from baseline: 1.30 (SD1.27), to 2 years-treatment: 1.55 (SD 1.25) [$p < 0.05$]. At baseline, 27 patients were anti-JCV positive (51.9%). According to grouped values, before treatment, index JCV was < 0.4 in 37.8%; 0.4-0.9 in 13.5%; 0.9-1.5 in 10.8%; and > 1.5 in 37.8%. After 12 months (N:21): < 0.4 : 52.4%; 0.9-1.5: 4.8%; > 1.5 : 42.9%. And after 24 months (N:29): < 0.4 : 24.1%; 0.4-0.9: 6.9%; 0.9-1.5: 24.1%; > 1.5 : 44.8%. In 44.1% of patients, baseline JCV index was maintained < 0.9 after 2 years. 9.6% increase levels above 0.9. No patient with > 1.5 index decreases below < 0.9 .

Conclusion: Titers of anti-JCV antibodies > 1.5 before starting natalizumab, predicts stable positive values after 1 or 2 years of treatment. It is important to measure periodically JCV index in cases with low value, as there is a considerable percentage of variation that could modify the risk of PML and could influence in therapeutic decisions.

Disclosure: Nothing to disclose

EPO2343

Parry Romberg: neurological manifestations after 20 years

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Background and aims: Parry-Romberg syndrome (PR), is characterized by slow and progressive atrophy of 1 side of the face, primarily involving the subcutaneous tissues and fat. There have been reports of associated neurological complications, such as epilepsy, trigeminal neuralgia, facial pain, migraine, facial palsy, and ipsilateral cerebral hemiatrophy. Neurological involvement is unknown, but it has been described in 10% to 20% of the cases.

Methods: Case Report

Results: 36-year-old female with medical past history of autoimmune thyroiditis, presented with right hemifacial atrophy (V1 territory) beginning at age 16. The facial atrophy progressed during the 1st 10 years. Neurological symptoms were never reported till the age of 36, when she developed right trigeminal pain in V1 territory. Brain MRI showed right cerebral hemiatrophy, multiple white matter hyperintensities predominantly in the right hemisphere, and no morphostructural changes along the course of the trigeminal nerve. Pain remitted with carbamazepine. At the age of 37 she was admitted by binocular horizontal diplopia. Examination revealed right eye exotropia and hypotropia, with restricted adduction and supraduction. Neuroimaging didn't disclose new changes. The CSF showed oligoclonal bands corresponding to intrathecal IgG synthesis. She was treated with intravenous methylprednisolone, with no clinical benefit.

Conclusion: To our knowledge, this is the 1st PR case with neurological symptoms presenting 20 years after disease onset, when skin atrophy was already stable for the previous 10 years. In our patient, the autoimmune background (thyroiditis) and the presence of oligoclonal bands suggest that an autoimmune mechanism may contribute to the PR pathogeny.

Disclosure: Nothing to disclose

EPO2344

Progressive encephalomyelitis with rigidity and myoclonus with multiple autoantibodies as a first manifestation of thymoma

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Background and aims: Thymoma is frequently associated with paraneoplastic diseases, myasthenia gravis being the most common. Rarely, progressive encephalomyelitis with rigidity and myoclonus (PERM) is encountered and it is usually associated with anti-glycine receptor antibodies (GlyR).

Methods: We report the case of a 32-year-old male diagnosed with PERM with multiple antibodies as a paraneoplastic manifestation of thymoma

Results: The patient had a 6-day history of trismus, and progressive asymmetrical inferior limbs rigidity, associated with spontaneous and sleep induced hyperreflexia and piloerection, responsible for insomnia. Brain and spine MRI and electroencephalography were unremarkable. Cerebrospinal fluid (CSF) analysis showed mild pleocytosis (7elem/mL). Electroneuromyography (ENMG) emphasized rare fibrillations without neuromyotonic phenomena. Anti GlyR, anti-GAD and anti CV2 antibodies came back positive. Thoracic CT with iodine findings were consistent with thymoma. Initially, the symptoms improved after thymectomy and under treatment with immunoglobulins and methylprednisolone. He suffered a relapse a month after surgery with bilateral eyelid ptosis. Myasthenia gravis was excluded. He improved under immunosuppressive treatment. At 6-month and 1-year follow-up the patient is stable, the antibodies titer decreased progressively, and he currently has no immunosuppressive treatment.

Conclusion: A rapidly progressive stiff person syndrome in a young patient should be a red flag for PERM and it should not be tested only for GlyR antibodies. To conclude, PERM in the presence of multiple autoantibodies should always raise the suspicion of thymoma.

Disclosure: Nothing to disclose

EPO2345

Thrombin Activity Measurement in Human Cerebrospinal Fluid

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Background and aims: In many neurological manifestations coagulation proteins are known to be involved. Either being synthesized locally in the brain or penetrate from the systemic circulation- their presence and effects are well established. Thrombin is a central blood coagulation serine protease which affects in a dose-dependent manner neurons and glia cells in the central and peripheral nervous systems through protease activated receptors

Methods: We have developed a new method for thrombin direct quantitative measurement in cerebrospinal fluid (CSF). Thrombin activity was measured by a fluorescent substrate in the CSF of 32 patients from 6 groups: multiple sclerosis (MS), acute and chronic inflammatory demyelinating diseases of peripheral nervous system (CIPD/AIDP), non-inflammatory degenerative and cerebrovascular disorders (NI), CNS infection (CNSI), chronic and acute primary headache (CH and AH). Prolyl-endopeptidase and aminopeptidases were inhibited to ensure the specificity of the assay for thrombin detection.

Results: Significant increased thrombin levels were found in AH ($179.1 \pm 111.3 \mu\text{U}/\text{mg}$) and CNSI ($319.4 \pm 104.3 \mu\text{U}/\text{mg}$) groups in comparison to NI ($8.4 \pm 3.2 \mu\text{U}/\text{mg}$, $p < 0.05$ and $p < 0.002$, respectively). An interesting finding is the significant higher activity in the AH in comparison to the CH group ($p < 0.003$).

Conclusion: We have established a novel sensitive method for measuring thrombin activity in human CSF that allows to study the thrombin mediated pathology in various neurological disorders in humans. The differential thrombin activity found in the studied neurological disorders may indicate its potential as a prognostic factor and possible therapeutic target. Further study is needed in order to better characterize the CSF coagulation proteins levels during neurological manifestations.

Disclosure: Nothing to disclose

EPO2346

Brain volumetric analysis using Volbrain and comparative analysis with SIENA in patients with NMDA encephalitis

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Background and aims: Autoimmune anti-NMDAR encephalitis is an antibody-mediated disorder characterized by psychiatric symptoms followed by decreased consciousness, dysautonomia and seizures. Some reports suggest the existence of cerebral atrophy in the follow-up of these patients, with conflicting evidence regarding its presence and usefulness as a marker of prognosis.

Aim: The aim of this study is to define if there is sustained brain atrophy in patients with NMDA encephalitis.

Methods: In a longitudinal retrospective study, all patients with the diagnosis of anti-NMDAR autoimmune encephalitis with initial and control MRI study were included. Automated brain segmental analysis was performed using Volbrain and automated comparative analysis using SIENA. Parametric and nonparametric statistics were performed. Statistical mean and frequencies were calculated. T Student or χ^2 was performed to see the mean difference for volume changes analyzed.

Results: The mean time between the studies was 24 (4-84) months. Significant volume loss were identified in the white matter ($p = 0.001$), gray matter ($p = 0.001$), total brain volume ($p \leq 0.001$), cerebellar volume ($p = 0.035$), putamen volume ($p = 0.01$), thalamic volume ($p = 0.019$) and hippocampal volume ($p = 0.001$). In the simultaneous comparative analysis conducted by SIENA the mean brain volume loss is 334% (-3.65-5.60, SD 2.42).

Table III.
Brain volume differences by region in the follow-up

	Minimum	Maximum	Mean	Standard deviation	p
White matter difference	-139,73	354,53	28,9528	94,83093	,001
Grey matter difference	-66,26	210,03	9,1212	61,73685	,001
Brain difference	-114,71	123,28	19,2896	51,18562	<,001
Cerebellum difference	-7,30	699,97	46,9840	166,41816	,035
Brainstem difference	-4,64	79,43	4,2020	15,91088	,514
Caudate nucleus difference	-2,82	10,66	,1956	2,35606	,417
Putamen difference	-4,40	1,05	-,3608	1,07637	,001
Thalamus difference	-5,26	1,53	-,2620	1,37576	,019
Globus pallidus difference	-,91	8,00	,4196	1,64584	,795
Hippocampus difference	-2,56	2,28	,3404	1,20452	,001
Amygdala difference	-1,47	5,59	,2604	1,23363	,336

Segmental volumetry loss

Conclusion: Patients with antiNMDAR encephalitis have total brain volume loss and volume loss in certain brain regions. Various clinical manifestations seem to be the cause of this predilection by zones and indirectly we can infer that the most severe cases (dysautonomies, epileptic status) are the main factor that contributes to this finding.

Disclosure: Nothing to disclose

EPO2347

The neuropathological features of neurosarcoidosis are more widespread than imaging suggests

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Background and aims: To demonstrate the neuropathological appearances of a patient who died of severe leptomeningeal neurosarcoidosis and to compare with the antemortem imaging features.

Methods: A clinical case study is provided with antemortem imaging and brain autopsy examination.

Results: A 47-year-old man presented with a subacute encephalopathy with ataxia and ophthalmoparesis, uveitis, weight loss and cough. Investigations led to the diagnosis of systemic sarcoidosis. The brain imaging revealed a basal leptomeningitis involving the diencephalon and midbrain, but not elsewhere.

He was treated with steroids and azathioprine but deteriorated and died. His brain was donated to the centre for neurosarcoidosis for research.

At autopsy a marked and widespread granulomatous inflammation was seen which involved all parts of the brain, including those in which imaging had been normal antemortem. There was a vasculocentric granulomatous inflammation with invasion of surrounding parenchyma. In the areas in which there was MRI evidence for inflammation these features were more striking and included active vasculitis with fibrinoid necrosis.

Conclusion: These findings suggest that the leptomeningeal form of neurosarcoidosis is a more severe and more extensive disease than imaging suggests. A more aggressive form of treatment may lead to more favourable outcomes.

Disclosure: Nothing to disclose

EPO2348

White matter lesions in a patient with sarcoidosis: a diagnostic challenge.

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Background and aims: Neurosarcoidosis may present as granulomatous parenchymal inflammation or meningeal involvement. TNF-inhibitors may cause secondary demyelination.

Methods: Case report of a white matter disease (WMD) of the central nervous system (CNS).

Results: A 41-year-old female patient presented with a progressive diffuse headache with photophobia. Her past medical history was positive for systemic sarcoidosis and Crohn disease treated with prednisolone and infliximab for the last 4 years. Lumbar puncture revealed polymorphonuclear pleocytosis (64cells/mm³), 111mg/dL proteins, normal glucose and angiotensin-converter enzyme levels, and a negative microbiologic investigation including JCV-PCR. MRI showed a bilateral temporal T2/FLAIR hyperintense and T1 hypointense lesion, without restricted diffusion or enhancement after gadolinium. The headache subsided after IV methylprednisolone, and a mild cognitive impairment persisted. A presumptive diagnosis of neurosarcoidosis (aseptic meningitis) was made and oral prednisolone (1mg/kg/day) was started. Serum anti-MOG and anti-AQP4 determination was negative. After 4 months, MRI revealed extension of the lesions. CSF and blood infliximab titers were low and drug antibodies were not present. Anti-TNF therapy was stopped assuming a disorder secondary to infliximab, and prednisolone was slowly tapered. The patient remained stable (20 points on MoCA; no signs of progression on MRI). Repeated CSF analysis revealed normalization of cell count and chemistry, no oligoclonal bands, and a persisting negative PCR for JCV. She remained treated with prednisolone 40mg/day and vedolizumab.

Conclusion: This case seems to be an inflammatory disorder of the CNS associated with infliximab. The differential diagnosis between neurosarcoidosis and drug-induced meningitis associated with WMD is particularly difficult.

Disclosure: Nothing to disclose

EPO2349

To examine the impact of Multiple Sclerosis on bone health and explore mechanisms for this association.

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Background and aims: People with MS (PwMS) have an increased risk of osteoporosis and fractures. This may be due to shared risk factors such as low vitamin D and smoking.

Methods: We investigated associations with heel Bone Mineral Densitometry (BMD) and fractures in PwMS in UK Biobank, using BMD from 960 people with MS and 278,138 controls, and 47,466 fractures in 502,583 individuals. Multivariate linear (BMD) or logistic (fracture) regression adjusting for age, sex, ethnicity and current deprivation status was performed.

Results: Demographic characteristics were representative of the broader MS population. The odds ratio of fracture in MS was 1.4. 234/1781 PwMS in UK Biobank (13.1%) reported fractures. BMD T-scores were lower among PwMS (mean -0.649 ± 1.3 vs -0.336 ± 1.24). Lower BMD was associated with smoking (beta -0.1), alcohol consumption (beta -0.03), later menarche (beta -0.03), post-menopausal status (beta -0.18), epilepsy (beta -0.28), and vitamin D supplementation (beta -0.1).

In a model incorporating all individually-significant predictors, the effect of MS on BMD attenuated slightly (beta -0.11 , 95%CI -0.19 to -0.02) while the effect of MS on fracture risk reversed (OR 0.81, 95% CI 0.69-0.95). After adjustment for falls, the effect of MS on fracture attenuated (OR 0.90, 95% CI 0.78 to 1.04). No other exposures altered this association.

Conclusion: These results confirm in a large cohort that MS is associated with lower BMD and higher risk of fractures. Factors associated with BMD do not fully explain lower BMD in MS; increased rates of fracture appear to be driven by both decreased BMD and increased frequency of falls.

Disclosure: Nothing to disclose

EPO2350

Foramen Magnum Meningioma Presenting as Cervical Myelopathy in a Patient with Seronegative Neuromyelitis Optica Spectrum Disorder Overlap with Primary Sjögren's Syndrome

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Background and aims: Meningiomas are the most common primary tumours of the central nervous system (CNS). They are mainly benign and cause symptoms by compression. Foramen magnum meningiomas account for 1.8-3.2% of all meningiomas. Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the CNS primarily targeting the optic nerves and spinal cord, with a prevalence as high as 10 per 100000. Systemic autoimmune disorders including Sjögren's syndrome (SS) may coexist with NMOSD.

Methods: We report the case of a 52-year-old man with inflammatory disease of the CNS compatible with seronegative NMOSD overlap with primary SS, with a history of recurrent cervical and thoracic myelitis, in sustained clinical remission following immunosuppressive therapy with cyclophosphamide 8 years prior, and continuing oral corticotherapy with methylprednisolone. He was readmitted for persisting bilateral cervical paresthesia for a month and neurological examination revealed hypoesthesia in the C2 region bilaterally, tetramelic hypopallesthesia, slight motor deficit in the upper limbs and paraparesis 4/5 MRC.

Results: We performed magnetic resonance imaging of the cervical spine which showed a contrast-enhancing epidural mass compressing the spinal cord in the C1-C2 region and the medulla, raising the suspicion of a foramen magnum meningioma. The patient underwent complete excision of the mass and histopathological evaluation was consistent with a benign meningioma, i.e. WHO grade I.

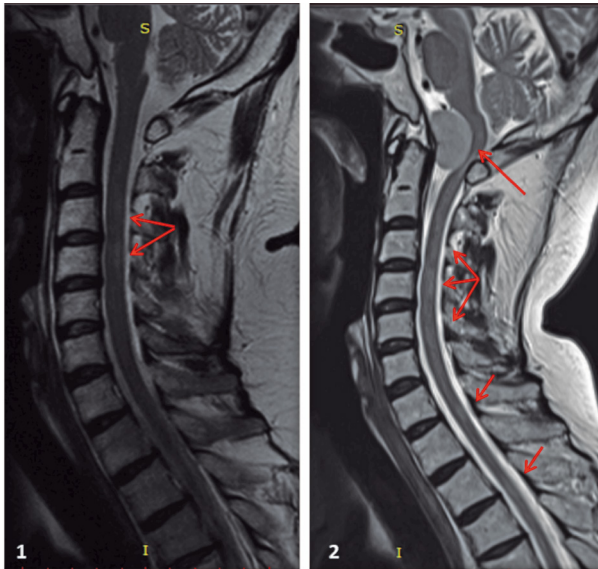


Figure 1. Cervical and thoracic spine MRI. Sagittal T2-weighted images showing T2-hyperintense lesions of myelitis in 2008 (1) and 2019 (2), with a contrast-enhancing epidural mass at the cervicomedullary junction, typical for meningioma (2).

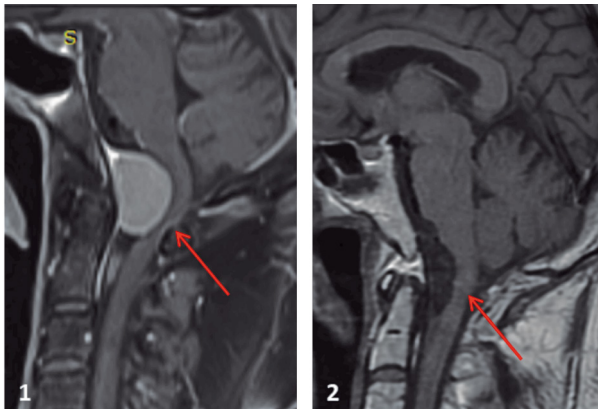


Figure 2. Cervical spine MRI. Sagittal T1-weighted image showing a contrast-enhancing epidural mass compressing the cervical spine in the C1-C2 region and the medulla (1) and postoperative T1-weighted image (2).

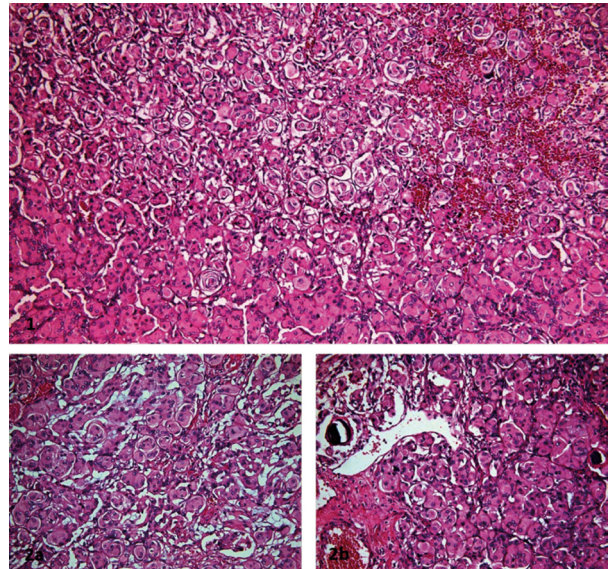


Figure 3. Histopathological specimens hematoxylin and eosin stained, 100 times enhanced (1) and 200 times enhanced (2a, 2b) showing proliferation of meningeal cells arranged in large lobules and nests of medium-sized epithelioid and spindle cells, numerous meningeal whorls and psammoma bodies, some calcified.

Conclusion: This case involved diagnostic difficulties before the current criteria for NMOSD were defined and we discuss here the differential diagnosis. The discovery of a foramen magnum meningioma was all the more surprising in the aforementioned background.

Disclosure: Nothing to disclose

EPO2351

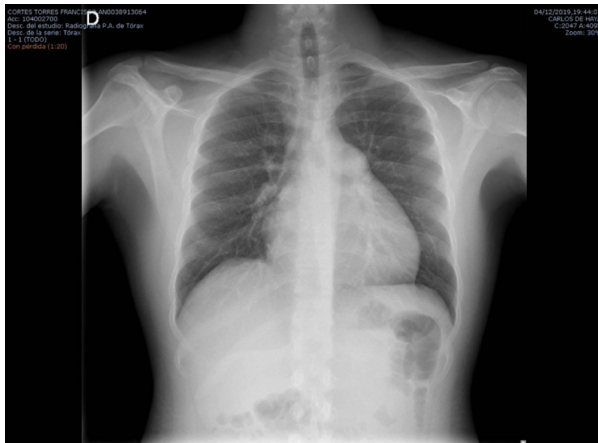
Secondary pulmonary hypertension in a patient with multiple sclerosis treated with teriflunomide: a case report.

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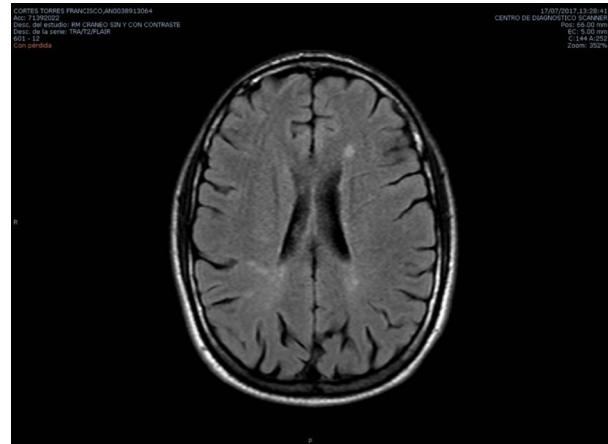
Background and aims: Teriflunomide is a disease-modifying drug approved for Multiple Sclerosis (MS). Its an overall well-tolerated treatment with an 11% rate of discontinuation due to side effects, such as hepatotoxicity, high blood pressure, headache and gastrointestinal disorders. Pulmonary hypertension (PH) is a chronic disease characterized by increased pulmonary vascular resistance (PVR) at the pulmonary arterioles, which causes a progressive overload and subsequent dysfunction of the right ventricle. Primary pulmonary hypertension has been described in patients with leflunomide, but teriflunomide has only been associated with secondary causes as lung interstitial disease.

Methods: We present the case of a 26-year-old man, diagnosed of MS in 2008, who presented an acute right-heart failure due to primary pulmonary hypertension. 8 months before he as started on teriflunomide because of IFNB-1A intolerance.

Results: Echocardiogram showed a severe pulmonary hypertension associated to a severe tricuspid insufficiency, without left heart disease. Chest angioCT ruled-out pulmonary thromboembolism and parenchyma abnormalities. Other diseases associated to HP were exclude as well. Teriflunomide was discontinued during the admission and the patient initiated treatment for primary pulmonary hypertension upon discharged.



Chest radiography



MR

Conclusion: We believe that pulmonary hypertension could be caused by the exposure to teriflunomide, as other causes were ruled-out and it has been previously described with leflunomide. Therefore, we consider that physicians should keep in mind this side effect, especially in patients with personal or family history of heart disease or pulmonary hypertension.

Disclosure: Nothing to disclose

EPO2352

Vogt-Koyanagi-Harada syndrome – Characterization of an 11 patient cohort

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Background and aims: Vogt-Koyanagi-Harada syndrome (VKHS) is a rare multiphasic inflammatory disorder, characterized by panuveitis, associated with neurological and cutaneous manifestations. To characterize a cohort of VKHS patients, concerning clinical, laboratorial and imagiological data.

Methods: Retrospective analysis of patients attending uveitis and/or neuroimmunology clinics, from 2008 to 2019, that fulfilled the diagnostic criteria for complete or incomplete VKHS (by the American Uveitis Society).

Results: 11 patients (8 women, mean age at onset 38±13,57 years), 7 had incomplete and 4 complete VKHS. All developed neurological manifestations: headache was the most common symptom (n=10), associated with nausea, stiffness of the neck and/or fever (n=7). In 3 patients the neurological involvement began in the prodromal phase (time to ocular disease 1 week to 3 months) and in other 6 patients in the acute ocular phase. 7 patients performed lumbar puncture, all had lymphocytic pleocytosis (median of 113 leucocytes, 1 case with high protein level). Brain MRI showed bilateral choroidal thickening in 4 patients, without involvement of the optic nerves. In the acute phase all patients were treated with corticosteroids and in the chronic phase immunosuppressive treatment was started: azathioprine (n=5), methotrexate (n=2), cyclosporine (n=1), corticosteroids (n=2) and adalimumab (n=1). The neurological symptoms recurred in 2 cases, one with transitory focal deficits (aphasia and right hemiparesis).

Conclusion: Neurological involvement was common and related to the beginning of ocular impairment, constituting a marker of disease activity. Neurological signs can precede the ocular disease and should be considered by the neurologist approaching an uveo-meningeal syndrome.

Disclosure: Nothing to disclose

EPO2353

An unusual association of chronic inflammatory demyelinating polyneuropathy (CIDP) and anti-contactin-associated protein-2 (anti-Caspr2) syndrome

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Background and aims: Anti-Caspr2 syndrome may present with several phenotypes including peripheral nerve hyperexcitability (e.g., cramps, fasciculations, myokomia, and neuromyotonia), central nervous system manifestations (e.g., insomnia, seizures, and limbic encephalitis) and dysautonomia (e.g., hyperhidrosis, labile arterial blood pressure and cardiac arrhythmias). It is due to the presence of antibodies that target the contactin-associated protein-2, a membrane protein of the juxtaparanodal region. Herein we report a CIDP patient who later developed an anti-Caspr2 syndrome.

Methods: Case report and literature review.

Results: A 73-year-old patient had been treated for CIDP with polyvalent intravenous immunoglobulins (IVIg, 1g/kg every 6 weeks) for 2 years when he developed insomnia, hyperhidrosis, labile blood pressure, diarrhea, weight loss, cramps, and stiffness. Electroneuromyography revealed fasciculation potentials, myokymia and neuromyotonic discharges at rest, in addition to a multifocal, predominantly motor axonal and demyelinating neuropathy with multiple conduction blocks. Anti-ganglioside antibodies were not detected in the serum. High-titer serum anti-Caspr2 antibodies were found. Cerebrospinal fluid examination showed a mildly increased protein level at 0.47g/L. Full body PET-scan was unremarkable. Symptom control was achieved with increased doses of IVIg (2g/kg for 5 days followed by courses of 1g/kg every 3 weeks).

Conclusion: Peripheral neuropathy is not a known feature of anti-Caspr2 syndrome. While the association of peripheral nerve hyperexcitability and CIDP has rarely been reported, this patient is, to our knowledge, the first case of anti-Caspr2 with CIDP.

Disclosure: Nothing to disclose

EPO2354

Stiff person syndrome: a case report

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Background and aims: Stiff person syndrome is a rare disease of the central nervous system, characterized by progressive stiffness and muscle spasms in the extremities and axial musculature. 60-80% have positive anti GAD antibodies and 10% have amphiphysin antibodies.

Methods: A 58-year-old woman from Equatorial Guinea started with weakness of lower limbs, stiffness and pain of the axial musculature that progresses over the time, with many accidental falls, leading to the need of using crutches for walking. On physical examination, she presented hyperlordosis with stiffness and hypertrophy of the dorsal-lumbar paravertebral muscles and painful muscle spasms of spinal and abdominal muscles, bilateral Hoffmann sign, bilateral incoordination of upper limbs and gait ataxia (more instability than expected due to slight rigidity of lower limbs).

Results: Analysis disclosed positive anti-GAD, anti-thyroperoxidase and anti-gastric ATPase antibodies. The EMG showed continuous motor activity. Diagnosis of stiff person with cerebellar involvement was made. Immunoglobulin and plasmapheresis treatment was unsuccessful, some improvement was observed with 1g/day of methylprednisolone for 5 days. However, the symptoms persisted, associating dysphonia and dyspnea with a restrictive pattern in spirometry (due to thoracic stiffness). Finally, it was decided to start treatment with rituximab with a great improvement of symptoms.

Conclusion: Stiff person syndrome with cerebellar component is rare. This patient had poor response to usual treatments, which requires finding therapeutic alternatives although its effectiveness has not been completely studied. We have to take in account that symptomatology guides the physician to take the decision and not the presence of positive antibodies.



Hyperlordosis with hypertrophy of the lumbar paraspinal muscles



Inability to bend down and touch their toes.

Disclosure: Nothing to disclose

EPO2355

The Clinical Efficacy of Intravenous Immunoglobulin in Neurology - A Retrospective Cohort Study at the Mater Misericordiae University Hospital

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Background and aims: Intravenous Immunoglobulins (IVIg) are blood-derived medicinal products prescribed for various medical conditions. Clinical evidence strongly supports the use of IVIg as 1st-line therapy in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Guillain-Barré syndrome (GBS) and Multifocal Motor Neuropathy. There are an increasing number of other neurological conditions where IVIg has been used despite limited evidence-based data. Careful consideration of the efficacy of IVIg in each indication is required as it is a limited resource.

To review clinical indications for IVIg use in neurology patients at the MMUH. To compare prescribing practices to international evidence-based guidelines.

Methods: All neurology patients treated with IVIg between 2016 and 2018 were retrospectively reviewed. Data collected included indication, dose, total number of IVIg courses, use of alternative therapies before IVIg and documentation of clinical benefit. Results were compared to international evidence-based guidelines and verified by a neurology consultant/registrar.

Results: 67 patients were included. IVIg was prescribed for 15 indications. The most common were GBS, Myasthenia Gravis and CIDP. 31 patients received IVIg for licensed indications, whereas 36 patients received IVIg for unlicensed indications. The level of evidence from international evidence-based guidelines supported the use of IVIg for most indications.

Conclusion: IVIg is prescribed for a range of neurological conditions at the MMUH, the majority of which are unlicensed. IVIg use was supported for most indications when compared to international evidence-based guidelines. However IVIg was prescribed for several indications despite limited evidence of efficacy. This study highlights the need for evidence-based clinical guidelines for IVIg use at the MMUH and Ireland.

Disclosure: Nothing to disclose

Infectious diseases 1

EPO2356

Varicella zoster virus (VZV) reactivation-induced myelomeningoradiculitis and cranial neuropathy without skin lesions

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Background and aims: Reactivation of varicella zoster virus (VZV) from latently infected human ganglia usually produces herpes zoster, characterized by dermatomal distribution pain and rash, often followed by postherpetic neuralgia. But it can also cause several neurologic dysfunctions such as meningoencephalitis, cerebellitis, isolated or multiple cranial nerve palsies, vasculopathy or myelopathy, even without skin lesions.

Methods: We present the case of a 72-year-old patient with myelomeningoradiculitis caused by VZV reactivation.

Results: A 72-year-old man with hepatocellular carcinoma treated with chemoembolization, presented to the emergency department with a 10-day history of urinary retention, lumbar pain and weakness of lower limbs. Upon admission, neurological exam revealed right facial palsy, weakness of lower limbs (grade 2/5) and bilateral Babinski sign. Ankle and knee jerk reflexes were abolished bilaterally and decreased sensation to vibration and touch was noticed with T10 sensitive level. Magnetic resonance imaging showed leptomenigeal and cauda equina contrast enhancement, hyperintense lesions in thoracic spinal cord (T2-T12) and subacute putaminal infarction. Cerebrospinal fluid (CSF) testing showed lymphocytic pleocytosis and elevated proteins, without malignant cells. PCR assay in CSF for VZV was positive. The remaining tests were negative. From these data, the diagnosis of VZV reactivation-induced myelomeningoradiculitis, facial palsy and ischemic stroke was made, without associated skin lesions. The patient was treated with intravenous acyclovir for 21 days and dexamethasone for ten days followed by oral tapering, with clinical improvement.



Image 1

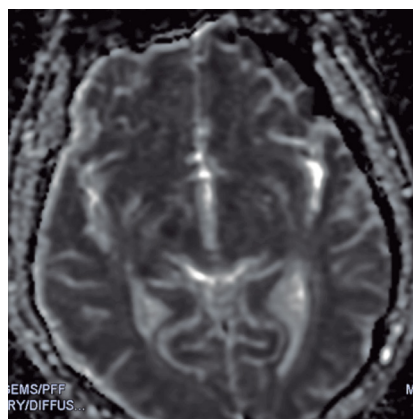


Image 2



Image 3

Conclusion: This case emphasizes the importance of considering VZV reactivation in patients (particularly immunocompromised) presenting with a constellation of symptoms of neurologic dysfunction, even in the absence of rash.

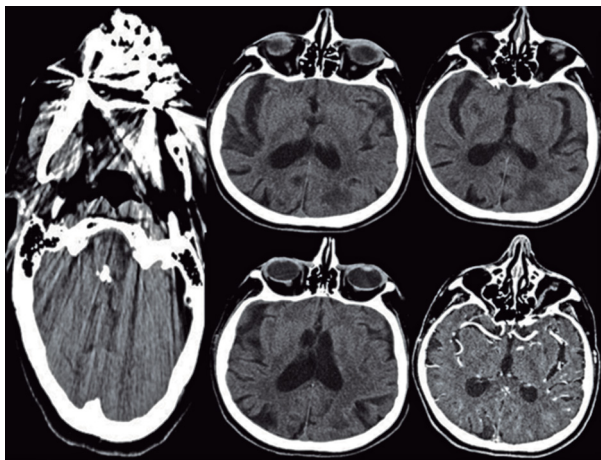
Disclosure: Nothing to disclose

EPO2357

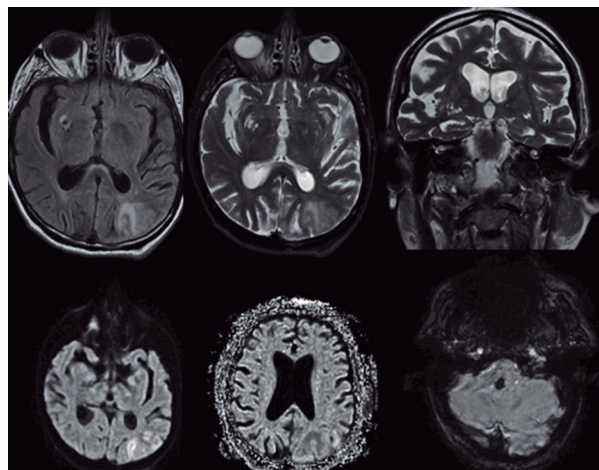
“Unusual presentation of cryptococcus neoformans: bilateral sublenticular invasion and meningoencephalitis”

G. Carvalho Monteiro¹, B. Povedano Margarit¹, J. Hernandez Cristobal¹, J.M. Celi Celi¹, D.E. Barbero Jiménez¹, F. Romero Delgado¹, A. Garcia-Puente Garcia², M. Torralba González de Suso¹, A. Yusta Izquierdo¹
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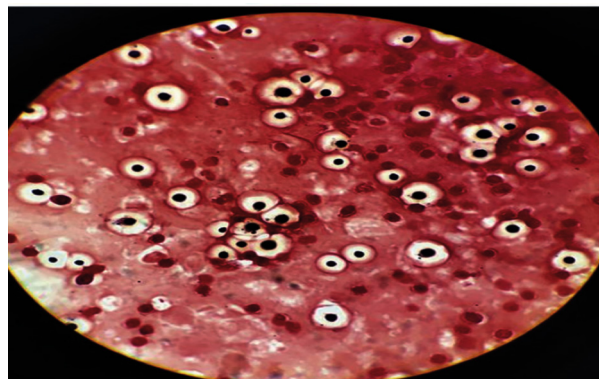
Background and aims: Disseminated cryptococcosis is a serious fungal infection with a high mortality rate in patients with AIDS and the 4th opportunistic disease that causes pneumonia and meningitis. Its most frequent form of presentation is Pulmonary but in the CNS the most common form is meningitis but less frequently it can occur as meningoencephalitis and/or pseudotumoral lesion (perivascular or cryptococomas gelatinous forms). The Neoformans cryptococcus has been isolated in excreta of pigeons, parrots and chickens being considered a zoonosis.



Methods: A 74-year-old male who presented abruptly about 7 am in the morning episode of language disturbance and temporo-spatial disorientation, activating stroke code. After assessment at 11:45h, past >4.5h since the beginning of the episode, presents NIHSS: 5 (Aphasia + mild right hemiparesis). Cranial CT and Angio CT are performed, visualizing hypodense area in the left parietooccipital border region without occlusion of large vessels, dismissing fibrinolysis and thrombectomy. Subsequently, it presents a 38° febrile peak. Performing lumbar puncture (33 leukocytes, 95% monocytes, Proteins 150, Glucose 50). Serum glucose 175. Visualization of yeast with Chinese ink. Positive CSF PCR for Cryptococcus Neoformans. HIV 1 positive and 50CD4.



Results: Fungal Meningoencephalitis is confirmed by initiating induction therapy with Liposomal Amphotericin B + Flucytosine and subsequently consolidation therapy with Fluconazole + antiretrovirals. In cerebral MRI, left parietooccipital meningoencephalitis with leptomeningeal thickening and vasogenic edema is described, in addition to gelatinous pseudocysts in sublenticular perivascular spaces.



Conclusion: We present a rare case of Cryptococcus Meningoencephalitis and unusual involvement of sublenticular pseudocysts.

Disclosure: Nothing to disclose

EPO2358

Dorsal myelopathy secondary to spondylodiscitis caused by streptococcus agalactiae in an adult with known underlying disease.

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Background and aims: We present a case of dorsal myelopathy secondary to spondylodiscitis caused by streptococcus agalactiae in an adult with known underlying disease.

Methods: 46-year-old female with a history of diabetes mellitus (DM) of undetermined evolution and abandonment of antidiabetic treatment. Go to emergency department due to acute urinary retention, temperature 38°C, proximal predominance flaccid paraplegia, areflexia in lower limbs, bilateral Babinski, tactile and algic hypoesthesia level D5, neck stiffness and meningeal signs. Cerebrospinal fluid compatible with acute bacterial meningitis. Espine MRI with left paravertebral abscess with extension to the spinal canal and extrinsic compression of the medullary cord (D4-D6), signs of myelopathy (D4-D7) and spondylodiscitis (D5-D6). Initially, empiric antibiotic therapy is prescribed and evacuating surgery and laminectomy are performed. Blood culture and paravertebral abscess culture were positives for *S. agalactiae*. After specific antibiotic treatment the clinical evolution is favorable.

Results: *S. agalactiae* is an asymptomatic colonizer of the organism that can infect the spine primarily by hematogenous spread. Adults who are at risk of infection are women in gestational and peripartum periods and patients with severe underlying diseases. In the few cases of spondylodiscitis due to *S. agalactiae* reported in adults, there is a predominance of the male sex, lumbosacral location, extravertebral extension in the form of paravertebral or epidural abscesses with spinal cord compression, and the existence of a predisposing factor of infection, highlighting DM among them.

Conclusion: Spondylodiscitis due to *S. agalactiae* outside the gestational and peripartum period most often affects adults with predisposing factors, highlighting DM among them.

Disclosure: Nothing to disclose

EPO2359

Diagnostic reliability and cost of routine determination of adenosine deaminase levels in cerebrospinal fluid.

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Background and aims: High levels of adenosine deaminase (ADA) in cerebrospinal fluid (CSF) along with other biochemical alterations suggest tuberculosis. We aim to evaluate diagnostic reliability and cost of measuring ADA routinely in CSF samples.

Methods: Observational retrospective descriptive study analyzing reason for requesting, final diagnosis and biochemistry of all CSFs in which ADA was requested from January 2017 until December 2018 at La Paz University Hospital.

Results: 201 CSFs with ADA determination were analyzed. Only 89 (44.3%) were requested due to a suspected CNS infection. ADA levels in CSF were considered high (>8U/L) in 26 (12.9%) samples; 25 (96.15%) of them pertaining to patients with possible CNS infection. Of the 26 samples with high ADA levels, 22 (84.61%) had other biochemical abnormalities and only 5 of these belonged to patients with final diagnosis of CNS tuberculosis. There was no CSF sample with normal levels of ADA from which a tuberculosis diagnosis was made. Sensitivity and specificity of ADA determination were 100% and 90%, respectively. Test positive predictive value was of 19%. The price of ADA determination in a single sample of CSF is 12€. In our study, the extra cost of ADA determination when CNS infection is not suspected is of 1164€, and it ascends to 1476€ taking into account cases of suspected CNS infection but lack of biochemical abnormalities in CSF.

Conclusion: Due to the low incidence of CNS tuberculosis in our environment, routine CSF ADA determination does not seem profitable unless CNS infection is suspected and CSF is abnormal.

Disclosure: Nothing to disclose

EPO2360

Rhino-orbital mucormycosis causing multiple cranial nerve palsies: a case report

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Background and aims: Mucormycosis is a rapidly progressive fungal infection frequently seen in diabetic and immunosuppressed patients. Rhino-orbital mucormycosis is the commonest form presenting with chemosis, ptosis, proptosis, ophthalmoplegia and visual loss.

Methods: We report a patient with multiple cranial nerve palsies.

Results: A 55-year-old man known for diabetes mellitus, chronic renal insufficiency on dialysis, diabetic peripheral neuropathy and left foot diabetic ulcer, presented with diplopia. He complained of unilateral headache starting 4 days earlier. Upon admission he had normal vital signs and an isolated abducens nerve palsy. Laboratory findings included high glucose levels, ketoacidosis and high C-reactive protein. Cranial CT scan showed opacification of the left ethmoid, sphenoid and maxillary sinuses and the patient was put on antibiotics. The following day the patient evolved ptosis and complete external and internal ophthalmoplegia on the left, hypoesthesia of the left half of the face and unilateral visual loss. Brain MRI depicted edema and diffusion restriction of the oculomotor muscles of the left eye and of the optic disk, periorbital soft tissue gadolinium enhancement, and opacification of the nasal and paranasal cavities. Rhinoscopy revealed multiple necrotic lesions and the biopsy yielded *Rhizopus arrhizus*. Isavuconazole was promptly initiated and the patient was transferred to the maxillofacial surgery department for treatment.

Conclusion: Mucormycosis is a medical emergency and rapidly evolving multiple cranial nerve palsies in a diabetic patient should raise suspicion of this condition. Necrotic lesions in the oral maxillary or nasal mucosa could be easily missed unless specifically looked for. Early radical surgical treatment may be life-saving.

Disclosure: Nothing to disclose

EPO2361

Stroke in HIV-infected patient due to thrombosed cerebral aneurysm leading to diagnosis of aneurysmal vasculopathy

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Background and aims: HIV – associated cerebral aneurysmal vasculopathy is a rare complication of HIV-infection among other vascular changes such as vasculitis, stenosis, aneurysms and accelerated atherosclerosis.

Methods: We report a case of a 29-year-old patient with AIDS who suddenly developed left hemiplegia and left central facial palsy during hospitalization in the Department of Infection Diseases for measles.

He was 1st diagnosed with HIV at the age of 5, being one of the children who acquired an HIV infection parenterally more than 25 years ago (Romanian "1987-1990 cohort"). The initial workup included lumbar puncture that showed protein level of 60mg/dl, fluid glucose level of 40mg/dl (blood glucose level of 95mg/dl), 2/mm³ white cells, negative cryptococcal latex antigen fixation, negative rapid plasma reagin and negative cultures for bacteria, fungi and tuberculosis.

He was transferred to the Neurology Department for further investigation. He underwent an MRI and angiography (MRI-MRA) that showed acute infarction in the distribution of right MCA deep territory, bilateral multiple fusiform aneurysms and thrombosed cerebral aneurysm arising from the intracranial segment of the internal carotid artery (M1, M2 segments).

Results: In collaboration with a neurosurgeon and an interventional neuroradiologist, the surgical/endovascular treatment options were inappropriate considering potential risks, particularly bleeding in the brain or loss of blood flow to the brain.

Conclusion: Although cerebral aneurysmal vasculopathy in adult patients with AIDS is a rare condition, it should be properly considered in the differential diagnosis in patients with AIDS who developed stroke or intracranial hemorrhage.

Disclosure: Nothing to disclose

EPO2362

An unusual presentation of sciatic neuropathy after influenza A virus infection

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Background and aims: Peripheral neuropathies caused by infectious agents have a complex pathophysiology. They can be classified as postinfectious or parainfectious neuropathies. The 1st usually appears several weeks after the onset of the disease and is thought to be an autoimmune reaction. The latter develops during the acute infection or shortly after, and is either a direct consequence of the infection or an unusual hyperimmune response.

Methods: A previously healthy 45-year-old woman was admitted to intensive care for complicated influenza A virus pneumonia. 10 days after admission, the patient began experiencing excruciating pain with neuropathic characteristics (allodynia, hyperalgesia and dysesthesia) in the left leg, along with motor limitation involving tibial and peroneal nerve territories. Blood workup was unremarkable (including CK, cryoglobulins, antiganglioside antibodies, infectious serologies and immune study). Lumbar puncture was normal, with negative oligoclonal bands. Lumbar and dorsal MRI were normal, but an MRI directed to the sacred plexus showed marked thickening and hyperintensity of the left sciatic nerve with diffuse contrast enhancement. Nerve conduction studies revealed axonal sensory-motor neuropathy of the left sciatic nerve. (figure-1)

Results: A 3-day trial with methylprednisolone (1g endovenous), along with 1200mg gabapentin, 30mg baclofen, 35mg amitriptyline and 20mg subcutaneous morphine daily resulted in gradual pain and motor deficit improvement. The patient is currently on physical rehabilitation program.

Conclusion: Neuropathies can result directly from bacterial/viral infections, but also from indirect/parainfectious autoimmune responses to the infection. In this patient, parainfectious influenza A neuropathy was the most likely mechanism. To our knowledge, is the first reported case.

Disclosure: Nothing to disclose

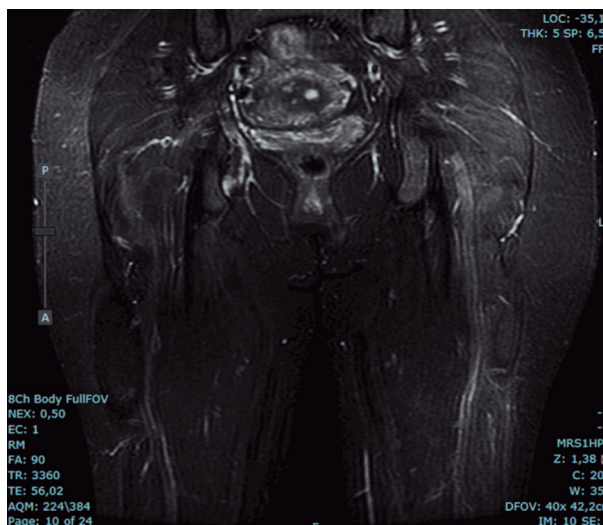


Figure 1- Hyperintensity of the left sciatic nerve

EPO2363

Severe human herpesvirus 7 (HHV-7) encephalitis in a patient with rheumatoid arthritis

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Background and aims: HHV-7 encephalitis is a rare cause of encephalitis in both immunocompetent and immunosuppressed patients. The reported symptoms in HHV-7 encephalitis are seizures, cognitive problems or abnormal electroencephalogram (EEG) and the pathogenic role is controversial. Therapeutic experience is derived from isolated cases, “in vitro” antiviral efficacy studies. Ganciclovir, foscarnet and cidofovir inhibit the replication of HHV-7 but therapeutic indications are still poorly defined.

Methods: We present the case of a patient with rheumatoid arthritis under immunosuppressive treatment who developed severe HHV-7 encephalitis with torpid evolution despite of foscarnet treatment.

Results: 69-year-old woman with a history of rheumatoid arthritis with a positive centromeric pattern under treatment with prednisone and leflunomide, deep vein thrombosis in chronic treatment with acenocoumarol, hypertension and morbid obesity. She presents with 2 generalized tonic-clonic seizure, followed by sensitive aphasia, inattention and psychomotor restlessness. The EEG showed left frontotemporal epileptic activity and antiepileptic treatment with levetiracetam, lacosamide, valproic acid, carbamazepine and clobazam was subsequently initiated. The brain MRI showed left frontoparietal cortex enhancements compatible with meningoencephalitis in diffusion sequence. The cerebrospinal fluid (CSF) showed 88leukocytes/mm³ with and 96.3mg/dL proteins. Empirical treatment with Acyclovir and Ampicillin was initiated and changed to foscarnet after C-reactive protein (CRP) in CSF resulting in HHV-7. She had a torpid evolution and after 19 days died.

Conclusion: The pathogenic role of HHV-7 in encephalitis is controversial but it should be considered and aggressively treated in immunosuppressed patients. The current case reports the evolution of HHV-7 encephalitis which can contribute to the current knowledge of this serious disease.

Disclosure: Nothing to disclose

EPO2364

Empyema due to *Listeria monocytogenes* presented as “stroke-mimic”

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Background and aims: Subdural collection as meningitis by *Listeria monocytogenes* is a rare complication that occasionally requires surgery. So far, a case of subdural empyema caused by *Listeria monocytogenes* infection has been reported with good evolution after only medical treatment using combined antibiotic therapy. The presentation as stroke-mimic has not been reported so far.

Methods: We present the case of a 78-year-old male with metastatic colon adenocarcinoma in active treatment with chemotherapy, who presents with a “stroke-mimic” consisting of right hemispheric syndrome secondary to subdural collection due to *Listeria monocytogenes* induced meningitis, showing excellent evolution after antibiotic treatment and surgical treatment.

Results: 78-year-old male with colorectal adenocarcinoma with liver metastases surgically treated and active chemotherapeutic treatment, presents with right hemispheric syndrome showing right oculocephalic preference, left hemiplegia and heminegligence and fever. Multimodal CT did not show any anomalies. Brain MRI identified a right parietal subdural collection and meningoencephalitis with leptomeningeal uptake. The patient was empirically covered with acyclovir, cefotaxime, vancomycin, ampicillin and metronidazole and underwent right frontoparietal craniectomy. *Listeria* was detected in CSF and brain biopsy and Ampicillin was administered for 6 weeks due to the presence of cerebritis and ventriculitis associated with meningitis. The patient had a complete recovery with physiotherapy and is currently under chemotherapeutic treatment again, Eastern Cooperative Oncology Group(ECOG) 0.

Conclusion: This is, to our knowledge, the 1st case of subdural collection as a complication of *Listeria monocytogenes* undergoing surgical treatment and antibiotic therapy with an excellent evolution, which may suggest that surgical treatment could be a good option for these patients.

Disclosure: Nothing to disclose

EPO2365

A case of Bannwarth syndrome with acute onset of severe tetraparesisI. Goursky¹, Y. Brant², A. Astapenko¹, S. Likhachev¹¹Department of Neurology, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus, ²Neurological department, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

Background and aims: Lyme disease is endemic in Belarus. Bannwarth syndrome is a rare variant of neuroborreliosis, which is characterized by painful radiculopathy, neuropathy, limb weakness and facial palsy, as well as lymphocytic CSF pleocytosis. Here we describe our own observation of Bannwarth syndrome, to highlight the possibility of acute onset of profound neurologic deficit in Lyme disease.

Methods: Medical records were analyzed of the female patient, who admitted our facility 01.10.2018.

Results: At 15.10.2018 the patient developed lower back pain, irradiating to the right leg. Lumbar spine MRI at 26.09.2018 was unremarkable (small disc protrusions). Physical examination on admission was consistent with a diagnosis of sciatica, and during the first 3 days treatment was successful in relieving pain. Beginning from the 4th day, the patient experienced increasing pain, demanding narcotics; also neck pain emerged. At the 7th day the patient developed progressively headache, left facial and abducens palsy, and severe distal tetraparesis, neck stiffness. CSF examination demonstrated protein 1.6g/l, glucose 1.8mM, and lymphocytic pleocytosis of 96/ul. Aciclovir, ceftriaxone and dexamethasone were started. Brain MRI demonstrated no other findings, but contrast enhancement of the left facial nerve. During the following day, the symptoms subsided, and a positive serology result for *B. burgdorferi* was received. The patient was transferred to the infection hospital, and was asymptomatic after 3 weeks.



Brain MRI (T1), demonstrating contrast enhancement of the left facial nerve.

Conclusion: This case demonstrates a possibility of neurologic emergency in Lyme disease. Other remarkable feature of this case is the absence of history of tick bites and erythema migrans.

Disclosure: Nothing to disclose

EPO2366

Progressive multifocal leukoencephalopathy of the cerebellar peduncle in a patient with Myasthenia gravis immunosuppressed with azathioprine: Case report and review of the literature

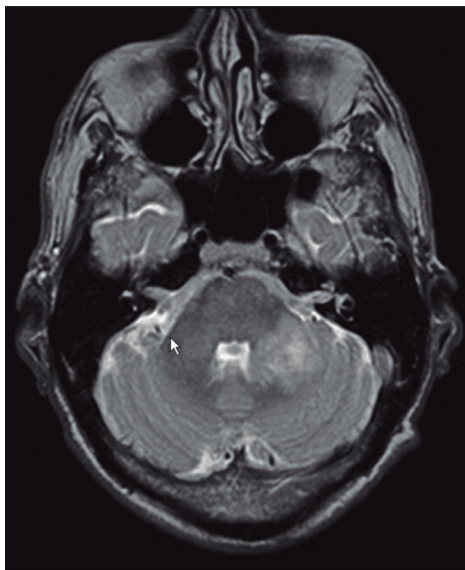
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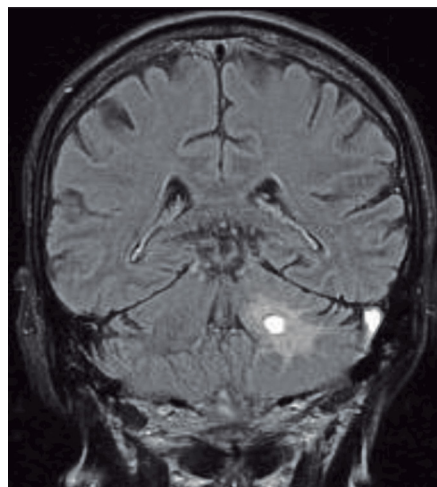
Background and aims: Progressive multifocal leucoencephalopathy (PML) is a rare opportunistic infection of the central nervous system with JC-polyomavirus affecting most often patients with hematological malignancies, HIV infection or treatment with monoclonal antibodies or immunosuppressants.

Aims: To present an unusual presentation of PML and treatment course including pembrolizumab

Methods: A 71-year-old patient with generalized myasthenia gravis with acetylcholine-receptor antibodies (AchR-gMG) and resected thymoma 20 years earlier presented with a progressive unilateral cerebellar syndrome. In addition to symptomatic therapy he was treated with low dose steroids and azathioprine since 2009. 2014 a slight pancytopenia occurred, which was tolerated. A brain MRI showed a T1-hypointense, T2-hyperintense lesion of the left cerebellar peduncle without contrast enhancement, the cerebrospinal fluid (CSF) displayed no pleiocytosis or other routine pathologies.

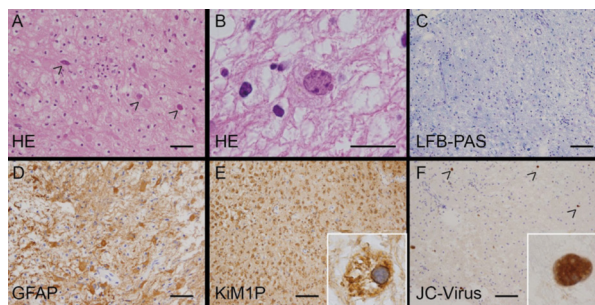


MRI T2-weighted image before biopsy



MRI coronar FLAIR image one month later

Results: Biopsy of the lesion proved demyelination with JC-virus in astrocytes and oligodendrocytes, 24,000 viral copies/ml were detected in the CSF. After withdrawal of immunosuppressants viral copies dropped to 360/ml, clinical deficits remained unchanged and MRI lesions progressed. Pembrolizumab (2mg/kg) was given, the patient died 3 weeks later.



Neuropathological findings: F: JC-virus in astrocytes and oligodendrocytes (SV40-staining)

Conclusion: Our patient suffered from a biopsy proven PML while being immunosuppressed with azathioprine for AchR-gMG. Immunosuppressants were discontinued, CSF JC-Virus copies dropped quickly and pembrolizumab was given, but he died 14 weeks after symptom onset. PML caused by azathioprine is rarely reported, though analysis from the US Adverse event reporting system calculated on reporting odds ratio of 15 for this drug. When hematological adverse events like pancytopenia occur, like in our patient, discontinuation of azathioprine seems advisable.

Disclosure: Nothing to disclose

EPO2367

Neurological manifestations of Mycetoma

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Background: Daoud Research Group, khartoom, Sudan.

Introduction: Mycetoma is a chronic specific granulomatous progressive and disfiguring subcutaneous inflammatory disease. It is caused by true fungi (Euomycetoma) or by higher bacteria (Actinomycetoma), in 2015 Mycetoma was named as one of the neglected tropical diseases by the WHO. It mainly affects lower limbs, upper limbs, back and rarely head and neck and other sites. It's mainly transmitted through trauma with infected sharp objects.

Objectives: To determine the neurological manifestations of mycetoma.

Methodology: A cross-sectional community based study.

Results: Almost 160 patients were included in the study, 90% of them were male. 2 patients presented with entrapment neuropathy, 1 presented with proximal neuropathy, 1 patient has peripheral neuropathy, 1 patient has dorsal spine involvement presented with spastic paraplegia with sensory level, 1 of our patients has cervical cord compression, and 1 patient has repeated attacks of convulsion due to tumor like mass caused by fungal infection affecting the right cerebral hemisphere.

Conclusion: Although it is rare clinicians should highly suspect neurological involvement in mycetoma patients. Mycetoma infection (with bacterial or fungal) can cause peripheral or central nervous system damage at the level of formation of papule and discharging sinuses which can lead to entrapment neuropathy, or direct destruction of the bone which can cause nerve damage or cord compression. A rare manifestation due to spread of infection from the skull to the brain causing convulsion or hemiplegia.

Disclosure: Nothing to disclose

EPO2368

Herpes simplex encephalitis in a patient treated with tofacitinib

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Background and aims: Tofacitinib is a JAK-1 and JAK-3 inhibitor used to treat rheumatoid arthritis and is known to increase the risk of herpes zoster infections but there is little known about herpes simplex infections.

Methods: We present a case where a 62-years-old patient was treated with tofacitinib due to rheumatoid arthritis and psoriasis. Previously, he has been treated with infliximab and methotrexate which were discontinued after a Hodgkin lymphoma was diagnosed. He also had a herpes virus simplex encephalitis 19 years before.

Results: The patient was admitted due disorientation symptoms preceded by fever. A lumbar puncture was performed were a slightly increase in proteins and an increase un white blood cells (mononuclear predominance) were objectivated. A PCR show positivity for HSV-1

The tofacitinib treatment were discontinued and acyclovir treatment was started (10mg/kg/8h) with a satisfactory evolution. After his discharge, he started acyclovir 200mg every 12h and the immunosuppression was changed to pimecrolimus.

Conclusion: The use of tofacitinib was related with an increase of the cutaneous herpes zoster affection and rarely with HZV encephalitis. This is thought to be related with a decrease in interferon- γ and a diminished CD4 T-cell proliferation. The HVS may be underreported due the benignity of the cutaneous affection but in patients with previous CNS infection, this drug should be used with caution.

Disclosure: Nothing to disclose

EPO2369

A case of multiple tuberculous brain abscesses with pulmonary miliary tuberculosis

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Background and aims: Tuberculous brain abscess is a rare manifestation of central nervous system tuberculosis. It resembles a pyogenic brain abscess clinically and radiologically, and poses a problem in diagnosis and treatment.

Methods: A 57-year-old male patient visited to the emergency room with fever and general weakness for four days. Physical examination showed a blood pressure of 169/98mmHg, a body temperature of 38.1°C. Chest computed tomography showed peribronchial centrilobular nodules and small consolidations with ground-glass opacities in the both upper lungs, suggestive of the possibility of active pulmonary miliary tuberculosis.

Results: The patient was initiated with a 4-drug anti-tuberculous therapy. On the 3rd day of admission, he showed drowsiness with decreased verbal responses, global aphasia, and right hemiparesis with motor grade 1 on upper extremity and grade 2 on lower extremity. Brain magnetic resonance imaging (MRI) showed multiple and variable sized round T2 high signal intensity lesions with marked diffusion restriction and rim enhancement with perilesional edema in the both cerebral hemispheres, suggestive of multiple brain abscesses. To differentiate tuberculous from pyogenic abscesses, magnetic resonance spectroscopy (MRS) was done and revealed large lipid peak around 1.3ppm, suggestive of high possibility of tuberculous abscess. Therefore, anti-tuberculous therapy was maintained, and the patient's neurological symptoms and signs were slowly improved.

Conclusion: We report a case of multiple tuberculous brain abscesses with pulmonary miliary tuberculosis. As in our case, it is possible to differentiate tuberculous from pyogenic abscesses by using MRS, which could be of value in influencing the management of such cases.

Disclosure: Nothing to disclose

EPO2370

Severe tick-borne meningoencephalomyeloradiculitis successful treatment with high dose intravenous immunoglobulin.

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Background and aims: Tick borne encephalitis is widespread viral neuroinfection with no specific therapy to date in Europe, Russia and North Asia. High dose intravenous immunoglobulins (IVIg) has not been tested systematically for treating severe cases of tick borne encephalitis. Although there are increasing number of case reports successfully treating other arboviral encephalitides with high dose IVIg, it is suspected that it may be beneficial for tick-borne encephalitis as well.

Methods: Case report

Results: We present 31-year-old male with acute onset progressive flacid tetraparesis, respiratory malfunction and bladder and bowel dysfunction. Cerebrospinal fluid (CSF) showed elevated protein and pleocytosis. Anti-TBEV IgM were positive in CSF, anti-TBEV IgG- neg. Other neuroinfections were excluded. Magnetic resonance imaging scans showed T2 weighted rhombencephalitis, longitudinal cervical and thoracic myelitis with gray matter involvement and cervical polyradiculoneuritis. Patient was further admitted to the intensive care unit with diagnosis of acute tick-borne meningoencephalomyeloradiculitis. Due to respiratory malfunction patient was put on artificial lung ventilation. On 5th day of illness patient received high dose IVIg (0.4g/kg) for 3 days. After that neurological deterioration stopped and gradually patients neurological status improved. On the 14th day of illness he was able to breathe spontaneously, started to develop movements in extremities. At the moment muscle strength in legs proximally and distally is 5/5, proximally arm muscle strength on the left side 2-3/5, on the right side 3/5, distally 4/5. He continues to receive rehabilitation.

Conclusion: Early intervention with high dose IVIg may pose a potentially successful treatment for severe tick-borne encephalitis.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases; Neuro-oncology

EPO2372

Pathogenic implication of HOX transcript antisense intergenic RNA (HOTAIR) in gliomas: a systematic review of pre-clinical and clinical evidence

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Background and aims: Gliomas present the most heterogeneous and aggressive primary tumors of the CNS with a very poor prognosis. Given the complexity of their pathogenesis, elucidation of the underlying molecular pathways and identification of diagnostic and prognostic biomarkers is important for effective personalized therapeutic strategies. HOX transcript antisense intergenic RNA (HOTAIR) is a long non-coding RNA with a pivotal pathogenic and prognostic role in several cancers, including gliomas.

Methods: A systematic literature search was performed on pre-clinical and clinical studies published in MEDLINE between 01/2000 and 11/2019, investigating the role of HOTAIR in gliomas, using the keywords “HOTAIR”, “gliomas”, “glioblastoma”, “HOX RNA” in various combinations.

Results: 32 articles were selected that demonstrate the role of HOTAIR in glioma pathogenesis, by promoting proliferation and invasiveness. HOTAIR inhibited apoptosis of glioma cells by regulating the activity of transcription factors (MXI1, E2F1, ATF5 and ASCL1), modulating the expression of cell-cycle-associated genes and related axes, such as Wnt/ β -catenin pathway, as well as by interacting with miRNAs (miR-326, miR-141, miR-148b-3p, miR-15b and miR-126-5p). HOTAIR was shown to enhance angiogenesis by upregulating VEGF expression, and affect the permeability of blood tumor barrier, altering the efficacy of chemotherapeutic agents. Clinical evidence suggests that increased serum and tissue HOTAIR levels of glioma patients have been associated with more malignant phenotype, poorer prognosis and reduced overall survival.

Conclusion: Accumulating evidence highlights the emerging pro-oncogenic role of HOTAIR in gliomas, and its potential use as a promising molecular prognostic biomarker, paving the way for future research regarding its therapeutic potential.

Disclosure: Nothing to disclose

EPO2373

Cerebrospinal fluid interleukin-10: a useful biomarker for atypical primary central nervous system lymphoma relapse.

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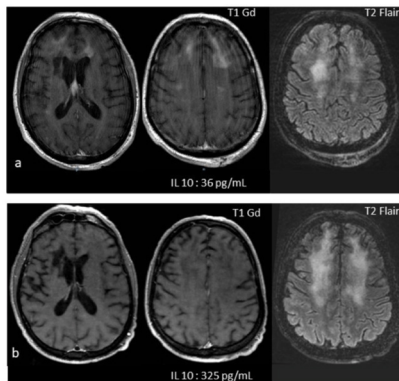
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Background and aims: Diagnosis of relapsing primary central nervous system lymphoma (PCNSL) is challenging as it may occur with atypical neuroradiological features.

Methods: We report on a 58-year-old man treated for a cerebral diffuse large B-cell lymphoma (DLBCL).

Results: After a 3rd line treatment consisting in Rituximab, Ifosfamide, Carboplatin and Etoposide was started, the neurologic status rapidly worsened with fever, epileptic seizures and coma, requiring a transfer to intensive care. Brain MRI showed a marked decrease of the enhanced lesions but an increase of bi-frontal Flair hypersignal, without diffusion hypersignal.

Blood tests revealed no metabolic, infectious or hematological disturbances. Body CT scan and spine MRI were normal. Electroencephalography showed slow activity but no sign of seizure. Results of the lumbar puncture were normal except from the cytokine assay which showed a major increase in IL10 (325pg/ml) while IL6 level remained low (14pg/ml). A brain biopsy performed in the right frontal lobe, in an area with Flair hypersignal but no contrast enhancement confirmed the progression of the lymphoma, with a typical form of DLBCL.



T1-weighted gadolinium-enhanced and T2 Flair brain MRI before (a) and after (b) Rituximab, Ifosfamide, Carboplatin and Etoposide (RICE) treatment failure, and CSF IL10 level (pg/ml).

T1-weighted gadolinium-enhanced and T2 Flair brain MRI before (a) and after (b) Rituximab, Ifosfamide, Carboplatin and Etoposide (RICE) treatment failure, and CSF IL10 level (pg/ml).

Conclusion: Interleukin-10 is well known in ocular lymphoma where its value in the aqueous humor allows the diagnosis of the disease. By analogy, certain studies have confirmed its diagnostic and prognostic capacity in PCNSL. In our case, even in the absence of clear MRI progression, the major elevation of CSF IL10 level, directed us towards the diagnosis of progression, which was confirmed by a brain biopsy. Larger studies are needed to confirm CSF IL10 level diagnostic value in atypical PCNSL relapses

Disclosure: Nothing to disclose

EPO2374

MAPK signalling pathway inhibition allows long-term tumour control in adult gliomas

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Background and aims: The aim of this study was to identify predictors of response to RAF inhibitors in adult patients with BRAF-mutant primary brain tumours.

Methods: We performed a retrospective research in 5 institutional databases for all adult patients with BRAF-mutant primary brain tumours treated with RAF/MEK inhibitors (February 2012-September 2019). The clinical data and MRI scans of patients identified through this research were collected from referring centres and centrally reviewed.

Results: 29 patients were included in the study, 15 receiving RAF inhibitors as single agents and 14 receiving a combination of RAF/MEK inhibitors. 9 patients developed treatment-related adverse events (9/21, 43%), including one grade 3 toxicity (CTCAEv5.0). Best RANO response was partial response (PR) in 13 cases (13/27, 48%), stable disease (SD) in seven (7/27, 26%) and progressive disease in seven (7/27, 26%). Patients achieving PR experienced prolonged tumour control (median response duration: 13 months) together with clinical improvement (median increase in Karnofsky Performance Status: 10 points). Median tumour shrinkage in the whole cohort, measured using RANO criteria, was -38%. Predictors of response included younger age ($p < 0.01$), ganglioglioma/pleomorphic xanthoastrocytoma histology ($p = 0.015$) and early treatment ($p = 0.018$). Median progression-free survival in the whole cohort was 5.9 months, differing based on histology ($p < 0.001$) and grade ($p = 0.0017$). 6 patients were rechallenged with different RAF/MEK inhibitors at progression, 4 of which achieved a novel long-lasting condition of tumour control.

Conclusion: Treatment with RAF/MEK inhibitors allowed long-lasting tumour control, especially in younger patients with gangliogliomas or pleomorphic astrocytomas.

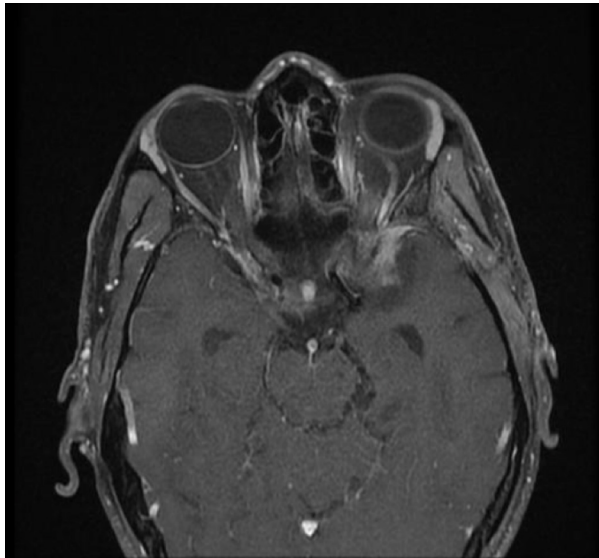
Disclosure: Nothing to disclose

EPO2375

A case report of a patient with T-lymphoblastic leukemia / lymphoma

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Background and aims: T-lymphoblastic lymphoma (T-LBL) is neoplasm of immature T-cell precursors. T-LBL that was localized only at central nervous system, represent less than 5% of cases, and did not had the subsequent evolution for a systemic usual acute lymphoblastic leukemia.



MRI of the brain- tumor in the left cavernous sinus

Methods: Somatic and neurological status, laboratory tests: flow cytometric (FCM) immunophenotyping of cerebrospinal fluid, antiphospholipid antibody, rapid plasma reagin (RPR) test, HIV-testing, computed tomography (CT) of chest and abdomen, magnetic resonance tomography of the head (MRI), lymphocytic choriomeningitis testing, trepan biopsy of bone marrow.



CT of chest

Results: We present a clinical case of a 44-year-old patient admitted to the emergency department with complaints of progressively increased headache, stiffness of the neck. The patient was admitted with meningo radicular irritation syndrome, with MRI data for tumor in the left cavernous sinus. Patient was with history for peripheral facial nerve palsy and MRI with data for extraaxial tumour formation in the same area. Biopsy was performed 3 months earlier and the histology showed partially hyalinized connective tissue. Slightly increased troponinI-marker was found in the blood tests-1761.4 and C-reactive protein 25.4, normal X-ray on thorax. Examination of cerebrospinal fluid showed lymphocytic pleocytosis. Trepan biopsy of bone marrow was without pathological changes. CT of the chest and abdomen showed mediastinal tumor, lymphadenomegaly, infiltration of the left ventricular myocardium. FCM immunophenotyping of cerebrospinal fluid gave the diagnose T-LBL. Intrathecal chemotherapy was started.



MRI of the brain

Conclusion: CNS T-LBL is a rare disease with incidence approximately 51 cases per 10,000,000 per year. Differential diagnose include different conditions like aseptic meningitis, granulomatous angiitis, neurological infections. FCM immunophenotyping of cerebrospinal fluid could help to make the right diagnose.

Disclosure: Nothing to disclose

EPO2376

Pathophysiology and mechanism of ischemic stroke in cancer patients.

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Background and aims: Numerous types of cancer are accompanied by ischemic stroke. The purpose of this study is to assess the risk factors, bio-markers of stroke and the mechanism of cerebral infarction among cancerous diseases.

Methods: 156 patients presented by acute ischemic stroke were divided into 2 groups: the 1st group included 78 ischemic stroke patients associated with different types of cancer and the 2nd group (control group) included 78 ischemic stroke patients not associated with cancer. Both groups were compared regarding the risk factors, previous thrombotic activity, sub-types and the bio-markers of stroke.

Results: Cancer patients presented by acute ischemic stroke were accompanied by a significantly less incidence of diabetes mellitus, hypertension, dyslipidemia, and coronary heart disease and atrial fibrillation than non-cancer patients ($p < 0.001$). While, levels of bio-markers of inflammation like erythrocyte sedimentation rate and C-reactive protein, and stroke bio-markers like fibrinogen, and D-dimer, all together were highly elevated in cancerous disease group of patients presented by cerebral infarction than in non-cancerous group ($p < 0.01$). The prevalence of deep vein thrombosis, pulmonary embolism, and myocardial infarction was significantly higher in patients with cancer than in control patients without cancer ($p = 0.008$, $p < 0.01$ and $p < 0.01$ respectively). The most common stroke etiologies were atherosclerosis of large arteries and stroke of undetermined cause in a cancerous group of patients.

Conclusion: Pathophysiology and mechanism of ischemic stroke in cancerous disease patients were due to different risk factors, bio-markers of stroke, and sub-types in comparison with non-cancer patients.

Disclosure: Nothing to disclose

EPO2377

Pembrolizumab-induced demyelinating cranial nerves neuropathy and neuromuscular junction disorder: a case report

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Background and aims: Introduction. Checkpoint inhibitors are widely used in the treatment of solid tumors and new classes of immune-related adverse events (IRAEs) are reported. Pembrolizumab is an anti-PD1 agent, that has been related to cases of encephalitis, neuromuscular junction disorders, and demyelinating polyradiculopathy. Here we describe a case of a patient presenting a complex neurological disorder following treatment with pembrolizumab.

Methods: Case report. A 72-year-old patient was treated with pembrolizumab for a lung adenocarcinoma (EGFR-, ALK-, PDL1 90%). After 3 administrations he presented with fatigue, ptosis, ophthalmoplegia, dysarthria, and dysphagia. MRI of the brain and spine ruled out SNC progression. Electromyography (EMG) did not display axonal or demyelinating neuropathy, nor myopathy. Patterns of myasthenia or Lambert-Eaton disease were not seen in repetitive nerve stimulation, even if increased jitter was registered in frontal muscle in single-fibre EMG. The concomitant evidence of an altered Blink reflex was helpful in suggesting a demyelinating neuropathy (DN) of cranial nerves. A drug-related neuroimmunological disorder was suspected, pembrolizumab was stopped and patient underwent 2 subsequent cycles of intravenous immunoglobulins, with a slow improvement of ocular motion, dysarthria and partial normalization of Blink reflex. The patient finally died after 8 months for an aggressive local tumor progression.

Results: Discussion. IRAEs from anti-PD1 agents are very rare conditions. Thus far, only 1 case of DN following pembrolizumab was described, but this is the 1st report responding to IVIg.

Conclusion: Conclusion. Neurological IRAEs are insidious conditions, requiring a prompt diagnosis to avoid any delay of treatment which could modify the course of disease.

Disclosure: Nothing to disclose

EPO2378

Paraneoplastic Neurological Syndrome with unidentified onconeural antibodies

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Background and aims: The definition of Paraneoplastic Neurological Syndrome (PNS) is based on the combination between existence of cancer, “classic” PNS and “well characterized” onconeural antibodies. However, in recent years new antibodies have been described that are not included in the most available panels. On the other hand, other antibodies remain to be characterized.

Methods: We describe 2 case reports of PNS with unidentified antibodies.

Results: An 83-year-old man with Merkel cell carcinoma treated with pembrolizumab in the past developed subacute cerebellar degeneration. The restaging revealed cancer relapse. A 60-year-old man with inguinal melanoma who underwent surgery and focal radiotherapy developed paraparesis and sensitive ataxia. The MRI showed longitudinal myelitis with lateral columns predominance. In both cases, it was possible to identify by indirect immunofluorescence assay (IFA) a positive staining of granular and molecular layer of rat cerebellum. The subsequent analysis with immunoblot (anti-Hu, Yo, Ri, CV2, amphiphysin, PNMA2/Ma2/Ta, recoverin, SOX1, titin, Zic4, GAD65, Tr/DNER) and transfected cells (anti-CASPR2, LGI1, NMDA receptors, AMPA1, AMPA2, GABAB) were negative. Further analyses made by an outside laboratory complemented the study with anti-AQ4, MOG, IgLON5 and DPPX which were negative. The antigens CARPVIII, rGlycine, mGluR1, mGluR5, rGABA-A, GLURD2, flotillin, RhoGTPase activating protein 26, ITPR1, Hommer 3 and neurochondrine were also investigated, all negative.

Conclusion: In both cases, a definitive PNS diagnosis could be established without a positive onconeural antibody finding. However, there were positive IFA staining pattern which were not followed by positive line blot typing assay. These could mean that some antibodies are still waiting to be discovered.

Disclosure: Nothing to disclose

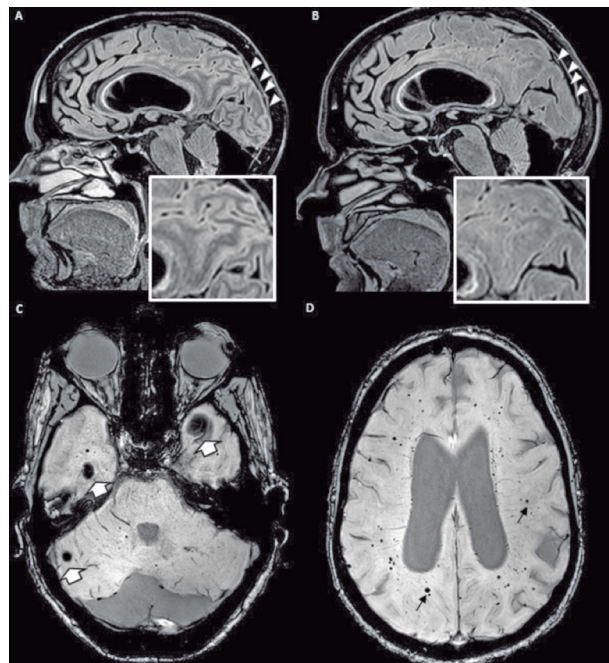
EPO2379

Challenging diagnosis of SMART syndrome with non-enhancing cortical lesion

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Background and aims: SMART syndrome often presents as a diagnostic challenge since no established criteria are available and clinical presentation may be quite varied.

Methods: A 49-year-old male with a remote history of medulloblastoma (29 years old), treated with surgical resection followed by chemotherapy and radiation therapy, presented to the emergency department because of a 3 days history of sudden onset of homonymous left hemianopia, confusion, significant postural instability and refractory migraine. Prior to this presentation he had rare episodes of migraine. At neurological examination he was disoriented with left homonymous hemianopia. The fundoscopic examination was also unremarkable. Brain CT scan showed multiple scattered calcifications in occipital and cerebellar lobe. Detailed haemato-immunological screenings and CSF examination was unremarkable. Electroencephalogram disclosed slowing activity in right hemisphere, but not epileptiform activity was detected. A brain MRI performed on day 3 showed gyriform cortical T2 hyperintensity with a correspondent T2 shine-through effect on DWI in the right parietal-occipital region (Figure 1 A). No cortical gadolinium enhancement was detected. Post-surgical changes were seen in the posterior cranial fossa. Several foci of reduced signal intensity were visible in SWI sequences, in line with radiation induced cavernous haemangiomas/cavernomas (Figure 1-C,D). A follow-up brain MRI performed 3 months (1B) later and EEG showed reversal of the previous abnormalities.



Results: SWI-sequence has a key-role in detecting radiation induced cavernous haemangiomas/cavernomas, highly suggestive of SMARTs, especially when other neuroradiological clues are lacking or unrevealing.

Conclusion: This case emphasizes the importance of performing a complete MRI-protocol in order to make a more rapid diagnosis, avoiding unnecessary procedures.

Disclosure: Nothing to disclose

EPO2380

Benign and malignant paragangliomas: clinical presentation and treatment outcomes in 38 patient

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Background and aims: Paragangliomas are tumors from cells of the neuroendocrine system. The incidence of paragangliomas is difficult to assess because of their rarity and complexity of diagnostics due to scarce symptoms. We aimed to study the clinic, the diagnostic methods, surgical risk and treatment outcomes among patients with paragangliomas.

Methods: Retrospective review of patients. The study included 38 patients with a diagnosis of paraganglioma treated in the Sverdlovsk Regional Oncology Center. Research was conducted epidemiological parameters, clinical presentation, tumor classification, Karnowski Index; classification of glomus tumors by U.Fisch and D. Mattox.

Results: More often paragangliomas was observed among women (76.3%). Malignant paraganglioma was rare tumor (7.9%). Most paragangliomas were localized (92.1%) in brachiocephalic area. Jugular, tympanic, yugulotympanic paragangliomas is characterized disacusia and dysphonia. Carotid paragangliomas was characterized a visible tumor formation or absence of clinic. The external carotid artery, especially the ascending pharyngeal artery is more often involved tumor's perfusion. The tumors of group C and D to the classification of U.Fisch and D.Mattox are prevailed. Interventional methods and surgical removal of the tumor were used. Embolization was complicated by the development of facial paresis and ischemic stroke in the basilar artery circulation. After open surgical removal, 31.3% patients have some complications: hypesthesia of trigeminal nerve, facial paresis, dysphonia, etc. 3-year patient survival was 96.7%.

Conclusion: The clinical symptoms of paragangliomas are variable and depended on localization. The main treatment for paragangliomas is the methods of microvascular and open surgery, which were successfully transferred by most patients.

Disclosure: Nothing to disclose

EPO2381

Optochiasmatic glioma - a rare, yet aggressive disease in adulthood

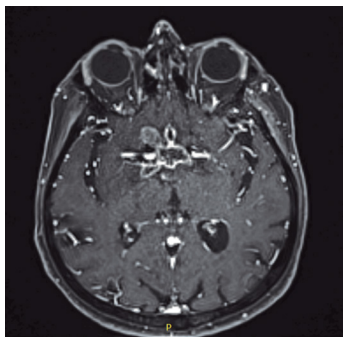
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Background and aims: Optic pathway glioma (OPG) is a type of tumor that occurs more frequently in children, having a favourable course and is often associated with neurofibromatosis type 1 (NF1). In the rare cases when OPG occurs in adulthood, the progression is aggressive, without an association with NF-1.

Methods: We report a clinical case of an optochiasmatic glioma in a 78-year-old female.

Results: The patient reported progressive vision loss in the right eye and temporal visual field loss in the left eye over 1 month. Brain MRI revealed the enlargement of the intracranial portion of the optic nerve, chiasm and right optic tract, with involvement of the hypothalamus. The lesion was described as T1 isointense, T2 and FLAIR hyperintense, with peripheral gadolinium enhancement, suggesting either an aggressive tumor with central necrosis or a granulomatous process. Extensive serum tests including quantiferon tuberculosis test, antinuclear antibodies panel, rapid plasma reagin, HIV, Toxoplasma, Borrelia, cANCA, pANCA antibodies, angiotensin converting enzyme were normal. Lumbar puncture was performed and the cerebrospinal fluid (CSF) tests including cytology, microbiological examination, angiotensin converting enzyme, VDRL, oligoclonal bands, Mycobacterium tuberculosis PCR were normal. Chiasmatic biopsy was performed and the histopathologic examination revealed a low-grade astrocytoma. The patient was referred to an oncology department for evaluation and oncologic treatment.



Axial T1 C+ (Gd): Optochiasmatic tumor with peripheral gadolinium enhancement

Conclusion: Although very rare in adults, OPG should not be missed in the differential diagnosis of progressive loss of vision accompanied by a chiasmatic lesion.

Disclosure: Nothing to disclose

EPO2382

The anxiety characteristics of newly diagnosed glioblastoma patients: preliminary results from the IMAGE study.

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Background and aims: Few studies have focused on the anxiety level (Bunevicius et al., 2017; Kilbride et al., 2007). Underestimating anxiety may have several consequences: a low treatment compliance, exacerbation of somatic symptoms or side effects of treatment, difficulties with understanding medical information and lower cooperation with the medical staff (Spencer, 2010). In the present study, we aimed assessing the characteristics of anxiety in a cohort of newly diagnosed glioblastoma patients.

Methods: At the beginning of their cycle of temozolomide cure and after radio-chemotherapy, 50 patients with glioblastoma were included. Inclusion criteria were: Karnofsky index (IK) $\geq 70\%$ and absence of cognitive disorder that could interfere with the completion of questionnaires. The characteristics of patients were as follows: mean age of 56.6 years ± 12.5 (70% were more than 50 years old); 20% were women. Anxiety level was assessed using the State-Trait Anxiety Inventory.

Results: The preliminary results showed that – at baseline – 21% of our sample reported high levels of anxiety. Correlation analyses showed that state anxiety was correlated with trait anxiety ($\rho=0.799$, $p<0.001$), quality of life (QoL) ($\rho=0.678$, $p<0.001$) and memory complains ($\rho=0.618$, $p<0.001$). Women had higher state anxiety scores than men ($t(27)=-2.4$, $p=0.02$). Any correlation was found with age, education level, lesional lateralization or depressive symptoms.

Conclusion: These preliminary results suggest that after radio-chemotherapy, few patients have a high level of anxiety. Moreover, the level of anxiety does not seem to be predictable by a specific factor, including the presence of depressive symptoms, age or education level.

Disclosure: Nothing to disclose

EPO2383

Wernicke's Encephalopathy Secondary to Malnutrition in Inflammatory Bowel Disease

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Background and aims: Wernicke's encephalopathy is an acute condition that requires urgent recognition and treatment to prevent neurological complications. Usually associated with thiamine deficiency due to chronic alcoholism, it can also appear in other cases of poor dietary intake, malabsorption, increased metabolic requirement or increased loss of thiamine in renal dialysis.

Methods: We present the case of a 26-year-old, non-alcoholic patient, diagnosed 1 year earlier with gastrointestinal inflammatory disease and pernicious anemia (under treatment), admitted to the neurology ward because of acute onset of walking disorder, nausea and vomiting. The patient presented intermittent confusion, ophthalmoparesis, horizontal nystagmus in both directions of gaze, appendicular and truncal ataxia.

Results: Laboratory tests revealed anemia and hypoproteinemia. Inflammatory tests were normal. Magnetic resonance imaging study of the brain revealed medial bythalamic lesions with petechial contrast enhancement, specific to Wernicke's encephalopathy. After intravenous nutrition (amino acids, electrolytes, dextrose and lipid injectable emulsion) with thiamine, cobalamine and pyridoxine supplements, the clinical status improved rapidly. We were able to dose the vitamins levels after 3 days of treatment and the results were in low normal range. Intrinsic factor, anti parietal cell and anti-gliadin antibodies were negative. Hystopathologic results from the gastrointestinal tract revealed chronic non-specific inflammation.

Conclusion: Wernicke's encephalopathy is a curable complication of inflammatory bowel disease if the treatment is started in early phases. Pregnancy and breastfeeding can increase the risk of thiamine deficiency in patients with history of malabsorption.

Disclosure: Nothing to disclose

EPO2384

The Third Side To A Coin: Hypophosphatemia Induced Myopathy

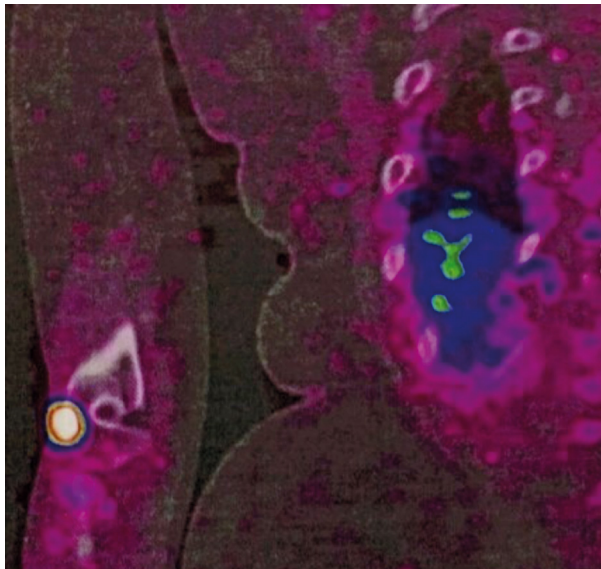
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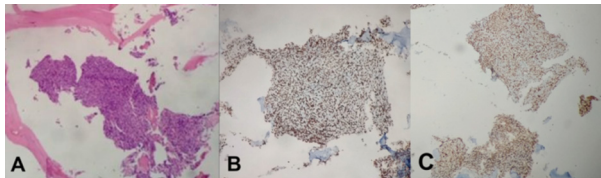
Background and aims: Endocrine myopathies represent a heterogenous group of disorders, which if identified early, are potentially treatable. When a patient presents with features suggestive of an endocrine myopathy the focus is usually on disorders of calcium homeostasis, including vitamin D deficiency and parathyroid imbalances, thyroid disorders or adrenal syndromes. We present this case to highlight, that disorders of phosphorus metabolism also present with a similar depiction, and can be easily overlooked.

Methods: We describe a 29-year-old female with diffuse myalgia, joint tenderness associated with insidious onset gradually progressive symmetrical proximal predominant weakness of lower limbs followed by upper limbs, with no wasting, spasticity, fasciculations, without higher mental, cranial nerve, sensory, or cerebellar involvement. Examination confirmed the proximal predominant weakness with reflexes being exaggerated and flexor plantar.

Results: Laboratorial evaluation revealed isolated hypophosphatemia with normal levels of calcium, parathyroid, and vitamin D. After endocrine consult, 24 hour urine phosphorus values done were found to be high. Simultaneous evaluation for presence of phosphatonins and tumour was initiated. FGF 23 levels were found to be elevated, with Dotanoc Galium Pet CT showing an FDG avid tumour in the lateral epicondyle of the right humerus. Histopathology confirmed SATB2, FL1 and vimentin positive phosphaturic tumour. Post excision and supplementation with phosphorus the patient improved significantly.



Dotanoc gallium PET CT showing tumour in the right lateral epicondyle.



A. Section shows bony trabeculae enclosing spindle cell lesion composed of bland looking spindled cells arranged in fascicles. B. Section shows tumour cells positive for SATB2. C. Section shows tumour cells positive for FL1.

Conclusion: The case describes a young woman presenting with diffuse myalgia and gradually progressive proximal predominant weakness of all four limbs who eventually was diagnosed to have tumour induced hypophosphatemia. After management her symptoms improved, highlighting the necessity to be cognizant about this amendable cause.

Disclosure: Nothing to disclose

EPO2385

Subacute myelopathy with axonal neuropathy: think about Acquired Copper Deficiency

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Background and aims: Acquired copper deficiency (ACD) is a rare condition usually seen after bariatric surgery. In addition to hematological disorders, patients with ACD can present central and peripheral neurological impairments.

The aim of our study is to describe the clinical, MRI and electrophysiological characteristics of neuromyelopathy due to ACD.

Methods: We assessed retrospectively the clinical, biological, spinal MRI and electrophysiological data of patients presenting in our patient with signs and symptoms of myelopathy associated with peripheral neuropathy with low plasmatic copper level.

Results: 2 female patients (age: 56 and 70 years old) with no medical history were included. Both patients presented for progressive paraparesis evolving for 3 and 6 months associated with urinary dysfunction. Examination showed proximal and distal muscular weakness in lower limbs, deep sensory impairment, Babinski sign, and absent ankle jerk. Spinal MRI revealed extensive cervicothoracic myelitis with no gadolinium enhancement. Nerve conduction studies showed an axonal sensory-motor neuropathy. Etiological assessment including CSF analysis, viral and bacterial serologies, vitamin B12 level and immunological tests was negative in both cases. Trial treatment with corticosteroids and vitamin B12 supplementation did not improve the symptoms. Subsequently, serum copper level revealed a plasmatic copper deficiency (Copper levels were 0.24 and 0.40 µg/mL respectively, normal range higher than 0.8 µg/mL). Copper supplementation and physiotherapy led to a clinical and radiological improvement in one patient and to symptom stabilization in the other.

Conclusion: ACD is a rare metabolic disorder mimicking Biermer disease. Physicians should remind this diagnosis facing an atypical myelitis associated with peripheral neuropathy since early copper supplementation could improve the prognosis.

Disclosure: Nothing to disclose

EPO2386

CNS Immunoglobulin G4-related disease: more than hypertrophic meningitis

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Background and aims: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated, fibro-inflammatory systemic condition that can affect a wide variety of organs mimicking a large number of disorders. The CNS involvement is characterized by hypertrophic pachymeningitis, with rare cases of leptomeningitis being described.

Methods: We report a case of leptomeningitis due to IgG4-RD.

Results: A 67-year-old woman, with past-medical history of pericardial effusion and chronic kidney disease.

1 month before hospital admission, she developed involuntary movements of the left lower limb that appeared only with sustained postures. 2 weeks later she noticed similar movements on left upper limb. Patient examination disclosed tremor and myoclonus of left limbs, both arising in posture, action and orthostatic positioning and disappearing at rest. The back-averaged EEG showed no epileptiform activity. However a levetiracetam trial led to complete cessation of movements. Brain-MRI showed dural and leptomeningeal gadolinium enhancement in the right high convexity. CSF revealed lymphocytic pleocytosis (64cel/mm³). Blood tests showed CPR and ESR elevation, p-ANCA, c-ANCA and IgG4 elevated titers. Thoracic-abdomen-pelvic-CT and PET/CT documented proximal aortitis and pericardial effusion. Meningeal biopsy confirmed aspects of IgG4-RD: circumferential fibrosis and IgG4 lymphoplasmacytic infiltration with IgG4/IgG ratio of 49%. She was treated with corticoids, azathioprine and later rituximab, with laboratory and imaging improvement.

Conclusion: The phenotype of IgG4-RD has been broadening. A neurological presentation including leptomeningitis is highlighted and may represent a different form of IgG4-RD. We emphasize the importance of considering the disease on differential diagnosis of unclear leptomeningeal disease.

Disclosure: Nothing to disclose

EPO2387

Recurrent posterior reversible encephalopathy syndrome in focal segmental glomerulosclerosis caused by NPHS2 mutations

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is a clinical-radiological entity with yet unclear pathophysiological mechanisms. We aim to describe the occurrence of relapsing PRES in a patient with focal segmental glomerulosclerosis associated with NPHS2 mutations.

Methods: Descriptive analysis of clinical, laboratory, imaging and genetic data.

Results: A 20-year-old woman was admitted with new-onset seizures and decreased consciousness. She had a 13-year history of chronic renal disease, presenting as corticoreistant nephrotic syndrome caused by 2 heterozygous variants in NPHS2 gene. At admission, she was under no immunosuppression and was considering options for renal replacement therapy. CT revealed bilateral parietal and right occipital, diencephalic and striatocapsular vasogenic oedema. Emergency dialysis and blood pressure control were initiated. Due to condition severity, steroids were added. There was gradual improvement. 4 weeks later, after a blood pressure fluctuation, a recurrence of PRES was seen, with clinical-radiological worsening. Again, with antihypertensive therapy and a short course of steroids, the patient improved. 9 months later, she was readmitted for uncontrolled blood pressure, headache and nausea. CT showed marked posterior fossa oedema with acute hydrocephalus. Aggressive blood pressure control resulted in symptomatic improvement and resolution of imaging findings. She is currently on peritoneal dialysis awaiting renal transplantation.

Conclusion: Recurrent PRES is a rare recognized complication of end-stage renal disease. To our knowledge, there are no reported cases of PRES in patients with NPHS2 mutations. We speculate whether genetically determined vascular changes contribute to disrupted blood-brain barrier function and increased susceptibility to recurrent PRES in this patient.

Disclosure: Nothing to disclose

EPO2388

Longitudinal Extensive Transverse myelopathy as a very rare presentation of Mixed Connective Tissue Disease: a case report

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Background and aims: Mixed Connective Tissue Disease (MCTD) is an autoimmune systemic disease characterised by positivity of anti-U1 ribonucleoprotein (RNP) antibodies and mixed clinical features typical of other rheumatological diseases (to which it owes its name). In some rare cases, neurological manifestations are described.

Methods: A 80 years old man came to our attention for a story of low-back pain and subacute progressive lower limb numbness (D10 level) with moderate weakness resulting in a severe ataxia. Bisphinteric retention completed the clinical picture. Spinal Cord MRI showed an extensive lesion from D9 to the medullary cone Gadolinium enhanced and DWI negative. CSF analysis revealed high level of proteins, 10 leucocytes/uL and oligoclonal band synthesis, PCR for neurotropic micro-organisms was negative. Serological differential diagnostic work-up led to the finding of a fine-speckled ANA positivity and high-titer anti-RNP positivity. MCTD diagnosis was made and IVIG treatment was administered, with weakness and numbness improvement. The patient is now undergoing rehabilitation.

Results: Myelopathy in MCTD is very rare and, for its features, can be confused with similar neurological entities. Anyway, finding a high titre of RNP when other ANA specificities are absent is highly predictive of MCTD, even though the full range of clinical involvement is not apparent that time.

Conclusion: Spinal cord involvement in MCTD is a challenging diagnosis due to its rarity, so an active case signaling of this entity has to be pursued, to improve our ability to promptly recognize and treat these patients. To our best knowledge this is the first case described of MCTD with myelopathy as presenting feature.

Disclosure: Nothing to disclose

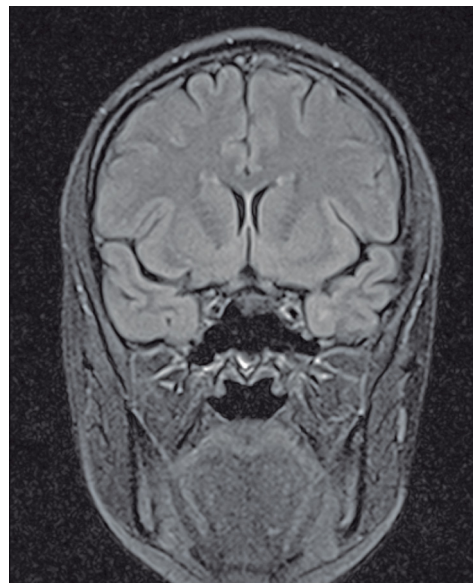
EPO2389

Severe neurology symptoms after desmopressin administration

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Background and aims: Desmopressin is a synthetic analog of vasopressin. It is mainly used in diabetes insipidus, patient with coagulation problems - for e.g. thrombocyte dysfunction, von Willebrand disease. - and in nocturnal enuresis. In coagulation problems, desmopressin usually used only before an operation. Desmopressin is known to reduce free water elimination and produce hyponatraemia, but its extent and rate of development in these patients were surprising.

Methods: We present 2 patients - a pregnant woman with von Willebrand disease and another young woman with thrombocyte dysfunction - who, both used the medication only occasionally and developed severe neurological symptoms - generalized tonic-clonic seizure and cerebral oedema - and serious hyponatraemia over 24 hours of use of desmopressin.



Diffuse cerebral oedema

Results: We will compare the 2 cases in a timeline, to highlight the differential diagnosis algorithm, the similarities and the differences; to show the course of the disease, the management and the result.

Conclusion: Since the „dramatic” symptoms of the hyponatraemia are mainly neurological the 1st consultant at ER is usually a neurologist.

These cases show that how important to be aware of the medications side effects, mainly if it is not an „everyday” drug and complications manifested several hours after the administration.

Disclosure: Nothing to disclose

Neurorehabilitation 1

EPO2390

The use of transcutaneous electroneurostimulation in the treatment of children with enuresis.

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Background and aims: To study the effectiveness of various TENS modalities in the treatment of primary monosymptomatic nocturnal enuresis (PMNE) in children.

Methods: We observed 20 children aged 10 to 13 years old with a diagnosis of PMNE. The 1st group (10 children) underwent a course of high-frequency low-amplitude TENS (HL TENS) of the tibial nerves in tarsal canal using a current with a frequency of 100Hz, a duration of 100 μ s and an amplitude reaching a comfortable sensory response. The 2nd group (10 children) underwent a course of low-frequency high-amplitude TENS (LH TENS) of the tibial nerves in tarsal canal using a current with a frequency of 1Hz, a duration of 200 μ s and an amplitude reaching a comfortable motor response.

Results: Before treatment, the frequency of wet nights per week in 2 groups averaged 4.7 \pm 1.4. After treatment frequency of wet nights decreased in the 1st group to 3.5 \pm 1.6 and in the 2nd group, to 1.4 \pm 1.1. A decrease in theta index was observed on the EEG activity in 2nd group, on average, by 39% with the absence of significant changes in 1st group. A full recovery was noted only after a LH TENS in 2 patients.

Conclusion: Direct TENS of tibial nerve is effective in the treatment of PMNE in children. A more significant effect was found after applying a direct LH TENS, which was 1.7 times more effective than after using a HL TENS.

Disclosure: Nothing to disclose

EPO2391

Efficiency of transcutaneous electroneurostimulation in treatment of patients with Anxiety Disorders

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Background and aims: To study the dynamics of anxiety disorders with the use of a direct transcutaneous electroneurostimulation

Methods: 35 patients with autonomic dystonia syndrome accompanied by anxiety disorders were examined. In all patients ranges of Generalized Anxiety Disorder Scale-7 (GAD-7) were higher than 10 scores and averaged 16 \pm 0.5 scores. Quality of life were investigated by SF-36 questionnaire 12 patients underwent low-frequency high-amplitude direct transcutaneous electroneurostimulation (LH TENS) of the right median nerve 11 patients have been treated by high-frequency low-amplitude direct transcutaneous electroneurostimulation (LH TENS) of the right median nerve 12 patients received a course of LH TENS of the right tibial nerve.

Results: The decrease in the severity of anxiety disorders was most of all after LH TENS of the median nerve and averaged 45 \pm 3%, in second place - after LH TENS of the tibial nerve and averaged 28 \pm 5% and least of all after HL TENS of the median nerve (14 \pm 6%). There was also an improvement in the quality of life identified using SF-36 by 35% in patients after LH TENS of the median nerve, by 20% in patients after LH TENS of the tibial nerve and by 11% in patients after HL TENS of the median nerve.

Conclusion: Direct LH TENS is more effective than direct HL TENS in the treatment of patients with anxiety disorders. Stimulation of the median nerve was found to be more effective than stimulation of the tibial nerve by 66% in decreasing anxiety disorders and by 75% in improving quality of life.

Disclosure: Nothing to disclose

EPO2392

Improvement of bioelectrical activity of the brain with the use of direct transcutaneous electroneurostimulation of the right median nerve.

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Background and aims: To study the dynamics of bioelectric activity of the brain in patients with Insomnia after treatment by direct transcutaneous electroneurostimulation (TENS) of the right median nerve.

Methods: 19 patients with insomnia accompanied by increased slow EEG activity were studied. Patients were between 20 and 40 years old. All patients showed signs of an increased theta activity index in the posterior and parietal regions. Registration was carried out using ipsilateral ear referential montage. The theta activity index exceeded 25% and averaged 38%. All patients underwent direct transcutaneous electroneurostimulation of the right median nerve (TENS). 10 patients were managed by Low-frequency High-amplitude TENS (1Hz, 200mcs, 15mA). 9 patients underwent a course of high-frequency low-amplitude TENS (100Hz, 100mcs, 5mA).

Results: Theta activity index decreased in patients who underwent a course of low-frequency high-amplitude TENS by an average of 39%. In patients after high-frequency low-amplitude TENS, indicators of slow activity did not significantly change. A decrease in the severity of paroxysms of slow activity was also noted against the background of low-frequency and high-amplitude TENS with the absence of such dynamics after the application of high-frequency low-amplitude TENS.

Conclusion: The low-frequency high-amplitude TENS, in contrast to the high-frequency low-amplitude TENS, can improve the EEG indices in patients with insomnia. This improvement is manifested by a significant decrease in the index of theta activity in the posterior and parietal regions and a decrease in the severity of paroxysmal activity of the theta rhythm.

Disclosure: Nothing to disclose

EPO2393

Visuospatial therapy of a child with stroke: case report

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Background and aims: It is known that stroke has a devastating power for the future of child. The aim of this study was to describe the visuospatial therapy findings of a child with hemorrhagic stroke in the right fronto-parieto-temporal area, showing the progress after 8 months of therapy initiated early after acquired neurological injury.

Methods: Boy of 8 years suffered a sudden illness and was referred to the emergency hospital and diagnosed with hemorrhagic stroke in the right fronto-parieto-temporal area. Surgical procedures were performed. At the time of hospital discharge, there was guidance about the need for therapy care. Neuropsychological assessment revealed the severe deficit in visuospatial abilities in this child.

Results: A total of 62 visuospatial therapy sessions lasting 50 minutes were performed for 8 months. This therapy trains the child to do different visuospatial exercises both on motor and cognitive level. This training is built on the conceptual framework derived from the work of Luria's theory of restoration of neurocognitive functions (Luria, 1963, 1974). Neuropsychological assessment of child has revealed apparent progress in performance of 4 subtests which are designed to assess visuospatial abilities (copying of a table, mental rotation task, Head subtest, reconstruction of 3-dimensional designs).

Conclusion: According to result of this case report it can be assumed that visuospatial therapy can be used as a prospective treatment approach for children with stroke in the right fronto-parieto-temporal area.

Disclosure: Nothing to disclose

EPO2394

Botulinum Toxin Treatment for Cervical Dystonia – A Nation's PerspectiveS. Azzopardi¹, T. Dalli², D. Cauchi³, M. Mallia¹¹Department of Neuroscience, Mater Dei Hospital, Msida, Malta, ²Mater Dei Hospital, Msida, Malta, ³Outpatients Physiotherapy Department, Karen Grech Rehabilitation Hospital, Pieta, Malta**Background and aims:** The aim of this study was to analyse the cohort of cervical dystonia (CD) patients at the Maltese Botulinum Toxin (BoNT) Treatment Clinic.**Methods:** All CD patients being actively followed-up were included. Demographic data including treatment frequency, toxin formulation, dose administered and time interval between visits were recorded using the local database and medical records. The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) score was obtained prior to, and six weeks after treatment. Qualitative data regarding patients' expectations prior to treatment initiation and impact on quality of life (QoL) was gathered via questionnaire.**Results:** 16 patients (female=12, male=4) were treated. BoNTA was used in all patients; with a mean dose of 100U at an average of 4-monthly intervals. There was a statistically significant improvement in TWSTRS scores at 6 weeks, with the most significant change occurring in pain scores. Most patients entered treatment aiming to relieve pain. 66% reported a major impact of CD on their QoL, with BoNT having a moderately positive impact. However, 19% noted a decrease in efficacy of treatment over time. 31.3% made use of additional oral medications. All patients were referred for physiotherapy, with 58% complying with prescribed exercises. 25% were referred for assessment for deep brain stimulation. 19% were discharged due to clinical improvement.**Conclusion:** CD has a marked effect on QoL. BoNT is the treatment of choice; its efficacy is however neither sufficient nor enduring for a number of patients. Our data suggests it has a greater impact on pain control rather than functional ability.**Disclosure:** Nothing to disclose

EPO2395

An Efficiency Of The Electrophoresis With Mumiyo In The Complex Treatment Of Patients With Osteochondrosis Of The Cervical SpineB. Bakhriev, Y. Madjidova, M. Baxramov
Tashkent, Uzbekistan**Study aim:** To study effectiveness of mumiyo in patients with pain syndromes of osteochondrosis of the cervical spine.**Material:** We analyzed the treatment in 52 patients (male-23, female-29), treated in the neurological and physiotherapeutic departments with lesions of peripheral nervous system, including with cervical osteochondrosis: primary -22 and secondary – 30 (with plexitis – 69.2%, with brachial nerve neuritis – 31.8%). The age of patients from 26 to 60 years old; To evaluate all indicators, we used: visual analogue scale (VAS), neck disability index (NDI). The VAS was used to measure the degree of pain on a scale of 0 to 10 points. The NDI is a 6-point scale (0, 1, 2, 3, 4, 5), with a score of 0 indicating no pain or disability and 5 indicating insufferable pain or complete disability.**Results:** Patients with acute pain syndrome (plexalgia, pain in the cervical spine) were prescribed mumiyo electrophoresis from the 1st day of admission. From 4-5 days of admission to the treatment complex, additional physical therapy and massage were prescribed. According to the results of the VAS scale, pain after treatment decreased from 4.95±1.55 to 2.28±1.37 score. Agree to the results of the NDI scores declined from 12.50±4.55 to 7.10±4.18.**Conclusion:** Thus, analysis of the material showed that differentiated complex treatment of patients with lesions of the peripheral nervous system using mumiyo electrophoresis, massage and exercise therapy gives good results, which allows them to be widely used in the rehabilitation of these patients.**Disclosure:** Nothing to disclose

EPO2396

EFFICIENCY OF EXARTA KINESIOTHERAPEUTIC TECHNOLOGY IN PATIENTS WITH OSTEOCHONDROSIS OF THE Lumbar spine

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Study aim: To study the effectiveness of the Exarta kinesiotherapeutic technology (EKT) in the treatment of patients with pain syndromes of osteochondrosis of the lumbar spine.

Material: We studied 30 patients with back pain (male-11; female-19), aged 28 to 56 years, in 2 groups: the main group "A" - 15 (male-5; female-10) who took medication with EKT; control group "B" - 15 (male-6; female-9) patients who received only drug therapy (DT).

Results: As a result of studies, it was found that the joint use of DT with EKT is more effective in the treatment of osteochondrosis of the lumbar spine. According to the results of the VAS scale, pain after DT and EKT decreased to 2 ± 1.42 points, in the control group to 3 ± 1.09 points. The Mann-Whitney U test (Uac) is 62.5. The critical value of the Mann-Whitney U-criterion (Ucr) for a given number of compared groups ($n_1=15$; $n_2=15$) is 64. $Uac \leq Ucr$ 64, therefore, differences in the level of trait in the compared groups are statistically significant $p < 0.05$.

SABS results in the main group are 6 ± 1.38 points; in the control group, 5 ± 1.49 points. The Mann-Whitney U-test is $Uac \leq Ucr$ 64 ($p < 0.05$).

Conclusion: The obtained data show that usage of EKT with DT leads to a significant reduction of pain and improved function in short time compared to classical therapy without usage of EKT.

Disclosure: Nothing to disclose

EPO2397

Low-frequency Transcranial Magnetic Stimulation; a Potential Therapeutic Tool in the Treatment of Autism Spectrum disorders

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Background and aims: Autism Spectrum disorders are a group of early-onset neurodevelopmental pervasive disorders defined by a core triad of symptoms: qualitative abnormalities in reciprocal social interaction, communication and restricted, repetitive and stereotyped behaviours. Affecting 1% of the population and accounting for 58 disability-adjusted life-years (DALYs) per 100,000 population, autism causes a significant burden to health and social services. The heterogeneous nature of autism has impeded effective targeting. The prefrontal cortex (PFC), pivotal in socio-emotional processing, is thus proposed as a target, to modulate implicated regional dysfunction in connectivity and excitability. Repetitive transcranial magnetic stimulation (rTMS) is an emerging tool in psychopathology. Data suggests low-frequency stimulation-induced inhibition of the PFC could mediate the elevated excitation/inhibition imbalance. Consequent interneuron attenuation causes functional reorganisation of the PFC, resulting in core symptom alleviation. The aims of the report are to establish the evidence behind rTMS to design an effective proposal to further establish the therapeutic benefits of rTMS in autism.

Methods: A literature review was conducted using search terms: 'rTMS', 'ASD', 'Autism', 'LFS' and 'PFC'. PubMed, google scholar and Omid were used to identify appropriate data.

Results: Data suggests low-frequency stimulation-induced inhibition of the PFC could mediate the elevated excitation/inhibition imbalance. Consequent interneuron attenuation causes functional reorganisation of the PFC, resulting in core symptom alleviation.

Conclusion: Although available TMS studies in autism are preliminary, they provide promising evidence for therapeutic benefit including reductions in repetitive behaviours, attentional-processing and Event-Related Potential (ERP) normalisation.

Disclosure: Nothing to disclose

EPO2398

Effects of electrothermophototherapy on spasticity in pediatric patients with neuromotor dysfunction

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Centro Universitário Filadélfia, Londrina, Brazil

Background and aims: Spasticity is a motor disorder characterized by velocity-dependent increase in muscle tone associated with exacerbation of the myotactic reflex. Cryotherapy and thermotherapy provide an effective, practical means to reduce spasticity of muscles resulting from a central nervous system dysfunction. This study aims to analyze the effects of cryotherapy and thermotherapy on spasticity.

Methods: Cross-sectional study with intentional sampling consisting of 20 pediatric patients with spasticity of Instituto Londrinense de Educação para Crianças Excepcionais (ILECE/Centro – Londrina/PR). It was evaluated the passive amplitude of motion (goniometry) and the level of spasticity by the Modified Ashworth Scale, before and after the physiotherapeutic intervention in muscles with spasticity. The physiotherapeutic treatment (cryotherapy/30min; UST) was managed in 15 sessions during 5 weeks, lasting 50 minutes each session. The ice pack (cryotherapy) was applied to the muscle belly to be treated, with a duration of 30 minutes at 15°C, and in the same session, continuous therapeutic ultrasound (Sonopulse, IBRAMED – Brazil) was applied with a frequency of 1MHz and intensity of 0,5w/cm² in the tendon of the analyzed muscle. The temperature of the thermal agents before, during and after the physiotherapeutic intervention was constantly monitored by the infrared thermometer. The Spearman correlation was used for the analysis of the non-parametric variables and the Pearson correlation for the parametric variables.

Results: The results found indicates increased muscle flexibility and reduced the degree of spasticity.

Conclusion: This study was effective in decreasing muscle spasticity with consequent improvement in the amplitude of joint movement.

Disclosure: Nothing to disclose

EPO2399

Probiotics and aerobic physical activity improve symptoms of MetS, muscle and nerves structure and posture in overweight patients.R. Bubnov¹, L. Kalika², M. Spivak³

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Background and aims: Metabolic syndrome (MetS) can be associated with neuropathy, muscle wasting and postural imbalance. Modulating gut microbiome and exercises can improve MetS, nerve and muscle health.

The aim: was to study lifestyle-modifying interventions efficacy on MetS manifestations according to ultrasound markers of neuromuscular and metabolic health.

Methods: We included 20 overweight patients (age 37-65 years), BMI>30, waist circumference (WC)>110. 6 patients underwent lifestyle modification – increased physical activity and aerobic exercises (yoga, plank and walking 10K steps daily); 6 patients were given probiotics (L. casei IMV B-7280/B. animalis VKB/B. animalis VKL strains (108 CFU/day, 10 days); 8 remained controls. All patients underwent general clinical, lab tests; multiparameter abdominal, neuromuscular ultrasound (US), measuring visceral fat (VF), liver elastography; dynamic US of postural stability.

Results: We detected increasing visceral fat (to 26±6mm), liver size and stiffness (to 175mm and 7.5kPa accordingly), muscle and nerve lesions on US; pelvic floor hypomotility in obese patients. Weight, BMI, WC and VF decreased after probiotic administration. Aerobic physical activity improved postural parameters, decreased BMI and WC, did not decrease VF. Muscle impairment in overweight manifested as follows: increased echogenicity, smaller hypoechoic bands (3-6cm vs 5-10cm); lower motility, contractility; improved after treatment. Neuropathy was in 10 patients with MetS; US demonstrated decreasing fascicles diameter from 1.9 to 0.5-1mm after both intervention. Liver size and stiffness decreased in all patients.

Conclusion: Probiotics and aerobic physical activity improve symptoms of MetS, muscle and nerves structure and posture in overweight patients.

Disclosure: Nothing to disclose

EPO2400

Arm crank ergometry with blood flow restriction technique as a feasible strategy for improving hand function in chronic stroke survivors - A randomized controlled study

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Background and aims: Arm function has been significantly related with muscle strength and improves activity after stroke. Low intensity aerobic exercise combined with blood flow restriction (BFR) can facilitate improvements in muscular strength. The objective of this study was to determine the effectiveness of combined arm crank ergometry with BFR to improve arm strength and function in stroke survivors.

Methods: Participants with stroke were randomised into experimental and control groups and performed arm crank ergometry with and without BFR respectively daily once, 4 days/week for 10 weeks. Vascular occlusion was achieved using blood pressure cuffs inflated to 60% of brachial artery occlusion pressure just below the shoulder joint (Fig1). After 3 minutes of warmup at self selected pace the participants were instructed to maintain the cadence between 50 to 60 r.min⁻¹ for 12 minutes. Data was collected from 10 participants at baseline, 5th and at the end of 10th week. The Fugl-Meyer (FM) motor assessment for upper extremity was the primary outcome measure.



Figure 1. Participant performing arm crank ergometry with blood flow restriction to the arm.



Blood flow restriction strap.

Results: 1 way ANOVA between the groups at the end of 10th week showed highly significant improvement in the scores of FM ($F=17.883$, $p<0.05$). Correlation in linear model between scores of FM with progressive weeks showed positive correlation in both experimental ($r^2=0.9508$) and control group ($r^2=0.9908$). Compared to the control group FM scores in the experimental group showed a net improvement of 7.29%.

Conclusion: Arm crank ergometry with BFR is a feasible strategy for stroke rehabilitation to strengthen upper limb.

Disclosure: Nothing to disclose

EPO2401

Role of Home based Targeted-CASP therapy in post stroke rehabilitation.

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Background: There is a need for a low cost, easy to apply, non-institutional regimen for significant functional recovery in post-stroke patients.

Aim: To study the effectiveness Targeted-Corrected-Assisted-Synchronized-Periodic therapy (T-CASP) in post-stroke rehabilitation.

Methods: This was a prospective quasi-randomised double-blind control study. The study was conducted in tertiary-care centre. Post stroke-Patients recruited on OPD-1 (Monday) and OPD-2 (Friday) were grouped under cases and controls respectively. All patients were assessed for power, spasticity, cognition, depression, functional level at baseline, 3 months and 6 months using standard tools of assessment. Caregivers were trained in T-CASP therapy and asked to carry it out at their homes as per protocol.

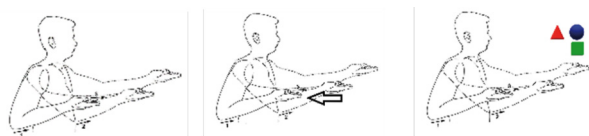


Figure 1: A) Passive Phase: Passive moment by examiner. B) Resistance Phase: Movement against Resistance. C) Cognitive Phase: Targeted movements towards different objects while naming them. Targeted CASP Therapy (Corrected-Assisted-Synchronized-Periodic) therapy.

Results: Baseline patient characteristics and outcome parameters were comparable between 2 groups. Significant difference was seen at 3 and 6 months between the 2 groups in Ashworth scale score for spasticity ($p=0.012$ & 0.001), MRC score for power ($p=0.021$ and 0.0001), Adden-Brookes score (Hindi) for cognition ($p=0.025$ & 0.010), BDI score for depression ($p=0.001$ & 0.001). Barthel scores were higher in T-CASP group but the difference was not significant ($p=0.219$ & 0.080). However, on subcomponent analysis percentage of people who were able to walk (93.3 vs 76.7 %), transfer to/from bed/chair (80 % vs 70%) and climb stairs (63.3% vs 50%) independently at 6 months was significantly higher in T-CASP group.

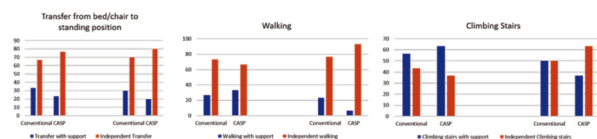


Fig 2 Percentage of people able to A) Transfer, B) Walk, C) Climb Stairs independently at 0 and 6 months in Conventional and CASP group.

Conclusion: Targeted-CASP therapy is a low cost, home based post stroke physiotherapy regimen which benefits all the aspects of post stroke rehabilitation.

Disclosure: Nothing to disclose

EPO2402

Bilateral recurrent ischemic stroke, Foix-Chavany-Marie Syndrome and tachycardia-induced cardiomyopathy – case report of an unusual course

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Background and aims: The heart may have an impact on the recovery process after stroke.

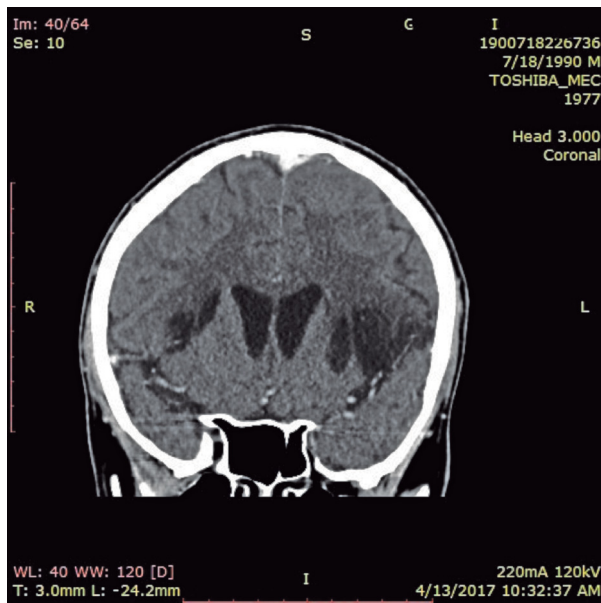
Foix-Chavany-Marie Syndrome (FCMS)- paralysis of the facial, tongue, pharynx, larynx and masticatory muscles with automatic-voluntary dissociation due to lesions of the opercular regions of descending fibres.

Tachycardia-induced cardiomyopathy is a reversible cause of heart failure and dilated cardiomyopathy.

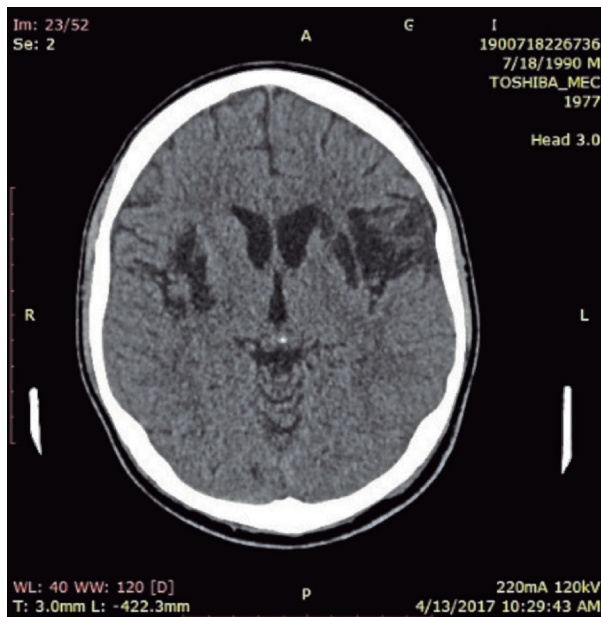
We report a 3 years follow-up of a patient with bilateral recurrent ischemic stroke and the above mentioned clinical features.

Methods: Case report

Results: A 27-year-old man, daily consumer of energizing beverage and alcohol, developed right faciobrachial monoplegia (MRC 2/5) and speech disturbances. After one week he becomes sleepy, mute and unable to swallow in addition to left complete hemiplegia. EKG revealed fast atrial fibrillation (ventricular rate 165/min) and dilated cardiomegaly (ejection fraction 38 %) by echocardiography. CT scan showed lesions in the left frontoparietal lobe, left lenticular nucleus and capsular lenticular on the right. He went under a gradual rehabilitation program, with a multidisciplinary approach, under EKG monitoring because of the high risk of cardiovascular events during the exercises, including speech therapy, kinetotherapy, robotic devices and psychological support. After 2 months right motor deficit recovered and the left hemiplegia improved significantly, including after 2 years from the event. Regarding FCMS, only mild dysarthria and hypophonia, but no dysphagia was noticed. The cardiomegaly and ventricular functions returned to normal within 1 year.



CT scan - 6 months after the stroke



CT scan- 6 months after the stroke

Conclusion: Into our best knowledge, this is the first case of FCMS with a cardiac abnormality that with multidisciplinary rehabilitation program recovered significantly from his neurological deficit and cardiac malfunction.

Disclosure: Nothing to disclose

EPO2403

How a vibro-tactile brain-computer interface paradigm can affect the Coma Recovery Scale-Revised in patients with disorders of consciousness?

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Background and aims: Persons diagnosed with disorders of consciousness (DOC) typically suffer from motor disabilities, although their cognitive abilities might be intact, they are difficult to assess, but brain-computer interface (BCI) technology can help.

Methods: 20 DOC patients performed 10 vibro-tactile P300 BCI sessions over 10 days with 8-12 runs on each day. Patients were in a stable chronic stage, 11 were diagnosed with a minimally conscious state (MCS) and 9 with unresponsive wakefulness syndrome (UWS) based on the Coma Recovery Scale-Revised (CRS-R). Changes of the BCI classification accuracy were investigated over the 10 days, and the changes of the CRS-R score before and after 10 vibro-tactile P300 sessions. Stimulators were fixed on both wrists and one foot, instruction was to mentally count either the stimuli on the left or right wrist, which induces the P300.

Results: The grand average accuracy of the BCI paradigm in the 1st session for all patients was 40%, in the best session it was 88% and the median accuracy of all sessions was 21%. In the 1st run 10 patients had a classification accuracy above chance level (>23%). In the best run every patient reached an accuracy $\geq 60\%$. 12 out of 20 patients showed an improvement of 1 to 7 points in the CRS-R score after the VT3 BCI sessions. 6 patients didn't show change in the CRS-R and 2 patients showed a decline in the score for 1 point.

Conclusion: The improvement of the CRS-R score after the 10 vibro-tactile sessions is an important fact for future studies.

Disclosure: The research for this study is partly funded by g.tec medical engineering GmbH and Guger Technologies OG.

EPO2404

Reliability of H-reflex as a paraclinical measure in neurorehabilitation of progressive multiple sclerosis patients with leg spasticity and gait problems

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Background and aims: Leg spasticity (LS) and gait impairments (GI) are common problems in progressive multiple sclerosis (PMS).

The study aim was to check whether H-reflex can be a reliable measure in the setting of physiotherapy for LS/GI.

Methods: 50 PMS patients (age 22-65 years, mean 45.3±9.4; duration 2-24 years, mean 10.6±6.9; EDSS 1.5-6.5, mean 5.3±1.4; leg spasticity 0-10 NRS 1-10, mean 7.0±2.0) enrolled into an inpatient physiotherapy program for LS/GI were studied. Modified Ashworth Score (MAS), Timed 25-Foot Walk (T25-FW), and the Barthel index (BI) together with soleus H-reflex (H/M ratio) were taken at the beginning and after a 4-week physiotherapy program.

Results: Before the therapy, there was no correlation between H/M ratios and clinical measures (EDSS, duration, NRS, MAS). Only T25-FW and total H/M correlated marginally (p=0.04). Following the physiotherapy program, there was a significant improvement in spasticity (p<0.00001) and gait (p=0.0004) measures, while BI did not change (p=0.60). In spite of the improvements, the H/M ratios did not change following therapy. The baseline H/M ratios did not correlate with change in clinical measures. The change in clinical measures did not correlate with change in H/M ratios too.

Conclusion: Regarding level of impairment, therapy-associated change or prediction of therapy effects, within the setting of physiotherapy for LS/GI in PMS patients, the H-reflex does not seem to be a reliable measure.

Disclosure: Nothing to disclose

EPO2405

Induced neuroplasticity via TMS in subjects with ischemic stroke.

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Background and aims: Stroke is the leading cause of disability and the third most common cause of death. Between 55% and 75% of the subjects who have suffered a stroke have functional motor limitations present even 3-6 months after the event. In the last 2 decades, significant progress has been made in understanding the mechanisms of brain plasticity.

Purpose of the study: To underlie the peculiarities of cerebral plasticity in patients with ischemic stroke during the acute phase and to investigate the rs6265 polymorphism of the BDNF gene under the influence of transcranial magnetic stimulation (TMS).

Methods: We conducted a controlled clinical study on subjects with ischemic stroke, in the territory of the middle cerebral artery. All the subjects received a neurological complex evaluation and DNA sequencing (Sanger method) for rs6265 BDNF.

Results: The dynamics of the TMS group was statistically better compared to the control group according to all the applied scales: mRS, NIHSS, Barthel, Orpington, 9-peg-hole test, Mini-Mental State Examination. The Spearman correlation confirmed that the presence of the motor evoked potential (MEP) is a significant factor for the rehabilitation of patients with ischemic stroke. The subjects without the rs6265 polymorphism had better results than those with the polymorphism, according to all the used clinical scales.

Table 1. The correlation between MEP and the 9 Peg Hole test, TMS group

	mRS dynamics		9 Peg Hole test dynamics				
	Mean	Abs. value	From N/A to „value“	Positive dynamics	Negative dynamics	N/A-N/A	From „value“ to N/A
MEP present at both visits	-1,03	32	0	29	3	0	0
MEP absent at 1st visit, and present at the 2nd one	-1,00	5	5	0	0	0	0
MEP present at 1st visit, and absent at the 2nd one	0,80	5	0	0	0	0	5
MEP absent at both visits	-0,40	5	0	0	0	5	0

Table 1. The correlation between MEP and the 9 Peg Hole test, TMS group

Table 2. Distribution of 9-Peg Hole test values by sex, age and hemispheres affected by stroke during the acute period

Gender	Age	Paretic hand (1st visit)			Paretic hand (2nd visit)			Non-paretic hand (1st visit)			Non-paretic hand (2nd visit)		
		Valid N	Mean, sec	SD	Valid N	Mean, sec	SD	Valid N	Mean, sec	SD	Valid N	Mean, sec	SD
Female	30-39	1	22.10		1	18.70		1	15.80		1	14.50	
	40-49	1	24.30		1	19.60		1	16.80		1	18.40	
	50-59	2	39.55	21.43	2	41.15	27.79	2	17.25	0.50	2	17.80	0.85
	60-69	10	31.34	9.51	12	34.58	19.20	10	18.72	1.65	12	19.45	2.52
	70-79	11	43.64	19.89	10	34.95	17.98	11	25.02	4.07	10	25.44	4.54
	80-89	3	33.97	1.10	4	34.31	11.72	3	29.03	0.46	4	29.23	0.42
	90-99	0			1	30.30		0			1	45.70	
	Femai		36.46	15.46	31	33.95	17.05	28	22.02	4.93	31	23.19	6.54
	Male	30-39	0			0			0			0	
40-49		1	39.56		1	23.50		1	17.45		1	17.80	
50-59		5	54.57	26.20	3	44.21	33.25	5	20.59	3.37	3	22.97	2.25
60-69		24	42.85	22.17	19	34.35	19.42	24	21.80	2.88	19	21.81	3.08
70-79		10	55.69	24.97	13	45.25	24.03	10	28.11	4.15	13	27.82	3.89
80-89		1	32.10		2	34.40	18.10	1	29.30		2	28.35	2.62
90-99		0			0			0			0		
Barbañi		41	47.07	23.12	38	38.57	21.77	41	23.26	4.43	38	24.20	4.44

Table 2. Distribution of 9-Peg Hole test values by sex, age and hemispheres affected by stroke during the acute period

Table 3. Genotypic distribution according to the presence / absence of the BDNF rs6265 polymorphism (abs., %)

		%	ABS.
CONTROL GROUP	G/G (no polymorphism)	70	33
	G/A+A/A (polymorphism)	30	14
TMS GROUP	G/G (no polymorphism)	71	34
	G/A+A/A (polymorphism)	29	14
TOTAL	G/G (no polymorphism)	71	67
	G/A+A/A (polymorphism)	29	28

NUCLEOTIDES: G – GUANINE, A - ADENINE

Table 3. Genotypic distribution according to the presence / absence of the BDNF rs6265 polymorphism (abs., %)

Conclusion: We recommend the application of the TMS method in all subjects with ischemic stroke during the acute period. Genotyping the subjects with stroke, based on the rs6265 polymorphism, should be further used in studies regarding neuroplasticity after stroke for subsequent modulation of the personalized neuro-recovery interventions.

Disclosure: Nothing to disclose

EPO2406

Pilot Study: Dry needling for treat the spasticity in multiple sclerosis.

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Background and aims: Dry needling is semi-invasive technique physiotherapy where work on trigger points causing spastic patterns of patients. MS is a disease that presents spasticity by lesions in the pyramidal pathway, conditioning alteration in ambulation, balance, sphincter control, motor weakness. The object is to assess the decrease in the taking of medications for spasticity in patients with MS as a consequence of dry needling; and observe the effectiveness of this according to the scales of assessment of spasticity.

Methods: Patients with MS (McDonald criteria 2010) without the use of steroids during the month before inclusion.EDSS>2.5. After a detailed explanation of the study, 20 subjects provided written informed consent for their participation Assessment sessions (questionnaires, explorations and medication log diary) conducted, as well as treatment sessions once a week for a period of 4 months. There were reassessments 1 months after having performed the therapies. The questionnaires carried out through a personal QR code for each subject of the study. There were 18 sessions in total that included 12 treatment sessions (puncture, stretching and reeducation) and 6 assessment sessions

Results: Of the patients analyzed so far, it is observed that 75% have decreased the pyramidal score on the EDSS scale, after the sessions. Also, a high percentage of improvement was found in the analysis of the quality of life questionnaire MSQol54.

Conclusion: Dry puncture in patients with multiple sclerosis reduces spasticity, and could improve the quality of life, being a technique to be considered in patients with spasticity.

Disclosure: Nothing to disclose

ePoster Sessions

Monday, May 25 2020

Ageing and dementia 3

EPO3001

Atypical mutations in patients with clinical Alzheimer's disease: report of three emblematic cases

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Background and aims: Apart from well known mutations in APP and Presenilin genes, additional hereditary factors in early-onset Alzheimer's disease (EOAD) remain largely tentative. We describe 3 cases of early-onset dementia clinically suggestive of AD with concurrent detection of mutations in SQSTM1, PRNP, and NPC2.

Methods: 3 patients presented in their 50s with a slowly-progressive history of episodic memory impairment, leading to the loss of their functional autonomy. They all performed neuropsychological evaluation, brain-MRI, fluorodeoxyglucose (FDG)-18F-PET, lumbar puncture, amyloid-PET. In keeping with the early onset of symptoms, genetic analysis with next generation sequencing (NGS) covering the spectrum of common and rare dementias was performed.

Results: Neuropsychological evaluation outlined an amnesic syndrome of hippocampal type in all patients. MRI showed brain atrophy in temporal-mesial lobes, with FDG-PET hypometabolism in the same areas in patients #1-#2, while patient #3 had minimal brain atrophy, but fronto-temporal and right-parietal hypometabolism. Low CSF beta-amyloid levels with concurrent evidence of amyloid deposition at the amyloid-PET were found in patients #2-#3, only. 3 unexpected mutations were detected in patients #1-2-3, respectively: SQSTM1 (P392L), PRNP (R208H), and NPC2 (V30M).

Conclusion: While a causal link between mutations in SQSTM1, PRNP and NPC2 and other neurodegenerative diseases - fronto-temporal dementia and amyotrophic lateral sclerosis, prion disease and Niemann-Pick type-C, respectively - has been uncovered, the role of these genetic variants in AD pathogenesis remains undefined. Larger studies are needed to define whether they play a specific causal role or are risk factors for the development of AD.

Disclosure: Nothing to disclose

EPO3002

Measuring benefit of cognitive rehabilitation in Alzheimer's disease

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Background and aims: Assessing the benefit of cognitive rehabilitation (CR) for patients and caregivers remains difficult

Methods: An observational, prospective study was conducted in 33 patients with AD and their caregiver during a clinical, individualized CR program, compared to 17 patients with AD who benefited from standard follow-up. CR consisted of 1 weekly session during 3 months at home, followed by one monthly contact for 9 months. Usual follow-up consisted in 2 counselling sessions in 1 year at the memory clinic and a few phone contacts. Evaluation of patient's dependence in activities and objective and subjective caregiver's burden was performed with a research quantitative scale at one year follow-up.

Results: Analyses with repeated measure ANOVA showed decreased patient's dependence for adapted activities at 1 year in the CR group compared to the control one. Subjective percentage of caregiver's burden was also decreased after one year in the CR group with our research functional scale. Global cognition slightly decreased in both groups over 1 year.

Conclusion: This observational study in a clinical setting is in line with the benefit of CR for patients with mild to moderate AD reported in most recent randomized controlled trials. The benefit obtained for adapted activities remained after 1 year, even if global cognition declined. More importantly, caregiver's subjective burden related to all individually relevant daily activities evaluated within the CR program was decreased after 1 year. Those results emphasize CR efficacy for AD patients and their caregivers in a clinical setting.

Disclosure: Nothing to disclose

EPO3003

Accelerated neuroaxonal retinal thinning in Alzheimer's disease

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Background and aims: A significant reduction of neuroretina thickness in Alzheimer's Disease (AD) has been demonstrated. Longitudinal studies investigating neuroaxonal thinning rates over time in AD and age-matched cognitively unimpaired subjects (CS) and possible correlations with disease progression are still lacking. Here, we assessed the neuroaxonal retinal thinning rate in AD, Mild Cognitive Impairment (MCI) and CS.

Methods: 68 consecutive subjects (16CS, 24MCI, 28AD) underwent OCT with measurement of peripapillary RNFL and macular GCL at baseline and at a mean follow up time of 2.5 years. Neuropsychological tests, both at baseline and follow-up, were available in AD and MCI groups. Group differences in yearly thinning rates were tested with one-way ANCOVA with age, sex and RNFL/GCL baseline values as covariates

Results: AD showed a significantly higher yearly thinning rate of RNFL global thickness (mean \pm S.D.) than CS (-1.66 \pm 0.58 vs -0.62 \pm 0.4 μ m, p=0.037) and a higher thinning rate of the RNFL superior quadrant thickness than both CS (-3.57 \pm 1.21 vs 0.07 \pm 0.74 μ m, p= 0.001) and MCI (-1.28 \pm 0.45 μ m, p=0.01). MCI patients with pathological CSF A β 42 and p-tau values showed a higher decay in GCL volume than MCI with normal values (p=0.032). RNFL and GCL thinning over time was positively associated with worsening in cognition.

Conclusion: Our findings prompt further studies to validate neuro-retinal OCT as a cost-effective, objective and easy to handle neurodegeneration marker in AD, for monitoring the disease course and to test the effects of neuroprotective interventions

Disclosure: This work was carried out within the framework of the Ivascomar project of the Italian Ministry of Research (CTN01_00177_165430), Cluster Tecnologico Nazionale Scienze della Vita "Alisei", Italian Ministry of Research and partially supported by Regione Lombardia (POR FESR 2014-2020) within the framework of the NeOn project (ID 239047)

EPO3004

Changes in antidiabetic drug prescription among patients with dementia and diabetes mellitus: Longitudinal analyses using Swedish national registers over 14-years.

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Background and aims: Dementia may impact self-management of diabetes mellitus (DM), but it's unclear how it affects antidiabetic drug prescription. Herein we investigated the long-term changes in antidiabetic drug prescription among DM patients with and without dementia.

Methods: We performed an open-cohort study using 5 Swedish national registers – the Swedish Dementia Registry (SveDem), Prescribed Drug Register, Cause of Death Register, Patient Register and Total Population Register (TPR). We identified 13,483DM - dementia patients registered in SveDem from May 1st, 2007 until October 16th, 2018 and propensity-score matched 13,483DM patients without dementia (controls) extracted from the TPR. Matching criteria included age, sex, comorbidity score, and index date (dementia diagnosis date). Yearly proportions of 7 antidiabetic drug classes (insulin, metformin, sulfonylurea derivatives, thiazolidinediones, dipeptidyl-peptidase-4 inhibitors (DPP-4i), glucagon-like peptide-1 agonists and sodium-glucose co-transporter-2 inhibitors) were determined from the total yearly antidiabetic drug usage, in years 2005 to 2018. Regression analyses were used to analyze the slope (β coefficients with 95% confidence intervals) of yearly changes in drug proportions.

Results: With one-year increments, DM-dementia patients had steeper percent increase in insulin use (β 1.65% [95% CI 1.35%;1.94%] vs 1.32% [1.19%;1.45%]), steeper decline in metformin

(-1.25% [-1.56%;-0.93%] vs -0.77% [-0.98%;-0.56%]) and less pronounced increase in DPP-4i use (0.42% [0.34%;0.50%] vs 0.76% [0.67%;0.84%]). Difference in average insulin usage was particularly high after dementia diagnosis (67% in dementia vs 58% in dementia-free).

Table 1. Beta coefficients for percent change in antidiabetic drug usage with yearly increments

	Dementia Cases β (95% CI)	Dementia-Free Controls β (95% CI)
Insulin	1.65 (1.35; 1.94)*	1.32 (1.19; 1.45)*
Metformin	-1.25 (-1.56; -0.93)*	-0.77 (-0.98; -0.56)*
Sulfonylurea derivates	-1.22 (-1.42; -1.03)*	-1.07 (-1.15; -0.99)*
TZD	-0.18 (-0.21; -0.15)*	-0.13 (-0.19; -0.08)*
DPP4i	0.42 (0.34; 0.50)*	0.76 (0.67; 0.84)*
GLP1a	0.1 (0.07; -0.12)*	0.29 (0.22; -0.36)*
SGLT2i	0.06 (0.05; -0.08)*	0.18 (0.15; -0.21)*

TZD, thiazolidinediones; DPP4i, dipeptidyl-peptidase-4 inhibitors; GLP1a, glucagon-like peptide-1 agonists; SGLT2i, sodium-glucose co-transporter-2 inhibitors;
Beta coefficients represent slope of percent change in antidiabetic drug usage with advancing time (one-year increments) derived from the linear regression analysis.
*p-value<0.001

Table 1. Beta coefficients for percent change in antidiabetic drug usage with yearly increments

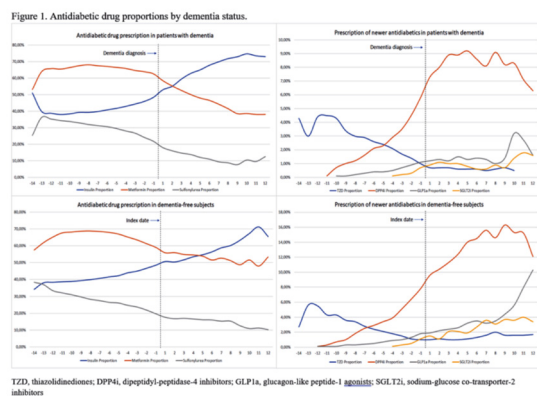


Figure 1. Antidiabetic drug proportions by dementia status

Conclusion: Compared to dementia-free subjects, dementia patients experienced more frequent insulin prescription, less frequent metformin and DPP-4i prescription, suggesting lower likelihood of receiving more modern antidiabetic drugs in dementia patients.

Disclosure: This work has been supported by the Swedish Brain Power, Swedish Research Council (2012-2291, 2016-02317, 2018-02843), Alzheimerfonden, CIMED, Stockholm County Council, the Swedish Associations of Local Authorities and Regions, the Swedish Order of Saint John/Johanniterorden, Swedish Society for Medical Research, FORTE (the Swedish Council for Health, Working Life and Welfare, dnr: 2017-01646), the Swedish Stroke Association, Margaretha af Ugglas Foundation and the Stiftelsen för Gamla Tjänarinnor.

EPO3005

Kinesin, amyloid precursor protein (APP)-vesicle transport motor interacts with Rab effector, EHBP1L1 via the tetratricopeptide repeat domain of KLC1.

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Background and aims: Mutations of the amyloid precursor protein (APP) cause for the formation of amyloid- β peptides. These peptides play a key role in Alzheimer's diseases. The tetratricopeptide repeat (TPR) domain of kinesin light chain 1 (KLC1) may be responsible for binding APP either directly or via interaction with C-jun N-terminal kinase-interacting protein 1 (JIP1). However, the binding partners of the TPR domain of KLCs have not yet been fully identified.

Methods: We were used the yeast 2-hybrid system to identify the binding proteins that interact with the TPR domain of KLC1. The binding affinity was quantified by measuring β -galactosidase activity. Direct interaction between binding proteins and KLC1 in mammalian cells as well as in vitro was assayed using the co-immunoprecipitation with the antibodies. The cellular co-localization in cells was used the immunocytochemistry.

Results: We revealed an interaction between the TPR domain of KLC1 and EH domain-binding protein 1-like 1 (EHBP1L1), which is Rab8/10 effectors that associates with Bin1 to generate membrane curvature to excise the vesicle at the endocytic recycling compartment and accumulate on Rab8-positive enlarged lysosomes. EHBP1L1 bound to the six TPR motif-containing regions of KLC1 and did not interact with KIF5B (a motor subunit of kinesin-1) and KIF3A (a motor subunit of kinesin-2). The carboxyl (C)-terminal the coiled-coil domain of EHBP1L1 is essential for interaction with KLC1. When co-expressed in HEK-293T cells, EHBP1L1 co-localized with KLC1 and co-immunoprecipitated with KLC1, but not KIF5B.

Conclusion: These results suggest that kinesin 1 motor protein may transport of EHBP1L1-associated cargo in cells.

Disclosure: Nothing to disclose

EPO3006

Diagnostic whole-exome sequencing and C9orf72 repeat expansion testing in an Austrian cohort with early onset dementia

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Background and aims: Early-onset dementias (EODs, disease onset <age 65) are thought to be mainly genetic in origin, although a large proportion has no family history. High-penetrant mutations explain only few EOD cases. Whole-exome sequencing (WES) is a powerful diagnostic tool to detect pathogenic sequence variants in Mendelian conditions. We aimed to investigate the diagnostic yield in unrelated EOD patients.

Methods: WES and C9orf72 repeat expansion testing performed in 45 EOD patients: 38 AD, 4 FTD, 1 Lewy-body dementia and 2 cerebral amyloid-angiopathy patients. Exomes were enriched with the SureSelect Human All Exon v6 kit. DNA libraries were sequenced on a HiSeq 4000 instrument. Single nucleotide and copy number variants were screened in validated dementia genes. C9orf72 repeat expansion was conducted using a 2-step protocol with fragment length analysis and repeat primed PCR method

Results: 2 AD patients carried APP-duplications with 1 occurring de-novo (parents tested negative for the mutation). Furthermore, 1 FTD patient had a MAPT-mutation (c.1853C>T,p.Pro618Leu) and 2 AD patients carried PSEN1-mutations (c.617G>A,p.Gly206Asp; c.356C>T,p.Thr119Ile). 4 patients were homozygous for APOE4. No C9orf72 repeat expansion was found.

Conclusion: In 5 out of 45 patients a pathogenic variant meeting the American College of Medical Genetics and Genomics criteria for disease causation was revealed (diagnostic yield: 11.1%). 1 patient with a pathogenic variant and 1 homozygous for APOE4 (16.7%; 25%) had no family history. This emphasizes the importance of genetic testing in patients with negative family histories, particularly regarding homozygous APOE4 carriers having a lifetime-risk of 50-70 %.

Disclosure: Nothing to disclose

EPO3007

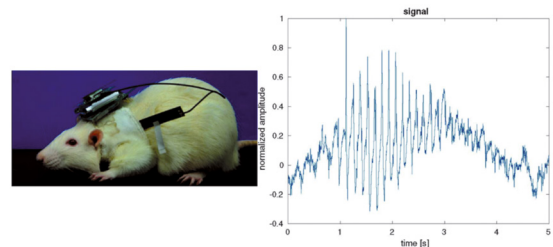
A smart closed-loop deep-brain stimulation system

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Background and aims: The Deep Brain Stimulation (DBS) has been found efficient to relieve patients from the symptoms of the Parkinson's disease (PD). Dejean, C. et al show the onset of the PD's symptoms can be predicted by detecting the presence of High-Voltage Spindles (HVS) waves in the brain Local Field Potentials (LFPs). The HVS is a synchronous spike-and-wave patterns in LFPs oscillating in the 5-13Hz frequency band. Suppressing HVS signals is found useful for delaying the progress of PD and deleting symptoms.

Controlling DBS is a promising solution trail for reducing the side effects induced by the DBS: this is our main objective in animal experiment context.

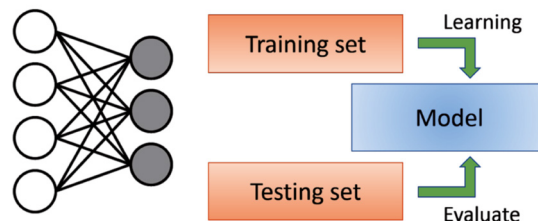


(a) Rat with neural prosthesis. (b) Signal recorded in LFPs.

Data extraction. Signal are extracted from rats with the PD.

Methods: A bipartite graph named Restricted Boltzmann Machine (RBM) is used to detect identify HVS signal. The 1st layer is fed with the observation and the hidden layer form a more significative latent representation.

We train one model for each PD rat with a session of 60s and we test each RBM with a second session of the same rat to evaluate it.



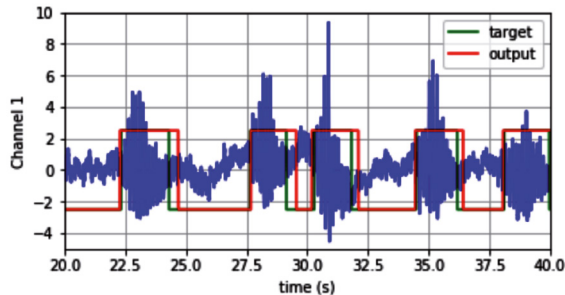
(a) The model.

(b) The method.

2a is a graph structure of a RBM with 4 visible neurons (white) and 3 hidden neurons (gray). Learning the cRBM consists in learning the weight of each links. 2b illustrate the method. We use data from a training set to learn the model and verify if the model remains efficient for new data of the testing set.

Results: The ground truth is heuristically defined to compare with the model prediction. Fig.3 gives the result for one rat with 6 hidden neurons.

The RBM succeed in detecting the HVS earlier than the ground truth for most rats by adapting automatically the detection of HVS for each rat.



Detection of the HVS. The result of the classifier is given in red and the green line is the ground truth to evaluate the model.

Conclusion: The model is fast, robust, capable to learn automatically from the data on real time.

The next step is the electrical implementation of the algorithm in the stimulator.

Disclosure: This work is supported by the doctoral school of Université Paris-Saclay and the Ministry of Science and Technology of Taiwan (MOST).

EPO3008

CSF/serum glucose ratio in Frontotemporal Dementia

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Background and aims: Neurodegenerative diseases affect cerebral glucose metabolism and induce inflammation. One such condition is amyotrophic lateral sclerosis (ALS), which is known to be characterized by a state of hypermetabolism that is associated with disease severity. Recently, it was demonstrated an increased resting energy expenditure and a state of hypercatabolism in Frontotemporal Dementia (FTD), an ALS' spectrum neurodegenerative disease. Although there is a relationship between cerebral glucose metabolism and dementia, serum and CSF glucose levels are less used biomarkers in its investigation, including in Frontotemporal Dementia (FTD). Our aim is to determine the relationship between CSF/serum glucose ratio and age of onset, disease duration, CSF biomarkers and MoCA score in patients with FTD.

Methods: Patients with FTD followed in a dementia outpatient clinic in a tertiary center and who did simultaneous CSF A β 42, Tau, glucose and serum glucose analysis were included. To study the associations between the investigated variables, Spearman's correlations and linear regressions were applied.

Results: 153 patients were included (mean age 63.3 \pm 9.2 years, 50.3% female). The CSF/serum glucose ratio correlates with MoCA score ($r=0.29$, $p=0.028$). Multivariate analysis showed independent associations between CSF/serum glucose ratio and MoCA ($\beta=0.006$, 95%CI=[0.001, 0.011], $p=0.019$), between age of onset ($\beta=0.004$, 95%CI=[0.002,0.006], $p<0.001$) and CSF glucose ($\beta=0.007$, CI=[0.004,0.009], $p<0.001$).

Conclusion: CSF/serum glucose ratio is lower in patients with early age of onset and lower MoCA scores, possibly associating an increased energy expenditure with a more aggressive disease.

Disclosure: Nothing to disclose

EPO3009

Driving behavior in Alzheimer's disease (AD) and amnesic Mild Cognitive Impairment (aMCI) carriers of the apolipoprotein e4 allele (APOE4)

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Background and aims: Although patients with AD and aMCI have driving difficulties, the literature regarding their severity remains inconclusive. 1 of the well documented genetic factors that affects cognitive functions is the APOE4. Cognitive functions play a major role for driving behavior. Our aim was to compare the driving behavior of carriers and non-carriers of the APOE4 in the clinical stages of mild AD or aMCI.

Methods: N=18 active drivers with aMCI or mild AD (M=71.61±9.25) carriers of the APOE4 and N=18 (M=73.89±8.10) non-carriers matched for clinical diagnosis. The 2 groups had no significant differences in age, years of education (carriers M=11.78±3.90, non-carriers M=11.56±4.69), general cognitive ability based on Mini Mental State Examination (carriers M=25.78±5.16, non-carriers M=25.61±3.31), and driving experience (carriers M=42.92±11.69, non-carriers M=45.73±8.57). All the patients undergone thorough neurological and neuropsychological assessment and participated in a driving simulation experiment including low and high traffic volume conditions.

Results: In low traffic volume conditions carriers of the APOE4 did not indicate any significant differences from the non-carriers. However, in high traffic volume conditions the APOE4 carriers drove significantly slower and with lower speed variation than non-carriers. No other significant differences were found.

Conclusion: Driving behavior of the APOE4 carriers seems to be affected in demanding driving scenarios even within the clinical stages of mild AD and aMCI.

Disclosure: Funding: This research was carried out within the framework of the Operational Program "Education and Lifelong Learning" of the National Strategic Reference Framework namely the Research Funding Program: THALES investing in knowledge society through the

European Social Fund, co-financed by the European Union and Greek national funds. The authors have no conflict of interest to report. The authors received no other funding for this study.

EPO3010

MiR-204-3p/Nox4 mediates memory deficits in a mouse model of Alzheimer's diseaseW. Tao¹, L. Yu¹, X. Zhu¹, Y. Xu², J. Chen³¹*Drum Tower Hospital, Nanjing, China, ²Nanjing, China,*³*Department of Neurology, Drum Tower Hospital of Nanjing University Medical School, Nanjing, China, Nanjing, China*

Background and aims: Oxidative stress plays a critical role in the pathogenesis of Alzheimer's disease (AD), and microRNAs (miRNAs) contributes to the oxidative stress and memory deficits in AD.

Methods: MiRNA microarray was performed using the hippocampus of 6-month-old APPswe/PS1dE9 (APP/PS1) mice. The miR-204-3p overexpression lentivirus (Lv-miR-204) was injected into bilateral hippocampus of APP/PS1 mice. The memory function was examined by Open field, New-object reorganization, Fear condition and Morris water maze tests. The beta-amyloid (A-beta) levels were determined by immunofluorescence and ELISA. The potential targets of miR-204-3p were predicted by Targetscan, and confirmed by luciferase assay and western blotting. Long-term potentiation (LTP) was recorded to evaluate the synaptic functions. The levels of 4-hydroxynonenal, 3-nitrotyrosine, and 8-hydroxy-2'-deoxyguanosine were detected by ELISA and the level of H₂O₂ was examined by spectrophotometry. Reactive oxygen species (ROS) was determined by fluorescence assay.

Results: MiR-204-3p was significantly downregulated in the hippocampus and plasma of 6-month-old APPswe/PS1dE9 (APP/PS1) mice and in the plasma of AD patients. MiR-204-3p overexpression attenuated memory and synaptic deficits in APP/PS1 mice. Lv-miR-204 treatment decreased amyloid levels and oxidative stress in the hippocampus. NADPH oxidase 4 (Nox4) was a target of miR-204, and Nox4 inhibition protected neuronal cells against A-beta induced neurotoxicity. Furthermore, GLX351322 treatment rescued synaptic and memory deficits, and inhibit oxidative stress and amyloid levels in the hippocampus of APP/PS1 mice.

Conclusion: MiR-204-3p attenuated synaptic and memory deficits and inhibit oxidative stress in APP/PS1 mice by targeting Nox4, and miR-204-3p overexpression and/or Nox4 inhibition might be a potential therapeutic strategy for AD treatment.

Disclosure: This study was supported by the National Natural Science Foundation of China and the Key Research and Development Program of Jiangsu Province of China.

EPO3011

Chronic somatic diseases increase mortality in dementia: a national registry-based cohort studyL. Taudorf¹, A. Nørgaard¹, H. Brodaty², T.M. Laursen³, G. Waldemar¹¹*Danish Dementia Research Centre, Department of Neurology, Rigshospitalet, Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark,*²*Dementia Centre for Research Collaboration and Centre for Healthy Brain Ageing, School of Psychiatry, UNSW, Sydney, Sydney, Australia,*³*The National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus BSS, Aarhus University, Aarhus, Denmark*

Background and aims: Mortality is known to be markedly increased in people with dementia. However, the association between multiple chronic conditions and mortality in dementia is not well clarified. The aim of this study was to investigate the impact of somatic diseases on mortality in dementia compared with the general elderly population.

Methods: In a cohort design, we linked data from nationwide registries on dementia status and somatic diagnoses from the Charlson Comorbidity Index (CCI). Our population comprised all Danish residents age ≥ 65 years from January 1, 2006 to December 31, 2015. We assessed mortality rate ratios (MRR) by comparing people with and without dementia stratified by CCI. The reference was defined as people without dementia with a CCI score of zero.

Results: Our population consisted of 1,558,015 people aged ≥ 65 years of whom 439,205 died. Of the 114,112 people with dementia, 77,409 died. MRRs were significantly higher in people with dementia and increased with higher CCI score. When comparing people with similar comorbidity load, the mortality was still significantly higher in people with dementia. After adjusting for CCI, age, sex and calendar year the mortality was 2.62 (95% CI: 2.59-2.64) times higher in dementia.

Conclusion: The comorbidity load was associated with increased mortality in both people with and without dementia. The increased mortality in dementia, even after adjustment for CCI, suggests that a dementia disorder in and by itself contributes with excess mortality, which may be further accentuated by increased frailty, disadvantageous risk factor profiles, and improper or insufficient treatment of other diseases.

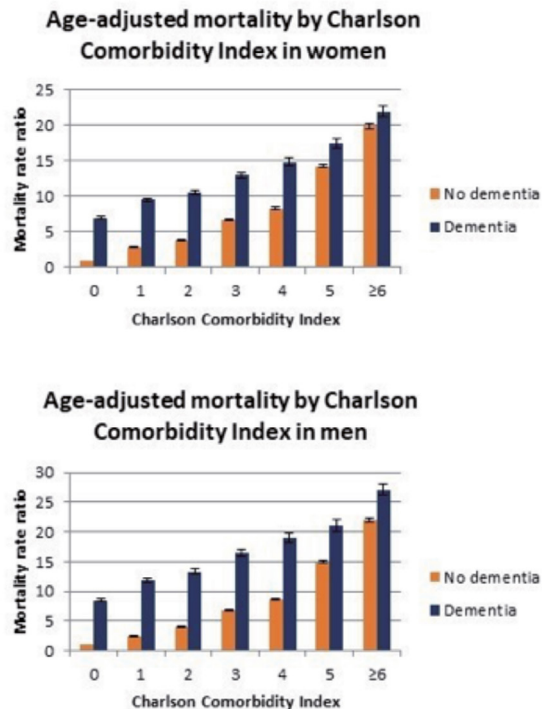


Figure 1. Mortality rate ratios adjusted for age and calendar year for women and men stratified by Charlson Comorbidity Index. Error bars represent 95% confidence intervals.

Disclosure: LT, AN, and GW reported grants received from the Danish Ministry of Health to the Danish Dementia Research Centre while conducting the study. TML reports no conflicts of interests.

EPO3012

Electrocortical Signal Complexity as Potential Biomarker of Cognitive Decline Progression from Normal Aging to Alzheimer's Disease through Mild Cognitive Impairment

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Background and aims: Pathophysiology beyond dementia is far from being understood. Non-linear analysis of EEG signal has been proposed as neurophysiological tool to assess cortical functioning in patients with cognitive impairment. We investigated changes in fractal properties of EEG signals by analyzing self-similarity of electrocortical activity through different levels of cognitive decline.

Methods: We analyzed data of patients with Alzheimer's disease ("AD"; N=24; age 68.4±9) and Mild Cognitive Impairment ("MCI"; N=21; age 65.6±9.9), group-matched by age, who underwent a standardized EEG. We selected also a group of healthy controls (N=27; age 68.8±6.2), age-matched with patients, with normal EEG. Power spectrum was calculated by applying a Welch's periodogram to selected electroencephalographic signal epochs using a standardized protocol. To investigate self-similarity of electrocortical activity, the power law exponent β was computed for each recording coordinate as minus the slope of the power spectrum vs frequency of signals in a Log-Log scale.

Results: We found significant lower β values among temporal-parietal-occipital sites of recordings in MCI subjects as compared to controls, while overall significant lower β values were observed in AD subjects as compared to controls among almost all site of recordings, except for the left frontal electrode. For each site of recording, an incremental gradient from AD to controls through MCI was observed in average β values.

Conclusion: We found a progressive decrease in β values from physiological conditions to dementia through MCI. Changes in fractal organization of EEG signal could represent an early electrophysiological biomarker of cognitive decline progression in AD.

Disclosure: Nothing to disclose

EPO3013

Rate of age-related cognitive decline and socioeconomic indicators in ageing population sample

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Background and aims: The objective of the study was to investigate the relationship between socioeconomic indicators and age-related dynamics of cognitive functions in an ageing Russian population.

Methods: Design: Longitudinal study. A random population subsample (3,153 people, initial age 47-74 years, prospective age 55-84 years) was formed from cohort of Novosibirsk residents (n=9,360, project HAPIEE). Repeated serial examinations of cognitive functions included the assessment of memory indicators (immediate and delayed recall), executive function (semantic verbal fluency) and processing speed (letter cancellation). Level of education and economic activity status were determined by standardized questionnaires. Economically active included participants with paid work in the past 12 months. Those who did not have paid work or who retired considered economically inactive. The mean follow-up period was 9.2 years (Median =9.3; SD=0.7).

Results: Persons with primary education had steeper rate of regress in memory (men: p<0.001; 0.025; women: <0.001 for delayed recall), than those with university education, independently of age. The accelerated decline in semantic verbal fluency among women with university education (p<0.001) is probably due to processing speed at initial examination in participants with primary education was relatively low. The termination of economic activity in men was associated with steeper rate of decline in memory indicators (p<0.001 and 0.001) compared to economically active participants, independently from age and education level.

Variables*	Wave 2		Wave 3	
	Men	Women	Men	Women
Observed, n (%)	1198 (38)	1955 (62)	1198 (38)	1955 (62)
Age*, years	60,0 (6,9)	60,6 (6,8)	69,2(7,0)	69,7(6,9)
Education, n (%)				
Primary	65 (5)	128 (7)	65 (5)	128 (7)
Vocational	283 (24)	593 (30)	283 (24)	593 (30)
Secondary	369 (31)	620 (32)	369 (31)	620 (32)
University	481 (40)	614 (31)	481 (40)	614 (31)
Economic activity, n (%)				
Active	898 (75)	1011 (52)	403 (34)	383 (20)
Inactive (retired persons)	294 (25)	938 (48)	786 (66)	1548 (80)
Cognitive functions, score				
Immediate recall	7,5 (1,3)	7,9 (1,2)	6,7 (1,6)	7,3 (1,4)
Delayed recall	8,1 (1,7)	8,6 (1,5)	6,9 (2,1)	7,7 (2,0)
Semantic verbal fluency	22,9 (8,0)	21,7 (7,6)	17,1 (5,5)	16,5 (4,9)
Letter cancellation	17,9 (4,7)	18,8 (5,0)	15,5 (5,4)	17,3 (5,7)
Hypertension, n (%)	795 (69)	1405 (74)	929 (78)	1621 (83)
Diabetes, n (%)	66 (9)	124 (10)	240 (20)	403 (21)
CVD **, n (%)	156 (13)	196 (10)	279 (23)	359 (19)
BMI **, kg/m ²	27,0 (4,1)	30,2 (5,4)	27,7 (4,6)	30,6(5,7)
Total cholesterol, mmol/l	5,5 (1,0)	6,0 (1,1)	5,2 (1,1)	5,6 (1,2)
Smoking status, n (%)				
Current smoker	364 (31)	80 (4)	454 (38)	113 (6)
Ex-smoker	469 (39)	125 (6)	326 (27)	79 (4)
Never-smoker	359 (30)	1744 (90)	411 (35)	1743 (90)
Marital status, n (%)				
Single/ divorced	122 (10)	805 (41)	186 (16)	1086 (56)
Married/ cohabiting	1070 (90)	1144 (59)	1006 (84)	851 (44)

*Values are presented as mean and standard deviation - M(SD) or n (%); **CVD - cardiovascular disease, BMI – body mass index.

Table 1. Characteristics of the population subsample of subjects who participated in two examinations (9 years of follow-up period, men and women, Novosibirsk, n=3153)

Education	Men, n=1198				Women, n=1955			
	Immediate recall	Delayed recall	Semantic verbal fluency	Letter cancellation	Immediate recall	Delayed recall	Semantic verbal fluency	Letter cancellation
(1) Primary	-161 (-197; -125)	-205 (-258; -152)	-474 (-678; -271)	-329 (-467; -192)	-086 (-111; 061)	-162 (-197; -128)	-290 (-423; -158)	-161 (-272; -050)
(2) Vocational	-089 (-107; -072)	-139 (-164; -113)	-619 (-716; -522)	-282 (-347; -217)	-063 (-074; 051)	-103 (-119; 087)	-585 (-645; -524)	-174 (-223; -125)
(3) Secondary	-084 (-099; -069)	-115 (-137; -093)	-606 (-691; -521)	-262 (-319; -204)	-058 (-069; -047)	-100 (-115; 085)	-581 (-640; -522)	-175 (-223; -127)
(4) University	-082 (-095; -069)	-123 (-142; -104)	-703 (-778; -628)	-242 (-292; -193)	-056 (-068; -045)	-078 (-093; -063)	-619 (-678; -559)	-169 (-217; -121)
P<0.01	<.001	.025	.229	.999	.208	<.001	<.001	.999
P<0.05	.999	.999	.999	.999	.999	.156	.999	.999
P<0.001	.999	.999	.556	.999	.999	.292	.999	.999

*Values are presented as Mean (95% CI); **Estimates of association are adjusted for age

Table 2. The association** between the rate of changes per year of cognitive function indicators* and education level (population sample, initial age 47-74 years, prospective age 55-84 years)

Economic activity status	Men, n=1183				Women, n=1925					
	n	Immediate recall	Delayed recall	Semantic verbal fluency	Letter cancellation	n	Immediate recall	Delayed recall	Semantic verbal fluency	Letter cancellation
(1) Active W2W3	399	-065 (-080; -049)	-096 (-118; -113)	-662 (-750; -574)	-251 (-308; -194)	381	-053 (-068; -038)	-078 (-099; -057)	-632 (-714; -549)	-188 (-253; -123)
(2) Active W2, inactive W3	512	-105 (-118; -092)	-148 (-167; -129)	-629 (-702; -557)	-265 (-313; -217)	651	-072 (-083; -061)	-105 (-120; -089)	-587 (-647; -528)	-170 (-217; -123)
(3) Inactive W2W3	272	-095 (-114; -076)	-141 (-169; -113)	-614 (-722; -505)	-272 (-347; -197)	893	-055 (-065; -045)	-099 (-113; -085)	-545 (-600; -491)	-166 (-210; -121)
P<0.01		<.001	.001	.999	.999		.128	.112	.999	.999
P<0.05		.071	.066	.999	.999		.999	.406	.333	.999
P<0.001		.999	.999	.999	.999		.109	.999	.999	.999

*Values are presented as Mean (95% CI); W2- wave2, data were collected from 2006 to 2008; W3- wave3, data were collected from 2015 to 2017; **Estimates of association are adjusted for age and level of education

Table 3. The association** between the rate of changes per year of cognitive function indicators* and economic activity status (population sample, initial age 47-74 years, prospective age 55-84 years)

Conclusion: The obtained results suggest that, higher education and continuous economic activity positively effect on cognitive decline in ageing. These results are consistent with cognitive reserve theory.

Disclosure: The reported study was funded by RFBR according to the research project № 19-013-00681.

EPO3014

Biomarkers based definition of limbic predominant long-lasting amnestic Mild Cognitive Impairment

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Background and aims: Previous reports described amnestic Mild Cognitive Impairment (aMCI) subjects with slow rate of cognitive decline, benign disease course associated to FDG-PET brain hypometabolism in the medial temporal lobe structures [1]. Clinical and post-mortem studies suggested the presence of both Alzheimer's disease (AD) and non-AD pathology [2]. The identification of aMCI with benign course has relevant consequences for both prognosis and treatment.

Methods: We selected 80 aMCI (Cohort1) using the following criteria: disease duration ≥ 4 years; available clinical follow-up; baseline CSF for amyloid- β 42, total-tau and phosphorylated-tau; FDG-PET assessed for individual brain hypometabolism [3] showing a selective medial temporal involvement, thus a non-AD brain pattern. We added 42 aMCI-due-to-AD with similar baseline clinical features and biomarker measurements, and both CSF positive for amyloidopathy and FDG-PET showing the typical AD temporo-parietal brain hypometabolism (Cohort2).

Results: Cohort1: disease duration 8.45 ± 3.37 years, no decline in MMSE, only 7% conversion to AD dementia. Cohort2: 81% conversion to AD dementia. The FDG-PET single subject analysis predicted stability in Cohort1 and progression in Cohort2, with high accuracy (AUC=0.88), sensitivity (0.85) and specificity (0.90). In Cohort1, the CSF biomarkers showed great variability as reflected in AT(N) classification, with lack of accuracy in predicting stability or conversion.

Conclusion: The specific brain hypometabolism pattern in Cohort1 was associated with clinical stability and slow rate of memory deficit progression at difference with Cohort 2 with AD metabolic pattern. These findings underline the key role of FDG-PET brain metabolism as a fundamental biomarker in the diagnostic and prognostic challenge of aMCI.

Disclosure: Nothing to disclose

EPO3015

A deficit in visual short-term memory distinguishes MCI and Alzheimer's patients from healthy aging

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Background and aims: To assess Short-Term Memory (STM) in Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) using a novel delayed reproduction task, which obtains a continuous measure of localization error and is potentially more sensitive than conventional correct/incorrect memory tasks.

Methods: 44 MCI and 41 AD patients plus 109 healthy elderly controls (EHCs) were recruited from clinics in Oxford, UK and Jena, Germany. They performed a "What was where?" task (Figure 1). Identification Accuracy (percentage correctly identified items) and Absolute Localization Error were measured. In addition, Misbinding Rate (erroneously localizing an item to the remembered location of another item in the memory array) was determined and errors modeled so that, for example, guessing response rate could be established.

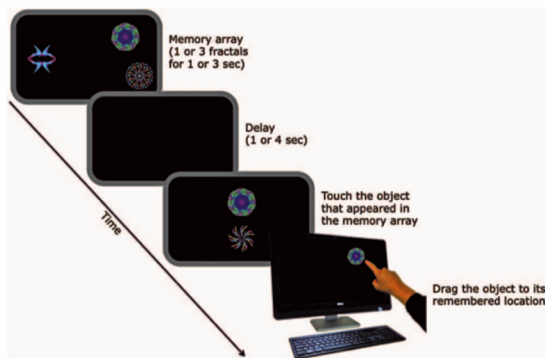


Figure 1 | "What was where?" Short-Term Memory task Participants were presented with either 1 or 3 fractals located randomly on the screen. After a 1- or 4-seconds delay, two fractals appeared at the center of the screen and participants were required to drag the remembered object to its original location.

Results: Both MCI and AD patients had significantly greater mislocalization ($p < 0.001$) and misbinding errors ($p < 0.001$) than EHCs. Importantly, no significant difference between AD and MCI cases was found on these measures. However, MCI cases were significantly more accurate at identifying objects ($p < 0.001$) and showed less guessing compared to AD ($p = 0.003$). EHCs identified the correct object more often ($p < 0.001$) and guessed less ($p < 0.001$) than MCI patients

Conclusion: STM deficits can be identified in AD. The sensitive memory measure used here was also able to detect STM impairment in MCI cases. This type of task might be a useful index of memory for future clinical trials in AD in its earliest stages.

Disclosure: Nothing to disclose

EPO3016

Management of idiopathic normal pressure hydrocephalus (iNPH) - a retrospective study

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Background and aims: Idiopathic normal pressure hydrocephalus (iNPH) is communicating hydrocephalus characterised by normal intraventricular pressures. The aim of this study was to assess the prevalence and management of iNPH in our institution.

Methods: This was a retrospective study carried out at a tertiary health care center. Retrospective case series analysis was conducted using the existing electronic medical record data (2009-2017) on patients with hydrocephalus.

Results: 42 (6.7%) patients with iNPH were identified, mean age 71.5±8.8 years, 21 male (mean age 71.5±9.3 years) and 21 female (mean age 71.5±8.5 years). Ataxia was recorded in 39, symptoms of dementia in 31, and urinary incontinence in 29 patients. 40 patients were treated surgically by placing a ventriculoperitoneal (VP) shunt. 1 of the 2 patients treated by endoscopic 3rd ventriculostomy (ETV) was subsequently treated by placing a VP shunt due to clinical deterioration. Significant improvements were noticed in cognitive and urinary symptoms, in the triad symptom sum score on the Japanese NPH scale, as well as in Evans' index and callosal angle (CA) on brain MRI ($p<0.05$). Significant positive correlation was found between age and gait disturbance (Spearman's $\rho=49.86\%$, $p=0.0017$), age and incontinence (Spearman's $\rho=35.22\%$, $p=0.0351$), age and triad symptom sum score (Spearman's $\rho=44.67\%$, $p=0.0056$), female gender and dementia (Spearman's $\rho=34.94\%$, $p=0.0367$), and among all three variables on the Japanese NPH scale ($p<0.0001$).

Conclusion: Treatment of iNPH with VP shunt showed significant improvement. A properly designed study is required to address the efficacy of ETV in the treatment of iNPH.

Disclosure: Nothing to disclose

EPO3017

Epidemiology of dementia in the very young and the oldest old - insights from prescription claims

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Background and aims: The epidemiology of dementia is shifting rapidly. Diagnostic improvements increase the identification of early onset disease while longevity increases dementia cases late in life.

This development will challenge health care systems in the near future, however, only little data is available on these cohorts. We use a prescription claims database to analyse the changing relationship of age and dementia incidence.

Methods: Insurance claims data covering 98% of the Austrian population were used. We identified patients aged <65 years (early onset) or ≥ 85 years (oldest age) that started treatment with an approved antedementive drug in the period of 2014-2015. Prescription incidence was calculated for 5-year groups using census data, and mortality was recorded through vital registries.

Results: 1076 people below the age of 65 were started on an antedementive drug, and 10414 above the age of 85. In the early onset group, 50% were female compared to 72% in the oldest old group (Figure 1). Cumulative incidence was 0.5/1000 person years in early onset and 33.9/1000 in the oldest old (Figure 2). During a median observation of one year, 5% in the early onset and 30% in the oldest old died (Figure 3).

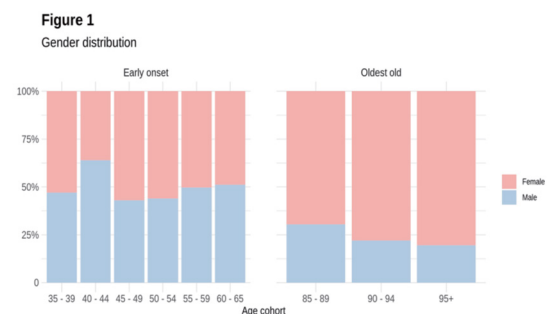


Figure 1 - Gender distribution

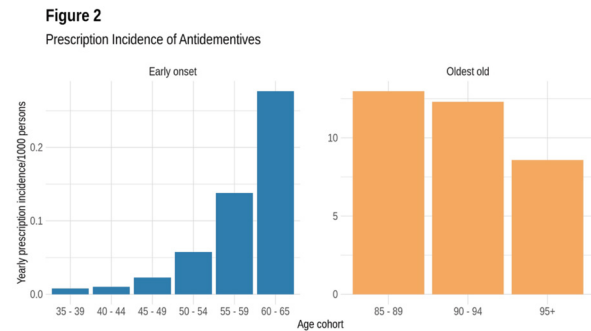


Figure 2 - Incidence

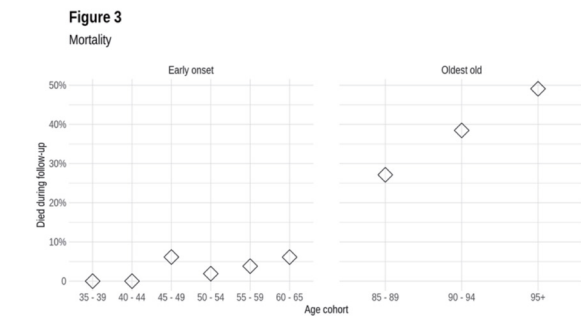


Figure 3 - Mortality

Conclusion: Antidementive medication is frequently started in the oldest old. Prescription in young people is rare but increases linearly with age, suggesting an interplay of age and heritable risk. Gender did not appear to confer substantial risk in this cohort, following the overall distribution in the population.

Disclosure: Nothing to disclose

EPO3018

Amyloid Imaging Findings in Familial and Sporadic Patients with Alzheimer's Disease

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Background and aims: Alzheimer's disease CAD is a multifactorial dementing disorder characterized by amyloid- β , tau deposition and neurodegeneration. There are differences between Familial and Sporadic AD in terms of age of onset as well as cognitive profile and patients' clinical presentation. In this study, we aimed to analyze difference of amyloid- β burden's brain locations between Familial and Sporadic Alzheimer's patients.

Methods: Clinical and imaging data of 17 familial and 18 sporadic Alzheimer's patients, that have no difference between the 2 groups in terms of sociodemographic characteristics and disease duration, from Alzheimer's Disease Neuroimaging Initiative (ADNI) were included in the study. Early-onset FAD (EOFAD), 17 patients, based on the underlying genetic mechanism are: 4 patients have mutation of APP, 11 patients have mutation of PSEN1, 2 patients have mutation of PSEN2. Flutemetamol radionuclide (F-18) marking amyloid PET images were used and analyzed with VINCI ("Volume Imaging in Neurological Research, Co-Registration and ROIs included").

Results: There was no significant difference between the 2 groups in terms of total amyloid burden. In the familial group, the amyloid burden was higher in the insular cortex, striatum, supra marginal gyrus, orbitofrontal cortex and cingulate cortex than in the sporadic group.

Conclusion: The findings of our study support other studies suggesting that frontal and extrapyramidal amyloid burden is higher in familial AD cases compared to sporadic cases.

Disclosure: Nothing to disclose

EPO3019

Deep Proteomic Profiling of CSF from Subjects with Alzheimer's disease Using DIA Mass Spectrometry

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Background and aims: The need for better biomarkers and biological understanding for neurodegeneration is evidenced by the lack of success in developing disease-modifying drugs. Here, we seek to address this unmet need by applying an optimized data-independent acquisition mass spectrometry (DIA-MS) workflow, to deeply characterize the proteomes of cerebral spinal fluids (CSF) from subjects with Alzheimer's disease (AD).

Methods: CSF samples were obtained from AD patients and healthy control subjects, and processed with in-solution digest. A sample specific spectral library was generated by shotgun mass spectrometric acquisition of fractions from the pooled sample. Quantification was performed with DIA-MS using 2hr LC gradients on a Thermo Scientific Q Exactive HF-X mass spectrometer. Data analysis was conducted using Spectronaut software (Biognosys AG).

Results: A CSF protein inventory was generated covering 4,390 proteins. Across all samples, 1,924 proteins were identified and quantified in single-shot acquisitions. The pool of quantified proteins comprises well-characterized biomarkers associated with AD and other neurological disorders including BACE1, APP, MAPT (Tau), SNCA, TREM2, YKL-40, and NEUG. Moreover, the depth and breadth of protein quantification cover numerous pathological mechanisms. Differential expression analysis identified 41 proteins that are significantly dysregulated between AD and control groups. We observed several classes of proteins both up/down-regulated in AD samples including apolipoproteins, components of the complement system, regulators of synaptic functions and markers for oxidative stress.

Conclusion: Optimized DIA-MS enables simultaneous quantitative characterization of close to 2,000 proteins, covering >90% of developmental markers, from CSF with a workflow that is scalable to 100s of samples.

Disclosure: Nothing to disclose

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EPO3020

Wake up stroke: is its characteristics different from that of stroke with known onset time?

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Background and aims: There is still treatment dilemma in many centers worldwide in the management of Wake up stroke (WUS). Both thrombolysis and mechanical thrombectomy have been recently started for acute stroke management in Nepal and these interventions are found to improve clinical outcome in WUS. Since WUS has not been previously studied in Nepal, we aim to study prevalence and clinical characteristics of WUS.

Methods: We prospectively evaluated all the admitted patients of ischemic stroke from 2019 September 1 to 2019 October 30 in Neurology department of Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Results: Among total 60 patients (31 female and 29 male), 15 patients (25%) were of WUS with no significant difference in age (66.2 ± 14.7 years vs 61.5 ± 19.4 years) and gender variation (male: 53.3% vs 45.9%, and female 46.7% vs 54.1%) from stroke with known onset time (SKOT). 10 patients were young stroke group (≤ 45 years), and all were under SKOT group. 6 patients presented with hypertensive crisis, and were all from SKOT group. Among risk factors, Smoking (66.7%) followed by hypertension (46.7%) was common in WUS, and Hypertension (51.1%) followed by smoking (48.6%) was common in SKOT. Cardioembolism was the most common stroke etiology in both WUS (33.3%) and SKOT (46.6%).

Conclusion: In our study, elderly patients are more prone to WUS than younger group. Hypertension and smoking are risk factors of stroke in both WUS and SKOT group, but SKOT group are likely to present with hypertensive crisis.

Disclosure: Nothing to disclose

EPO3021

Digging into stroke etiologies in young patients: A 20-year perspective

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Background and aims: Ischemic stroke (IS) in young adults has rising incidence in recent years with lifelong consequences and socioeconomic burden. A high proportion of this patients remain of undetermined etiology, limiting access to personalized preventive treatments.

We present a series of young patients with IS, with the aim of describing the clinical and epidemiological characteristics, risk factors, outcomes and etiologies.

Methods: Retrospective and descriptive study including all patients between 18 and 50 years with IS from a tertiary hospital in Madrid, Spain, during January 2009 – 2019 period.

Results: We identified 194 patients with IS (130 men, 64 women), 31 were 35 years old or less. Hypertension was the most important traditional risk factor (TRF) in the older group (45%) but was scarce like rest of TRF in the younger group (<15%).

MRI was performed in most of the patients (90%) and showed anterior circulation infarction in 51% of them. After extensive work-up, around 30% of IS remained of undetermined etiology. PFO with or without ASA was present in 10% of the patients. In the younger group, up to 50% of the strokes were classified as “other determined etiology”. Some of these unusual causes were: dissection, vasculitis, antiphospholipid syndrome, illicit drugs, pregnancy and puerperium.

Conclusion: IS in young adults remains a clinical challenge. The lack of TRF and the implication of unusual etiologies, more evident in the very young (less than 35 years old), reaffirms that further investigation and identification of risk factors in this population group is needed.

Disclosure: Nothing to disclose

EPO3022

Stroke etiology involvement in the occurrence of post-stroke seizures

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Background and aims: Nowadays, stroke is considered the leading cause of epilepsy in the elderly, ahead of degenerative diseases, tumors and head trauma. Post-stroke seizures (PSS) are a common complication of stroke constituting a serious morbidity. Many risk factors (RF) have been studied, the involvement of the different etiologies of stroke in the occurrence of epileptic seizures was discussed, but a disparity in different studies was noted.

Methods: A retrospective study was performed from 2009 to 2019 including patients who presented PSS after an ischemic stroke. Diagnostic workup consisted of anamnesis, neurologic examination, and radiologic exams. Multiple data have been collected. A complete etiological workup was performed and stroke etiology was determined using TOAST classification.

Results: 50 patients were included (36 men, 14 females) with a median age of 60 years, and of 55 years at the onset of PSS. In cardio-embolic stroke, PSS was observed in 18 cases (36%), and it was noted in 17 with atherosclerosis (34%). Other determined etiologies were seen in 6 cases (12%), arterial dissection in 3 cases (6%), and small-vessel disease in only one case. However, 5 cases (10%) remained unexplained with the diagnosis of cryptogenic ischemic stroke.

Conclusion: The implication of stroke etiology in the occurrence of PSS was discussed in different studies and results differ suggesting mostly a higher risk in cardio-embolic etiology in some, or in atherosclerosis in others. But more studies need to be performed.

Disclosure: Nothing to disclose

EPO3023

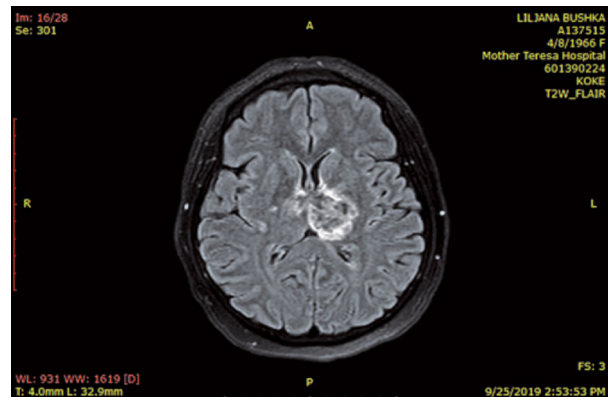
Bilateral Thalamic Infarct : A presentation of DCVT in basal veins of Rosenthal

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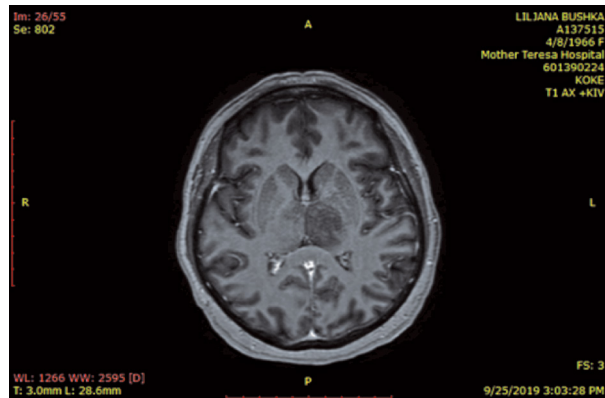
Background and aims: Deep Cerebral Vein Thrombosis (DCVT) is a term used for thrombosis of internal cerebral vein, vein of Galen and basal vein of Rosenthal. It is an uncommon cause of stroke. The diagnosis of DCVT is often missed. Hyperhomocysteinemia may be responsible about 40% of cerebrovascular diseases. We present the case of a 53-year-old woman with headache, vertigo, nausea and vomiting, diarrhea and a temperature of 37.5 degree Celsius for the last 2 days. She refers for frequent occipital headache during the last 10 years. MRI two days before was normal. It was initially thought to be meningoencephalitis.

Methods: This is a case report with literature review of a patient in our clinic.

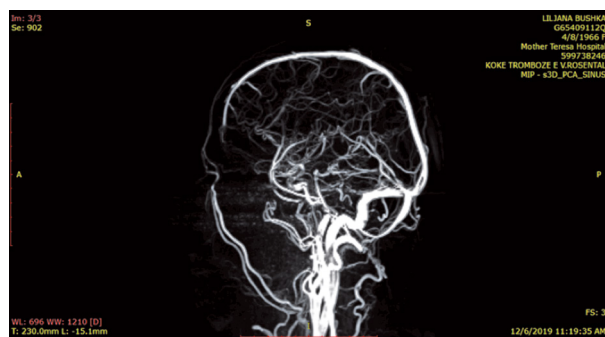
Results: The patient made multiple seizures with alteration of consciousness which were confirmed on EEG. MRI with contrast showed bilateral thalamic lesions. There was no visualization of vv. Rosenthal and hemosiderin was present, suggesting venous infarct with hemorrhagic transformation. Hyperhomocysteinemia was detected which is the possible cause of this thrombosis.



T2 -FLAIR: Bilateral thalami and basal ganglia hyperintensity on FLAIR images



T1 + IV contrast: Image showing hypointensity in bilateral thalami and basal ganglia



MPI s3D PCA Sinus

Conclusion: In our case just like most cases of deep cerebral venous thrombosis, the thalamus is affected bilaterally. Even though the prognosis in such cases is worse, compared to unilateral lesions, our patient recovered completely. A high index of suspicion is needed for early diagnosis of DCVT. It has favourable outcome, if recognized and treated early. MRI brain should be done early in cases of unexplained altered sensorium. If MRI is suggestive of DCVT, then MRV should be done for confirmation.

Disclosure: Nothing to disclose

EPO3024

The relationship between immature platelet fraction and TOAST classification in acute ischemic stroke

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Background and aims: Immature Platelet Fraction (IPF) is the indicator reflecting platelet production and the rate of platelet turnover. The increase of IPF means the increase of platelet activation. IPF is increased in the patient of acute coronary syndrome. It is caused by the elevation of thrombotic ability due to platelet activation. But the role of IPF in the patient of ischemic stroke is still unknown. We investigated the usefulness of IPF as the biomarker in the ischemic stroke.

Methods: This was a single-center study recruiting 285 acute ischemic stroke patients who had visited our hospital from March 2018 to March 2019. Whole blood samples were quantified via Sysmex XE-2100 hematology analyzer within 30min of blood sampling. High IPF was defined as more than 3.38%, it was set as above upper level of 95% confidence interval of all enrolled participants.

Results: We divided patients with cardiogenic ischemic stroke (CE, 87 patients, 30.5%) and with non-cardiogenic ischemic stroke (non-CE, 198 patients, 69.5%) by diagnostic criteria of TOAST classification. In this study, The mean [95% confidence interval] of IPF was 2.44 [2.17-2.74] in CE group, and 2.00 [1.83-2.17] in non-CE group. High IPF was significantly higher in CE group than that observed in non CE-group (21.8% vs 11.6%, $p=0.025$), but the its difference between 2 groups was not significant after multivariate logistic regression analysis.

Conclusion: CE group have a high IPF compared to non-CE group, but we should further demonstrate clinical significance of IPF in ischemic stroke classification.

Disclosure: Nothing to disclose

EPO3025

New outcome predictors in cerebral venous sinus thrombosis-case series

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Background and aims: Cerebral venous sinus thrombosis (CVST) is a rare case of stroke, usually affecting young people. During last decades outcome of CVST improved a lot, but predictors of outcome are still being analyzed, such as use of oral contraceptives. Most accepted score is based on findings of large International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT), but in recent years some studies analyzed other factors as prognostic inflammatory markers, most of which are derived from full blood count analysis. Aim of this study was to evaluate association between outcome in patients with CVST and certain blood parameters.

Methods: We analyzed case series of patients with CVST admitted to Clinic of Neurology, of Clinical Centre of Vojvodina in Novi Sad, during the last 2 years. Admission values of platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), and ICSVT score were calculated in 2 groups of patients based on modified Rankin Score (<3) three months after discharge.

Results: During 2 year period, 7 patients were admitted, 4 women, average age was 46 years. Only patient with unfavorable outcome that was admitted died during hospitalization. Patient with poor outcome had higher ISVCT Score (4 vs 1). LMR was lower in the poor outcome patient (4.07 vs 1.05), while PLR (132,3 vs 170) and NLR (4,72 vs 11) were higher.

Conclusion: Although underpowered, our analysis shows that simple full blood count subanalysis may be a useful prognostic marker in CVST

Disclosure: Nothing to disclose

EPO3026

Posthypoxic encephalopathy in patients after coronary artery bypass grafting: clinical and neuroimaging features

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Background and aims: Posthypoxic encephalopathy is a frequent complication after coronary artery bypass grafting (CABG), including stroke, delirium of the early postoperative period, postoperative cognitive dysfunction (POCD). Its more pronounced prevalence and severity during the operation with the cardiopulmonary bypass (CPB) still deserves discussion.

Purpose. To analyze the characteristics of various types of cerebral dysfunction in patients undergoing CABG.

Methods: Patients and methods. The study included 108 patients who received CABG for coronary heart disease in a planned manner. Group 1 included 28 patients operated on a beating heart. 80 patients were operated with CPB: 51 of them formed group 2, and 29 patients who also were given peptide methionyl-glutamyl-histidyl-phenylalanyl-prolyl-glycyl-proline for neuroprotection formed group 3. Neuropsychological testing and MRI of the brain in structural and functional techniques were carried out.

Results: Posthypoxic encephalopathy was diagnosed in 7% (group 1), 63% (group 2) and 27% (group 3) patients.

In group 1 functional MRI (fMRI) detected changing in functional connection of postcentral gyrus, right sensorimotor gyrus, amygdala and right intracalcarine cortex ($p < 0,05$). In group 2 fMRI revealed changing in functional connection of the medial prefrontal cortex with the posterior cingulate gyrus, temporal gyrus, insula, cerebellum. In group 3 MRI noted changing in posterior cingulate gyrus, frontal orbital cortex, amygdala.

Conclusion: In patients operated with CPB, cerebral complications are diverse and highly frequent. Performing MRI scans allows to identify morpho-functional changes in the brain. methionyl-glutamyl-histidyl-phenylalanyl-prolyl-glycyl-proline can be used as effective pharmacological neuroprotection strategy.

Disclosure: Nothing to disclose

EPO3027

Short-Term Effects of Transcranial Direct-Current Stimulation on Naming in Subacute Stroke Patients with Aphasia

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Introduction: Aphasia after stroke is a frustrating language disorder for which specialized speech and language therapy is the most efficient treatment. Various naming errors can be found in a stroke patient. We wanted to examine: Can tDCS improve effects of speech language therapy in a short post-stroke period.

Methods: 15 aphatic patients with subacute stroke, underwent anodal tDCS (A-tDCS, 15min, 1.5mA) over the left perilesional dorsolateral prefrontal cortex and standard speech and language therapy. Stimulation was done with the Soterix Medical 1 x 1 device, clinical standard in the field of non-invasive neuromodulation. 15 consecutive sessions (5 days per week for 3 weeks) were implemented. Logopedic evaluation was performed with Naming sub tests of Boston Diagnostic Aphasia Examination (BDAE) before and after application of tDCS.

Results: The mean age of patients was 62.20 (± 8.52), 66.66% were male. Treatment began an average of 37.86 days after stroke. Ischemic stroke was present in 14 patients, hemorrhagic in 1 patient. 11 patients had sensorimotor aphasia (global), 4 patients had motor (Broca's) aphasia. The average success on Naming sub tests before and after tDCS was: Responsive 25.76-44.43%; Confrontation 30.6-43.73%; Body-part 27.25-28.17%; Animal 19.22-29.61%. The correlation between the initial and final estimates on Naming sub test is very high, the average for the measured parameters is $r=0.897$

Conclusion: We found a significant beneficial effect of A-tDCS in all our aphatic patients, although with some inter-individual differences.

Disclosure: Nothing to disclose

EPO3028

Complications of mannitol therapy in patients with acute stroke - A prospective observational study

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Background and aims: Mannitol is one of the frequently used drug to treat cerebral edema resulting from ischemic and hemorrhagic strokes. Mannitol administration is associated with complications such as acute kidney injury and electrolyte imbalance.

Methods: We did a prospective longitudinal observational study of patients with acute stroke who received mannitol. Study was conducted in Father Muller Medical college from January 2019 till September 2019 after taking Institutional ethics committee clearance. After taking informed consent, nature of the stroke, presence of comorbidities and dosage of mannitol given was recorded. Serum electrolytes, Serum urea and creatinine were recorded at admission and in first week.

Results: Total of 72 patients were included in the study. Mean age was 57.7 \pm 14.6 years and Male:female ratio was 2.3:1. Ischemic stroke was seen in 42% patients and hemorrhagic stroke was seen in 58% patients. Patients received mannitol at the dose of 1-1.5gm/kg/day. Cumulative dose of mannitol was 180g \pm 177.3 grams. Serum sodium levels were significantly lower during 1st week compared to admission where as serum potassium and chloride levels were not significantly changed during therapy. There was statistically significant elevation in serum urea levels from admission to 1st week where as creatinine levels were not significantly altered. Total cumulative dose was compared to serum electrolyte levels and urea and creatinine at admission and first week and no significant changes were found

Conclusion: Low dose mannitol therapy doesnot produce significant electrolyte or renal function abnormality in patients with acute stroke.

Disclosure: Nothing to disclose

EPO3029

ACCURACY OF INTRACEREBRAL HEMORRHAGE VOLUME CALCULATION: COMPARISON BETWEEN A FULLY AUTOMATIC COMPUTERISED METHOD, ABC/2 and sABC/2

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Background and aims: Rigorous estimation of the intracerebral blood volume in patients with intracerebral hemorrhage (ICH) is of major importance since it guides important treatment decisions. We aimed to determine the accuracy of the ABC/2 and sABC/2 methods relative to a fully automatic computerised method (FACM) for measuring ICH volumes.

Methods: Neuroimaging data were prospectively collected for 73 patients with ICH. Agreement between FACM, ABC/2 and sABC/2 methods was evaluated using the Bland-Altman plots. FACM was considered the reference method.

Results: Median ICH volumes and 25-75IQR assessed with the FACM, ABC/2 and sABC/2 were 8.6mL (3.1–24.5), 6.2mL (2.2–17.8) and respectively 9.5mL (3.5–30.1). ABC/2 method systematically underestimated FACM with a mean difference of – 14.9mL (95% CI -6.3-2.08). Conversely, sABC/2 systematically overestimated FACM with a mean difference of 8.4mL (95% CI 3.74-13.1). Since we observed an increase in variability of the ICH volume differences assessed with the 3 methods as the ICH volumes increased, we created second Bland – Altman plots using the geometric means which showed an ABC/2 to FACM ratio of 0.7 and a sABC/2 to MVS ratio of 1.19.

Conclusion: Absolute haematoma volumes might vary depending on the technique used. Further work is needed to identify the most suitable methods for ICH volume measurement and to estimate their clinical impact.

Disclosure: Nothing to disclose

EPO3030

Exploring the prognostic value of left atrial volume index in cardioembolic acute ischemic stroke

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Background and aims: Left atrial volume index (LAVI) has shown to have prognostic implications in multiple cardiologic pathologies and recent studies proposed LAVI to be related with increased mortality in acute ischemic stroke (AIS). Our aim was to retrospectively evaluate the relationship between LAVI and cardioembolic AIS clinical characteristics and prognostic outcomes.

Methods: Demographics, comorbidity profile and stroke clinical characteristics and prognostic outcomes of patients with cardioembolic stroke due to atrial fibrillation admitted to a stroke unit of a tertiary hospital were analysed with SPSS®.

Results: In 131 patients, with a median age of 80 years and a majority of female (61.1%), hypertensive (86.3%), neither diabetic (74.8%) nor obese (70.4%) individuals, the mean LAVI was 42.85mL/m² and 89.4% had abnormal LAVI values (>28mL/m²). Patients with higher C-reactive protein levels at admission ($r=0.227$; $p=0.018$) and total anterior circulation infarcts (TACI) (71.16 vs. 53.38mL/m²; $p=0.009$) had increased LAVI. Significantly higher LAVI values were found in patients who died during hospital stay (90.27 vs. 63.78mL/m²; $p=0.018$), even after adjustment for confounding variables, and the ones discharged with higher Rankin scores (67.69 [3-6] vs. 52.14 [0-2] mL/m²; $p=0.014$; $r=0.311$; $p<0.001$), though this association was dependent on the presence of TACI. No significant relationship was found between LAVI and the remaining analysed parameters, namely long-term mortality and Rankin score at 6-month follow-up.

Conclusion: LAVI seems to have a possible in-hospital prognostic role, with an independent association with greater mortality. Bigger cohort and prospective studies should be pursued to clarify this association.

Disclosure: Nothing to disclose

EPO3031

The impact of thyroid function in the clinical features and prognostic outcome of acute ischemic stroke

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Background and aims: There is a bidirectional association between thyroid metabolism and stroke. Thyroid dysregulation following acute ischemic stroke (AIS) has been associated with greater stroke severity, higher mortality rates and a poorer long-term functional outcome. Our aim was to retrospectively evaluate the relationship between changes in thyroid function and clinical and prognostic outcomes of AIS.

Methods: Out of 1172 AIS patients, 96 (8,2%) had acute thyroid changes (TC) after stroke and were paired by gender with patients without thyroid changes (WTC). A statistical analysis was carried out considering demographic data, comorbidity profile, and clinical and prognostic stroke outcomes.

Results: The TC group registered a higher frequency of use of reperfusion therapy (38.5 vs. 24%; OR=1.99; 95%IC: 1.067-3.712), even after adjustment for confounding variables, higher average NIHSS score at admission (7.5 vs. 5; p=0.042) and higher mortality rates (6.3 vs. 0%; p=0.029). Cardioembolic strokes (34.4 vs. 17.7%; OR=2.434; 95%IC: 1.243-4.768) and total anterior circulation infarcts (37.2 vs. 21.1%; OR=2.225; 95%IC: 1.165-4.247) were more prevalent in this group. In the WTC group, there was a higher prevalence of small vessel disease (25.0 vs. 12.5%; OR=0.429; 95%IC: 0.200-0.917). There were no significant differences in NIHSS and Rankin scores at the time of hospital discharge and at six months, duration of hospital stay, stroke recurrence, and TOAST and OCSF classification.

Conclusion: Though retrospective, this study showed a link between TC following AIS and stroke severity and mortality. Nevertheless, this connection is complex and multiple factors intervene. Studies with larger cohorts should aim to clarify it.

Disclosure: Nothing to disclose

EPO3032

Atrial Fibrillation and Ischemic Stroke, Predicting Outcome

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Background and aims: Patients with atrial fibrillation (AF) are at increased risk of stroke, usually associated with poorer outcomes.

Methods: We present a cohort of patients with acute ischemic stroke admitted to Stroke Center, Department of Neurology, University Clinical Center of Republic of Srpska in Banja Luka in 2018. year. The main outcomes considered were mortality, NIHSS and modified Rankin score at admission and at discharge.

Results: Among 305 patients with acute ischemic stroke, 106 (34.8%) had AF. Overall, AF patients had higher risk of death at 30 days (43.3% versus 17.6%), higher NIHSS at admission (13.8 versus 11.5) and at discharge (7.8 versus 4.9), higher modified Rankin score at admission (4.4 versus 3.8) and at discharge (4.3 versus 3.2), compared with non-AF patients.

Conclusion: AF is highly prevalent among stroke patients and is one of the top risk factors associated with poor functional outcome. Stroke patients with AF have higher mortality compared with non-AF patients.

Disclosure: Nothing to disclose

EPO3033

Strokes in the young: a rising concern

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Background and aims: Trends have emerged internationally showing incidence of "young strokes" (stroke affecting people under the age of 45 years) is escalating. They have mechanisms of stroke when compared to older patients. Despite improvement in stroke care, it remains a leading cause of mortality and morbidity.

We aimed to analyse all acute stroke presentations under the age of 45 years over 12 months and to identify the mechanism.

Methods: A retrospective chart review was undertaken on all patients under the age of 45 years presenting with ischaemic stroke from January 1st 2010 to September 30th 2019 in a tertiary referral centre. Details regarding presentation, vascular territory, management, and aetiology were analysed. TOAST criteria was used to assign stroke mechanism

Results: A total 3420 patients presented with acute strokes over the 10 year period. One hundred and seventeen patients were enrolled. 74% were ischaemic strokes. The majority were cryptogenic (26%). "Other determined aetiology" accounted for 21%, 11% were secondary to small vessel disease, cardioembolic (11%), and 4% were from large vessel atherosclerosis. 6 patients were thrombolysed, and 2 underwent thrombectomy. The "other determined aetiology" was made up of carotid and vertebral artery dissection, hypercoagulability, antiphospholipid syndrome, vasculitis, and substance abuse. No patients had iatrogenic causes for stroke.

Conclusion: The mechanism of stroke in the young differs significantly. This population requires more extensive testing, and a meticulous search for risk factors and underlying pathologies. Further investigations into cryptogenic strokes can improve the long term outcome and decrease the burden of strokes on the healthcare system.

Disclosure: Nothing to disclose

EPO3034

How Does Hyperlipidaemia Influence Functional Outcome in Patients with Ischemic Stroke, Treated with Intravenous Thrombolysis?

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Background: The relationship between hyperlipidaemia and ischemic stroke is complex. There are number of trials that found no link between dyslipidaemia and ischemic stroke. On the other hand, epidemiological studies find modest relationship between high low-density lipoprotein (LDL) cholesterol level and the risk of ischemic stroke, while low LDL-cholesterol levels increase the risk of intracranial haemorrhage.

Aim: We aimed to evaluate the influence of hyperlipidaemia on 3-month functional outcome after ischemic stroke, treated with intravenous thrombolysis.

Methods: This retrospective cohort study included patients treated with intravenous thrombolysis for acute ischemic stroke in 10-year period. Lipid disorders were classified according to the Fredrickson classification. Primary outcome was defined as functional independence (modified Rankin score 0-2).

Results: Laboratory data on dyslipidaemia were available in 360 patients that received intravenous thrombolysis. Functional independence was achieved in 54.9% of cases. All types of hyperlipidaemia were significantly positively associated to favourable outcome. Patients with hyperlipidaemia type IIa had favourable outcome in 66.7%, those with type IIb in 57.6%, while those with type IV had favourable outcome in 75.8%. Patients with normal lipid levels were less likely to achieve favourable functional outcome.

Conclusion: We observed a protective effect of elevated lipid levels in patients treated with alteplase, leading to better 3-month functional outcome. This fact can be attributed to antioxidative effect of cholesterol and its neuroprotective effect, but also the use of statins, which were given to all patients with dyslipidaemia as a part of secondary prevention.

Disclosure: Nothing to disclose

EPO3035

Establishment of an Organotypic Culture System of Cortico-striatal Brain Slices to Investigate Cerebral Hypoxia ex vivo

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Background and aims: Unlike primary single cell cultures, organotypic brain slice cultures (OSC) conserve all major cell types in a three-dimensional tissue architecture allowing a profound study of morphological and (patho-) physiological changes. Importantly to note, only few OSC systems comprising the striatum as the primary affected structure in experimental ischemic stroke have been developed.

Methods: Cortico-striatal slices of neonatal mice were cultivated for 8 days in vitro (div). Cell viability was assessed by a lactate dehydrogenase (LDH) assay and by histological examination of cell morphology and tissue architecture. Furthermore, OSC were exposed to different concentrations of Triton X-100 and hypoxic-hypoglycemic conditions provoked by oxygen and glucose deprivation (OGD) on div 7.

Results: Histological fluorescence and Nissl staining revealed a better OSC viability when maintained in serum-free compared to serum-containing culture medium. Cell death peaked at div 1 and remained low thereafter until the end of cultivation period (<10%). A gradual increase of cell death in the OSC was induced by treatment with increasing concentrations of Triton (0.01%, 0.1%, 1%) for 24h or exposition to OGD for 25min, 90min and 5h with 24h reperfusion.

Conclusion: We provide an ex vivo OSC system of cortico-striatal structures that remains viable over 8 days in culture with inducible gradual cell death. Modulation of cell death by OGD in this OSC system represents a promising tool to study the effects of hypoxic-hypoglycemic conditions, complex interactions and novel treatment approaches.

Disclosure: Nothing to disclose

EPO3036

Effect of therapy on Stroke Mortality and Prognosis in a cohort of 121 patients with Atrial Fibrillation

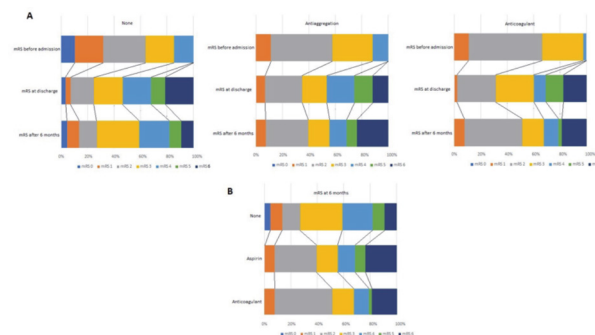
N. Rifino¹, C. Scaccabarozzi², V. Mantero², A. Aliprandi², D. Sangalli², G. Costantino², M.G. Filizzolo³, C. Ferrarese¹, A. Salmaggi²

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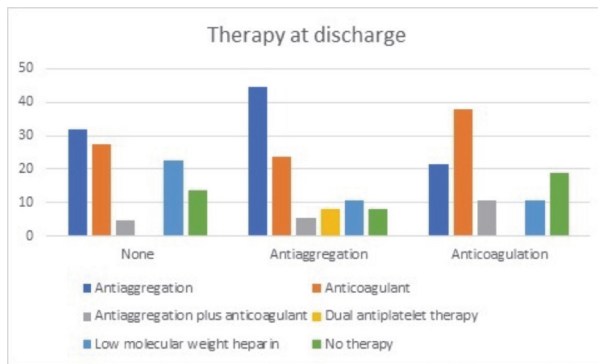
Background and aims: The incidence of stroke in patients with atrial fibrillation (AF) is greatly reduced by oral anticoagulation (OA). However, some patients are not treated with OA because of high bleeding risk. The effect of pre- and post-hospitalization treatment on the severity and prognosis of AF-related stroke is not clear.

Methods: Retrospective study including 121 patients with AF (known or unknown) admitted for ischaemic stroke between 2012 and 2013. We divided our population into 3 groups, depending on their treatment prior to admission (None-N; Antiaggregation-AGG; Anticoagulation-AC). We calculated their modified-Rankin scale (mRS) before admission and at discharge. Then, we considered subgroups distinguished by therapies at discharge and we calculated mRS at 6 months.

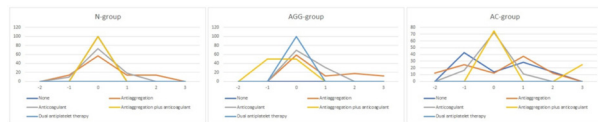
Results: Patients not treated or on anticoagulation prior to admission had a higher mortality-rate compared to those on antiplatelet therapy (N-21.4%; AGG-12%; AC-17.8%) (Fig.1a); however, patients in the N-group had a more severe stroke (mean-NIHSS: N-11.9; AGG-11.3; AC-9.7; median-NIHSS: N-12.5; AGG-9.5; AC-5). Mortality-rate at 6 months was greater in the AGG- and AC-groups (N-9%; AGG-23.7%; AC-18.9%) (fig.1b). Fig.2 shows the rate of patients according to their therapies at discharge for each group. The rate of patients with a worse mRS after 6 months was greater in the AGG- and AC-group compared to the N-group (N-19%; AGG-31%; AC-27%). No significant differences in mRS at 6 months were detected between patients according to their treatment at discharge(Fig.3).



A. Shift analysis of the mRS score before admission, at discharge and after 6 months for each group (Not treated, Antiaggregation and Anticoagulation). B. Shift analysis that compares the mRS score after 6 months for each group



Rates according to the therapies at discharge for each group



Difference between mRS at discharge and after 6 months for each group distinguishing patients according to their therapies at discharge

Conclusion: Our findings suggest that patients with AF receiving anticoagulant or antiplatelet therapy before stroke have a worse prognosis and a higher mortality during hospitalization and at 6 months compared with those not treated. Therapy at discharge did not affect functional status at 6 months.

Disclosure: Nothing to disclose

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EPO3037

Do patients over 80 years old benefit from reperfusion therapy in an acute stroke?

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Background and aims: Patients older than 80 have limited representation in the reported studies. This implies little evidence on the benefit of treatments in this age group. Our objective is to assess whether reperfusion treatments in stroke are safe and effective in this group of patients in our center.

Methods: In a retrospective series of 202 patients treated in an acute stroke, we carry out a comparative analysis between the groups over 80 years old and those under 80, mainly according with the functional outcome (modified Rankin scale after 3 months) and safety (symptomatic hemorrhages and mortality).

Results: 59 patients (29.2%) were over 80 years old. The previous Rankin and the NIHSS were significantly higher in the older patients; there were no significant differences in the previous ASPECTS or in the door-to-needle time in fibrinolysis between the groups. The percentage of Rankin less than or equal to 2 in the group <80 was 58.3% and 27.1% in the group >80; there were no significant differences in the number of symptomatic hemorrhages between both groups; mortality at 3 months was 35.6% in >80 and 10.1% in <80.

Conclusion: In our study, the efficacy and safety results are worse in the age group >80 compared to the younger group. The groups also differ in previous functional situation and in the severity of the stroke. We believe it is necessary to improve the treatment selection criteria in >80.

Disclosure: Nothing to disclose

EPO3038

SuPAR level's correlation with degree of disability, death and other inflammatory factors in patients with ischemic stroke.

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Background and aims: Soluble urokinase plasminogen activator receptor (suPAR) seems to be inflammatory biomarker elevated in cardiovascular disease, including stroke. The aim of this 3-year follow up prospective study was to evaluate suPAR levels in patients with a 1st ischemic stroke in correlation with inflammatory markers (CRP, PCT, NT-proCNP), marker of endothelial damage (endothelin 1-21, NT-proCNP) and to investigate the impact of suPAR and other markers on prognosis and death.

Methods: Fifty patients (mean age 73.7±11.9 years, 26F and 24M) with a 1st ischemic stroke were included in this study. Blood samples were collected on the first (suPAR1), third (suPAR2) and seventh day after stroke onset (suPAR3). Blood samples were analysed for suPAR, CRP, PCT, endothelin and NT-proCNP serum levels using enzyme-linked immunoabsorbent assay ELISA. The phone interview was conducted to collect follow-up information after 24 and 36 months (Rankin and Barthel scales).

Results: The positive correlation between suPAR levels and other inflammatory biomarkers (except endothelin 3) was observed. The negative correlation between suPAR1 and Rankin scale at 36 month was observed ($r=-0.406$, $p=0.003$). Logistic regression model revealed no significant effect of suPAR on death occurrence in first 24 months (suPAR1 ($p=0.203$), suPAR2 ($p=0.0953$), suPAR3 ($p=0.236$)). Non-significant effect was observed for dynamic of suPAR on death difference between suPAR1 and suPAR2 ($p=0.0865$) and between suPAR1 and suPAR3 ($p=0.20$).

Conclusion: suPAR level can be new potential inflammatory marker in ischemic stroke. There is no major impact on death, however suPAR level may be associated with the degree of disability or dependence in daily activities after stroke.

Disclosure: Nothing to disclose

EPO3039

Predicting outcome in intracerebral hemorrhage by transcranial duplex sonography

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Background and aims: Intracerebral hemorrhage (ICH) volume on admission and severity measured by NIHSS are the main prognostic factors in ICH. Transcranial duplex sonography (TDS) showed good correlation with CT scan measuring bleeding extent in acute phase. Our aim was to evaluate TDS in monitoring ICH and its relation with prognosis.

Methods: Prospective study of patients with supratentorial ICH evaluated within 24 hours of onset. All patients underwent CT scan and TDS exam on admission, 48 hours and at 7 days. Hematoma volume was determined using the formula $(\text{longitudinal} \times \text{sagittal} \times \text{coronal}) / 2$, Midline shift (MLS) was calculated according to the formula: $\text{MLS} = (A - B)$, in both techniques. Association of ICH volume and MLS measured by TDS with outcome at 3 months by modified Rankin Scale was evaluated.

Results: 45 patients were included. ICH was not measured by TDS in 12 cases due to the lack of transtemporal window. Mean age was 66.3 year-old and 23 (51.1%) were male. A significant correlation with CT between determinations was found for mean ICH volume ($r=0.791$, $p<0.001$ on admission; $r=0.708$, $p<0.001$ at 48hs; $r=0.672$, $p<0.001$ at 7 days) and MLS ($r=0.548$, $p=0.003$ on admission; $r=0.696$, $p<0.001$ at 48hs; $r=0.760$, $p<0.001$ at 7 days) measured with TDS. ICH volume measured by TDS was related with dependency at 3 months ($p=0.045$). MLS measured with TDS was associated with mortality at 3 months.

Conclusion: Hemorrhage volume and Midline shift measured by TDS are a useful tool for monitoring ICH at bedside and for predicting outcome.

Disclosure: Nothing to disclose

EPO3040

Idarucizumab for Dabigatran reversal in patients with acute ischemic stroke receiving intravenous thrombolysis: Our experience

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Background and aims: The use of direct oral anticoagulants 48 hours prior to acute ischemic stroke is a contraindication for intravenous thrombolysis (IVT) in the current guidelines. Idarucizumab is a humanized monoclonal antibody who can quickly reverse the anticoagulant effects of the thrombin inhibitor Dabigatran. Experience with Dabigatran reversal previous to IVT is limited. We present our clinical experience with three new cases of IVT after reversal Dabigatran effect with Idarucizumab.

Methods: We performed an observational, retrospective study of patients treated with IVT after Dabigatran reversal with Idarucizumab from January 2018 to December 2019 at our comprehensive stroke centre. Clinical, radiological and prognostic variables, including hemorrhagic complications, were collected.

Results: 2 women and 1 man of 78, 82 and 55 years with atrial fibrillation treated with Dabigatran 150mg (2 patients) and Dabigatran 110mg (1 patient) with an acute ischemic stroke (NIHSS 7, 16 and 8 respectively) were included. Activated partial thromboplastin time (aPTT) was abnormal in all cases. AngioCT revealed a distal occlusion not accessible by mechanical thrombectomy. IVT was initiated 10 minutes after the infusion of Idarucizumab 5mg, with a door-to-needle time of 95, 115 and 136 minutes. No thrombotic, systemic hemorrhage or symptomatic intracranial hemorrhage events were detected. At discharge, NIHSS were 0, 7 and 2. All patients were independent (Rankin modified score at 3 months was 0, 2 and 1).

Conclusion: In our experience, Dabigatran reversal with Idarucizumab is safe and may improve the prognosis of this patients. Specific protocols are needed to improve the door-to-needle time.

Disclosure: Nothing to disclose

EPO3041

Ramadan fasting and intracerebral hematoma: Incidence and outcomesS. Salama¹, K. Eltukhy², H. Egila³¹Mansoura, Egypt, ²Neurology, Mansoura University Hospital, Mansoura, Egypt, ³Department of Neurology, Faculty of Medicine, Mansoura University, Egypt, Mansoura, Egypt

Background and aims: Fasting over a prescribed period of time is a common religious tradition practiced by several prominent faiths in the world. It is also currently regaining interest as a medical practice, both as preventive and as therapy and/or simple choice of lifestyle. For the 1st time, we evaluate the effect of Ramadan fasting on incidence of intracerebral hematoma and its outcomes.

Methods: 69 patients enrolled in this study, 18 patients were fasting in Ramadan, 14 patients were not fasting and 37 patients 1 month later which isn't a recommended fasting month among Muslims. The in-hospital clinical course and mortality rate of these patients were recorded. They were assessed using routine lab, CT brain, National Institutes of Health Stroke Scale (NIHSS) score and Modified Rankin Scale (mRS) score.

Results: About 22% of fasting patients (8 patients) with intracerebral hematoma died, 28.6% non-fasting patients died (8 patients) and 20.5% of patients died in the month after Ramadan (16 patients) with no significant difference between the 3 groups ($p > 0.05$). Also as regard NIHSS, hematoma expansion and mRS, there were no significant difference between the 3 groups ($p > 0.05$).

Conclusion: Ramadan fasting showed neither protective effect nor worsening as regard incidence or bad impact on patients with spontaneous intracerebral hemorrhage.

Disclosure: Nothing to disclose

EPO3042

Atrial Fibrillation and Stroke or Stroke and Atrial Fibrillation?

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Background and aims: There is some controversy regarding if atrial fibrillation (AF) discovered after stroke was the cause of stroke and therefore preexisting (cardiogenic) or if it can be a stroke consequence (neurogenic). These 2 entities may differ in subsequent stroke risk. We aimed to study if patients diagnosed with AF after stroke had previous heart rhythm changes that could be associated to a higher risk of developing AF supporting the cardiogenic hypothesis.

Methods: We performed a case-control study and included patients admitted to a stroke unit from 2009 to 2019, with the diagnosis of ischemic stroke. In order to be included patients had to have a 24h ECG Holter monitoring performed before stroke occurrence. We excluded patients with previous diagnosis of AF. Our cases were patients that developed atrial fibrillation on the 1st 5 days after stroke. Controls were patients that maintained sinus rhythm. We collected data regarding sex, age, medication, personal history, stroke territory and time before stroke of the 24h ECG Holter recording. We compared the two groups regarding time (HR, PNN50, RMSSD, VarIndex, SDANN) and frequency (total power, VLF, LF, HF, LF/HF) domains of the ECG Holters.

Results: We included 9 cases and 11 controls. Cases were older than controls. There weren't other statistical differences between the 2 groups namely regarding time or frequency domains of the ECG Holters.

Conclusion: The absence of previous changes in the ECG Holters of patients that developed AF in the first days after the stroke supports the neurogenic hypothesis.

Disclosure: Education for Science by GAPIC

EPO3043

Diplopia – an atypical cause in an atypical location

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Background and aims: Diplopia has an extensive differential diagnosis, however posterior reversible encephalopathy syndrome (PRES) doesn't come to mind in first place. PRES is a clinical and radiological diagnosis, usually presenting with headache, seizures, vision disturbances and encephalopathy. Brain magnetic resonance (MRI) shows vasogenic oedema predominantly involving the bilateral parieto-occipital regions. With this case, we aimed to describe an atypical variant of PRES.

Methods: Case report.

Results: A 58-year-old woman, with known hypertension, presented with a 3-day history of binocular horizontal diplopia. Her blood pressure was 184/100mmHg and a left abducens palsy was the only finding at examination. Brain computed tomography scan showed no abnormalities and microvascular ischemia was deemed as first diagnostic hypothesis. However, her MRI showed hyperintense areas in fluid-attenuated inversion recovery (FLAIR) involving bilaterally the posterior mesencephalon, sparing the red nuclei, with extent to the left paramedian pons. These areas showed no restricted diffusion. Her blood pressure was lowered to normal range values and the diplopia resolved five days after admission. Her blood work and cerebrospinal fluid showed no relevant abnormalities, including sodium values. 9 days later, a second MRI showed almost complete resolution, favouring PRES diagnosis and excluding other entities. She was discharged completely asymptomatic.

Conclusion: In our case, the clinical and radiological improvement with only blood pressure control favours this atypical diagnosis. Isolated brainstem involvement in PRES is rarely reported, but as the classical presentation, is usually reversible. We highlight the importance of MRI imaging in diagnosing those cases, otherwise this interesting variant could be missed.

Disclosure: Nothing to disclose

EPO3044

The role of individual sensitivity to sodium in development of cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (CSVD) is 1 of the main causes of cognitive impairment, ischemic and hemorrhagic strokes. Sodium consumption could be 1 of the risk factors of CSVD, what could be connected with individual sensitivity of patients to its overindulgence with salt.

The aim is assessment of the role of individual sensitivity to sodium in development of CSVD.

Methods: The study included 73 patients (mean age 60.1±6.5, 48 (65.8%) women) with CSVD according to STRIVE criteria (2013). The control group consisted of 19 volunteers (mean age 56.9±5.4 years, 14 (73.7%) women). Individual sensitivity to sodium were estimated by measurement the buffer capacity of erythrocyte glycocalyx toward sodium and erythrocyte resistance to lysis in hypotonic solutions with decreasing concentrations. The relation between individual sensitivity to sodium and CSVD was estimated using receiver operating characteristic analysis (ROC-analysis) and binary logistic regression.

Results: ROC-analysis revealed the possibility of prediction of CSVD with measurement the buffer capacity of erythrocyte glycocalyx (AUC:0.723, 95% CI:0.610–0.836) and erythrocyte resistance to lysis in hypotonic solutions (AUC:0.708, 95% CI:0.578–0.839) and determined threshold values of these indicators. Using of logit-model showed greater reliability of the prediction of CSVD with both laboratory tests (p<0.000001, AUC:0.824, 95% CI:0.724–0.923).

Conclusion: The results revealed the possibility of prediction of CSVD by using laboratory tests of assessment individual sensitivity to sodium, which should be considered as independent risk factor of CSVD, but reduction in salt intake should be applied only in patients with exceeding of threshold values of the proposed indicators.

Disclosure: Nothing to disclose

EPO3045

Perineural Administration of Autologous Mesenchymal Stem Cells of Adipose Tissue in Patients with Cerebral Infarction

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Background and aims: We developed a unique technique for natural perineural migration of autologous mesenchymal stem cells (MSC) of adipose tissue to the area of cerebral infarction.

Methods: The method was used in addition to standard therapy of acute cerebral infarction. 35 patients were examined (aged 47-73 years, 61.25 mean); control group patients (n=20) were treated by standard therapy. Patients were subjected to intranasal perineural administration of MSC. Approximately 50ml of adipose tissue took from umbilical area. Cells were cultivated and then endoscopic threefold intranasal implantation of autologous MSC for 5-12x10⁶ cells was performed with the intervals of 5-9 days.

Results: All the patients showed only stable recovery of neurologic functions in 24 hours after each implantation of MSC.

Patients with cerebral infarctions showed statistically significant improvement of physiological functions control in 6 months after course therapy with MSC assessed by NIHSS. There were no repeated infarctions in the main group of patients for at least one and a half years. Administration of allogeneic SC to patients with cerebral infarctions (n=5) was ineffective.

Conclusion: Combination of standard therapy of cerebral infarctions with endoscopic perineural implantation of autologous MSC of adipose tissue is accompanied with activation of reparative processes leading to recovery of neurologic functions.

Disclosure: Nothing to disclose

EPO3046

MRI assessment of the relationship between small vessel disease and stroke outcome in patients on oral anticoagulants.

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Background and aims: Despite the fact that the disease of small vessels remains an important cause of both ischemic stroke and intracranial hemorrhage. Knowledge about the effect of small blood vessel diseases on the clinical course and outcomes in patients with stroke who received oral anticoagulation with atrial fibrillation is limited.

Methods: 240 patients aged 55-76 years was observed on the basis of the Uzbekistan stroke register, who received anticoagulation therapy after atrial fibrillation. The diagnosis of patients was substantiated by CT and NIHSS scale, as well as MRI (for assessing indicators of small blood vessel diseases) studies. Patients were evaluated both in the acute period and in the recovery period during the year. We evaluated the association of imaging modalities with clinical outcome, including repeated ischemic stroke, intracranial hemorrhage and death. Quality of life was assessed using a modified Rankin and Barthel scales.

Results: Small vessels disease was related to an increased risk of the composite endpoint (intracranial haemorrhage, ischaemic stroke, death: odds ratio (OR) 2.05, 95% p=0.005. In addition, confluent white matter hyperintensities were associated with increased disability OR 4.03; 95% CI 2.16–7.52; p<0.001) and mortality (HR 1.81, 95%CI 1.04–3.14, P 1/4 0.04).

Conclusion: In this study, we found that brain small vessels disease are associated with poor outcomes in patients with atrial fibrillation who received anticoagulant therapy after a stroke. cerebral microbleeds and white matter hyperintensities both were associated with an increased risk of a combined outcome during a follow-up period of one year.

Disclosure: Nothing to disclose

EPO3047

Abdominal Aorta occlusion as a cause of sudden paraplegia in the Emergency Department

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Background and aims: Abdominal aortic occlusion is a rare vascular emergency. It may occur due to embolization or thrombosis, in a concomitant vascular disease context. It typically presents with sudden-onset low back pain, whereas paresis or paresthesia are less frequent manifestations. The mortality rate is very high unless there is immediate treatment.

Methods: Non-applicable

Results: We present a case of a 72-year-old woman, with a history of ischemic stroke 2 weeks before, admitted to the emergency department with symmetrical and flaccid paraplegia, myotatic areflexia, pain and vibratory sensory deficit below the T10-12 level, flexor plantar reflex, livedo reticularis and bilaterally absent femoral pulses, confirmed by Doppler ultrasound. Abdominal and pelvic CT angiography revealed thrombosis of the abdominal aorta and both common iliac arteries. She was submitted to immediate thromboembolectomy, with successful revascularization and complete muscle strength recovery. Magnetic resonance imaging performed after 5 months ruled out any ischemic lesion of the spinal cord.

Conclusion: Acute paraplegia due to spinal cord ischemia is a rare condition and it is associated with a poor prognosis. Its mechanism is not yet fully understood, but is thought it is caused by an ischemic peripheral neuropathy, however more importantly would be a spinal cord ischemia, due to lower arterial blood flow through the intercostal, lumbar, sacral and pelvic radicular arteries. Abdominal aortic occlusion should always be considered in the differential diagnosis of acute paraplegia associated with limb ischemia signs, given its irreversibility without urgent surgical intervention.

Disclosure: Nothing to disclose

EPO3048

Does stroke location, assessed by a 24-hour CT scan, improve prediction of stroke outcome?

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Background and aims: Stroke is a major source of disability worldwide and, thus, predicting individual disability outcomes is a hot topic in stroke research. We intend to establish a relationship between the infarcted brain regions, assessed using the widely available plain head computerized tomography (CT), and the clinical outcome.

Methods: 459 patients with anterior circulation ischemic stroke submitted to revascularization were retrospectively assessed with CT imaging at 24 hours. The Alberta Stroke Program Early CT Score (ASPECTS), with the addition of the corona radiata, and lesion volume using the ABC/2 formula were calculated. Baseline and 3-month modified Rankin Scale (mRS), admission and 24-hour National Institutes of Health Stroke Scale (NIHSS) and other patient characteristics were obtained. Multivariate logistic regression models were used to study the influence of infarct location after adjusting for baseline mRS, admission blood glucose, infarct volume, 24-hour NIHSS, age and sex on outcome.

Results: Median baseline NIHSS was 14 [Interquartile range(IQR): 7-18], median age was 76 (IQR: 65-83), median 24-hour NIHSS was 7 (IQR: 2-16) and infarct volume was 9.1cm³ (IQR: 0.3-47.4). The insula was the most frequently infarcted region (53.8%). However, adjusted multivariate analysis revealed that the internal capsule and greater lesion volume (15cm³ intervals) were associated with worse outcome [Odds Ratio for good outcome: 0.40 (95% CI: 0.23-0.71) p<0.01; 0.88 (95% CI: 0.80-0.97) p<0.01, respectively].

Conclusion: Our study supports that lesion location, assessed by CT scan at 24h after stroke onset, independently impacts functional outcome.

Disclosure: Nothing to disclose

EPO3049

COL4A2 gene mutations as cause of cerebral small vessel disease, hemorrhagic stroke and intracranial vessels dolichoectasia

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Background and aims: COL4A1 and COL4A2 genes encode alpha subunits of type IV collagen, a vascular basement membrane component. Mutations in these genes have been recently identified as a cause of cerebral small vessel disease (cSVD), with an autosomal dominant transmission pattern. The disease can present with different phenotypes, including isolated cSVD, congenital porencephaly and multisystemic involvement – the HANAC Syndrome (Hereditary angiopathy with nephropathy, aneurysms and muscle cramps).

Methods: N/A

Results: A 54-year-old man from Guinea-Bissau presented in outpatient clinic with a 6-year-history of cognitive decline. He had a 12-year education and medical history of hypertension and hemorrhagic stroke at age 47 without relevant neurologic deficits. On examination he had decreased spontaneous behavior and speech, psychomotor slowing and scored 17/30 on Mini-Mental State Examination. Family history for stroke or dementia was unremarkable. Blood analysis showed only a slight and sustained elevation of the creatine-kinase and the patient confirmed that he felt muscle cramps frequently. Brain MRI showed confluent bilateral periventricular white matter hyperintensities, a left periventricular hemorrhagic sequel and diffuse cerebral atrophy. Angio-CT revealed diffuse tortuosity and dolichoectasia of the circle-of-Willis vessels, without aneurismal malformations. Genetic testing was performed through Next Generation Sequencing 7-gene panel for cSVD and it was identified the variant NM_001846.3:c.3448C>A(p.Gln1150Lys) of the COL4A2 gene, previously described as pathogenic.

Conclusion: COL4A2-gene mutation is a rare and less known cause of hereditary cSVD. COL4A1/A2 gene mutations should be considered in adults with cSVD, history of hemorrhagic stroke, muscle cramps and dolichoectatic intracranial vessels, even in the absence of aneurismal malformations.

Disclosure: Nothing to disclose

EPO3050

Stent-graft – a good choice of therapeutic approach in a variety of clinical situations

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Background and aims: Initially designed for endovascular treatment of aortic and peripheral aneurysms and arteriovenous fistulas, stent-grafts are now increasingly used for intracerebral vessels. The aim of our presentation is to illustrate the utility of stent-grafts in different clinical situations.

Methods: We present a series of 5 patients: a 46-year-old female with a giant aneurysm in the intracavernous segment of the left internal carotid artery, a 37-year-old female with an aneurysmal dilation of 1.5cm at the origin of the left internal carotid artery, a 36-year-old male with a post-traumatic right internal carotid artery dissection with a pseudoaneurysm in the C1 segment, a 47-year-old female with post-traumatic right direct carotid-cavernous fistula and a 73-year-old female with an iatrogenic lesion of the left vertebral artery after surgery for cervical myelopathy due to a herniated disk.

Results: All patients underwent digital subtraction angiography of the cerebral vessels and endovascular treatment with stent-graft, with optimal results and no intrastent stenosis at their follow-up visits. The therapeutic decision was made based on anatomic particularities of each case.

Conclusion: Stent-grafts represent a safe, effective and minimally invasive therapeutic alternative in a variety of clinical situations, which could become first-line therapy as experience with this kind of devices is continuously improving.

Disclosure: Nothing to disclose

EPO3051

Case report of bilateral intracranial internal carotid artery dissection in a patient with female phenotype, 46XY karyotype and homozygous MTHFR C677T mutation

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Background and aims: Multiple intracranial internal carotid artery (ICA) dissections occur more frequently in younger women compared to a single spontaneous cerebral arterial dissection (CAD).

Methods: Case report. Computed Tomography Angiography (CTA), Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography (MRA) and MTHFR genetical testing were performed.

Results: A 33-year-old patient presented with left>right anisocoria and headache. About a month prior a minor head trauma occurred, at the time no examinations were performed. Upon presentation carotid-cerebral CTA and head MRI showed right intracranial ICA dissection. No intracranial brain tissue damage was described. They administered acenocumarol. A week later, the patient was admitted to our hospital because of reoccurring right sided headache and immeasurably high INR. Neurological examination was negative. Repeated head MRI/MRA showed new, spontaneous left sided ICA C1 dissection next to the known right sided ICA C1-C2 dissection. Detailed medical history revealed primary amenorrhea, 46 XY karyotype on FISH examination and primary gonadal dysgenesis. Laboratory results showed MTHFR C677T homozygous mutation. Since limited data is available about the use of direct oral anticoagulants (DOACs) in ICA dissection, we continued administration of acenocumarol.

Conclusion: We present a case of bilateral (potentially spontaneous) ICA dissection in a patient with 46XY karyotype and homozygous MTHFR C677T mutation. A few cases of Turner Syndrome associated with CAD are mentioned in literature, but none with Swyer-syndrome. The detected MTHFR mutation might be an additional genetic risk factor. Further research is needed to prove the association between sex chromosome alterations and vasculopathy. The use of DOACs in such cases should be evaluated.

Disclosure: Nothing to disclose

EPO3052

The value of neuron-specific enolase in determining brain damage in the acute period of ischemic stroke

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Background and aims: Neuron-specific enolase (NSE) is an isoenzyme localized in neurons and released into the bloodstream by brain damage. Serum NSE levels can be valuable in patients with acute ischemic stroke (IS).

Methods: 42 patients in acute IS (23 women, 19 men) were examined, median age 55 [46; 61]. Blood samples were collected: 1st 72 hours (point-1) and 10-14 day (point-2). An enzyme immunoassay (ELISA kit) was used, control values (CV) 16.3 ng/ml.

Results: The NSE level at point-1 significantly exceeded CV and decreased in dynamics (20.4 [14.9; 36.8]→15.7 [12.8; 20.8], p=0.02).

In patients with a favorable outcome (mRS 0-2) the NSE level was significantly lower (point-2) compared with patients with a poor outcome (mRS 3-6) (13.6 [11.8; 17.4] and 16.9 [14.1; 21.9], respectively, p=0.03).

The correlation was determined between the NSE level at point-1 and the index Barthel (IB) at point-2 (r=-0.4), NSE at point-2 and IS severity (NIHSS) at point-1 (r=0.5) and 2 (r=0.7), a short-term outcome at point-2 (mRS) (r=0.5), IB at point-1 (r=-0.5) and 2 (r=-0.5).

Conclusion: The higher NSE level in the first 72 hours of IS, the worse the restoration of neurological functions by 10-14 days. The severe IS in the first 72 hours, the higher the NSE level by 10-14 days, meaning a more prolonged and massive damage to neurons. NSE can be considered a diagnostic and prognostic biomarker of brain damage in the IS acute period.

Disclosure: Nothing to disclose

EPO3053

Cognitive decline in patients in the preoperative period of cardiac surgery

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Background and aims: The study aimed to investigate the neuropsychological parameters and the frequency of mild cognitive impairment (MCI) in patients with coronary artery disease (CAD) in the preoperative period of cardiac surgery.

Methods: The study included 114 consecutive CAD patients scheduled for cardiac surgery, the mean age was 56.3 ± 5.25 years. The control group consisted of 40 healthy individuals, the average age of 55.1 ± 4.67 years. The patients were examined preoperatively with the Mini-Mental State Examination. A diagnosis of MCI was established based upon the Petersen's criteria. In addition, the CAD patients and healthy controls were underwent the expanded neuropsychological testing with assessment of psychomotor and executive function, attention, and short-term memory using the psychophysiological complex software "Status PF". The statistical analysis was performed using the STATISTICA 10.0.

Results: MCI was diagnosed in 48% of the CAD patients. It was found that the patients with CAD had lower complex sensorimotor reaction times, more errors, worse directed attention, memorization of words and meaningless syllables in comparison with healthy individuals.

Conclusion: The CAD patients preoperatively had the cognitive decline with impaired executive function, attention and short-term memory in comparison to the healthy controls. The data obtained in our study can be useful in developing an individual approach to preventing the development and progression of cognitive impairment in patients with CAD who underwent cardiac surgery.

Disclosure: The reported study was funded by RFBR and Kemerovo region, project number 20-415-420005.

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EPO3054

Reversible cerebral vasoconstriction syndrome: a dramatic case report

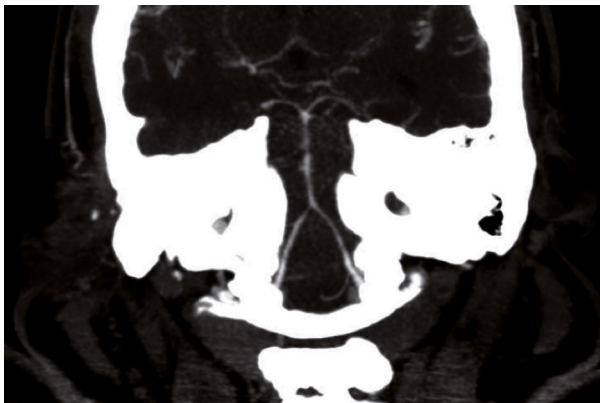
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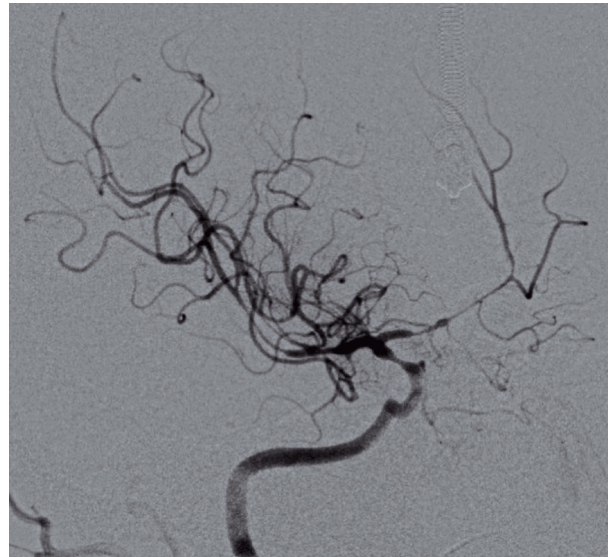
Background and aims: Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by severe headaches, with or without other acute neurological symptoms, and diffuse segmental constriction of cerebral arteries that resolves spontaneously within 3 months. The clinical outcome is benign in 90-95% of patients.

Methods: We present a 42-year-old woman, with a story of Sertraline medication. She began with a thunderclap headache. 5 days after, she started with low level of awareness, incoherent speech and loss of ambulation. She had no fever or other associated symptoms.

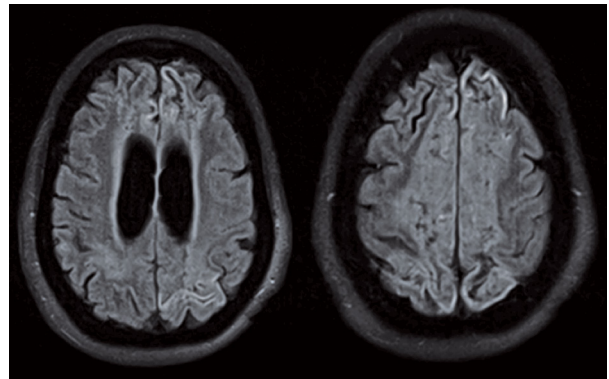
Results: The CT and MRI demonstrated multiple strokes located in arterial watershed and a cortical surface nonaneurysmal subarachnoid hemorrhage (NHSA). The cerebral Angiography showed multiple segments of narrowing in vessel caliber. 2 probable diagnoses performed: a vasculitis of the central nervous system and RCVS. The cerebrospinal fluid findings were normal. After 3 months, the follow up Angiography demonstrated a normal vessel caliber and diagnosis of RCVS was established. The clinical outcome was poor and patient follow-up showed a spastic tetraplegia and mutism. The follow up MRI showed a larger infarcts, especially in the territory of both anterior cerebral arteries. Our patient represents the 5% of cases of SVCR with poor prognosis.



CT- Angiography, multiple segments of narrowing in vessel caliber



Arteriography: cerebral vasoconstriction affecting basilar, vertebral and anterior cerebral arteries



Follow up MRI. Stroke in territory of both cerebral anterior arteries and arterial watershed regions

Conclusion: The RCVS represents an underdiagnosed entity to consider in middle-aged female patients with thunderclap headache and neurological deficit and combination of stroke and NHSA. There are some triggers described (like the serotonin reuptake inhibitors) but the etiology it's unknown yet.

Disclosure: Nothing to disclose

EPO3055

Posterior circulation ischaemic stroke: focal vasculitis 6 months after cervical Zoster

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Background and aims: Varicella Zoster Virus (VZV) vasculitis occurs by viral arterial transmural invasion after its reactivation in ganglion neurons. Diagnosis is confirmed by IgG VZV antibody in cerebrospinal fluid (CSF), with VZV PCR being positive in 30% of cases.

Methods: Case report of a woman with posterior circulation ischaemic stroke after cutaneous zoster infection.

Results: A 26-year-old woman, with a history of systemic lupus erythematosus (SLE) and chronic hepatitis B infection (inactive carrier), on prednisolone 15mg/day, mycophenolate 3000mg/day, and hydroxychloroquine 200mg/day. In January 2019, she was admitted for cutaneous cervical zoster (C2 territory) and right hemicranial headache, having completed 21 days of acyclovir (500mg IV q8h, 7 days followed by 14 days PO). 6 months later, she was for altered state of consciousness, dysarthria and left hemiparesis. Neurological examination disclosed gaze evoked nystagmus, left hemiparesis and left Babinsky sign. showed right pons and cerebellar hemispheres hyperintensities on DWI and T2/FLAIR. Blood tests showed controlled SLE activity markers CSF revealed pleocytosis (22 polymorphonuclear cells), hyperproteinorrachia (422mg/dL, traumatic puncture), glycorrachia 70mg/dL, negative CSF microbiological exams, and positive VZV PCR.

Brain MRI-angiography and transcranial Doppler ultrasound revealed stenosis of both vertebral arteries and distal occlusion of the basilar artery. She completed 21 days of IV acyclovir, with neurological improvement and maintained prophylactic acyclovir for 6 months and chronic antiaggregation.

Conclusion: VZV vasculopathy is a major cause of ischaemic stroke in immunocompromised patients and has a specific treatment. A high degree of clinical suspicion is required, as the disease might manifest quite sometime after the primary infection.

Disclosure: Nothing to disclose

EPO3056

Ruptured medullary bridging vein-draining dural arteriovenous fistula at the craniocervical region presenting with subarachnoid hemorrhage

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Background and aims: Background and Importance: Dural arteriovenous fistulas (DAVFs) at the craniocervical junction are rare vascular lesions with a potentially devastating natural history. Medullary bridging vein-draining DAVFs (MBV-DAVFs) at the craniocervical junction may present with both subarachnoid and intramedullary hemorrhage. Their complex angioarchitecture makes diagnosis challenging, with only a few published case reports so far.

Methods: Case Report

Results: Clinical Presentation: Here, we report a case of a MBV-DAVF presenting with acute subarachnoid hemorrhage. The fistula was supplied by a radiculomeningeal branch arising from the right vertebral artery at C1 level, while venous drainage occurred via an intradural perimedullary bridging vein that drained into the paravertebral venous plexus and the preponine venous system. There was an associated venous pouch, which presumably constituted the rupture point of the fistula. More distally there was also a stenosis of the outflow vein. Given the very small feeding branches and their very short security margin to the parent vertebral artery on the one hand and the venous outflow obstruction on the other, an endovascular approach was not deemed possible, and the patient was treated surgically with successful clipping of the bridging vein, with good clinical outcome and confirmed obliteration of the fistula on follow-up.

Conclusion: MBV-DAVF should be taken into consideration in the differential diagnosis of acute SAH. Their complex angioarchitecture makes diagnosis and treatment planning challenging. Currently, most of these patients are treated surgically since endovascular treatment is often too risky given the complex angioarchitecture of the lesions.

Disclosure: Nothing to disclose

EPO3057

The diagnostic yield of Holter ECG in a cohort of young ischaemic stroke patients

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Background and aims: Atrial fibrillation is a frequent cause of embolic strokes, but its prevalence is very low in young patients. The 24-hour Holter ECG monitoring takes more time to perform and read than most other exams done in this setting. We retrospectively looked at our young stroke patients to find the actual usefulness of this exam in our population.

Methods: We included all patients younger than 50-years-old admitted to the stroke unit of our centre since 2014 with the diagnosis of ischaemic stroke. We divided them in lacunar or non-lacunar strokes, and registered the results of the cardiologic exams performed.

Results: We found 100 patients (40% female) with a median age of 44-years-old (IQR: 40-48). 18% of the exams had relevant findings (64/346); Non-lacunar strokes had more positive exams (34/62 vs. 12/38, $p=0.02$). Only 2.3% of the Holter ECG exams were positive, while 38% of the echocardiograms had relevant findings (transthoracic: 26%; transesophageal: 56%); No patient with a normal transthoracic echocardiogram had a positive Holter ECG (0/65 vs. 2/21, $p=0.06$).

Table 1: Characteristics of the patients

Characteristics	All patients (n = 100)	Lacunar strokes (38)	Non-lacunar strokes (62)
Median age (IQR)	44 (40 - 48)	45 (40 - 48)	43 (40 - 47)
Female gender (%)	40	12 (32)	28 (45)
Hypertension (%)	36	16 (42)	20 (32)
Diabetes (%)*	12	9 (24)	3 (5)
Dyslipidemia (%)	29	14 (37)	15 (24)
Smoking (%)	38	17 (45)	21 (34)
Known heart disease (%)	11	3 (8)	8 (13)
Anticoagulant use (%)	4	1 (3)	3 (5)
Oral contraceptive use (%)	9	4 (11)	5 (8)
Previous stroke (%)	7	2 (5)	5 (8)

* $p < 0,05$ for lacunar vs. non-lacunar strokes

Table 1: Characteristics of the patients

Table 2: Summary of findings on cardiologic exams

Exam (positive/total)	All patients	Lacunar strokes	Non-lacunar strokes
ECG on admission‡	2/99	1/37	1/62
24-hour Holter ECG	2/88	1/33	1/55
TT echocardiogram*	25/96	4/37	21/59
TE echocardiogram	35/63	9/20	26/43
(Of which PFO)	26/63	7/20	19/43

TT: Transthoracic; TE: Transesophageal; PFO: Patent foramen ovale

* $p < 0,05$ for lacunar vs. non-lacunar strokes

‡ All but one patient – who had stopped anticoagulation despite a known permanent atrial fibrillation – performed ECG on admission. Retrospectively, both patients with atrial fibrillation on Holter ECG had an arrhythmia on ECG.

Table 2: Summary of findings on cardiologic exams

Conclusion: Our cohort showed a very low yield of 24-hour Holter ECG recordings, as was suggested by previous studies. We found that a normal transthoracic echocardiogram may be a predictor of a negative Holter ECG in this population. Based on these results, we suggest that the exclusion of atrial fibrillation should not lengthen admissions in young patients. In the case of embolic strokes of unknown source, monitoring heart rhythm during admission and using an event recorder after discharge is likely more effective.

Disclosure: Nothing to disclose

EPO3058

Gaseus-contrast transcranial doppler ultrasound for right-to-left shunt confirmation.

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Background and aims: Right-to-left shunt (RLSh) because of foramen ovale is an accepted risk factor for cryptogenic stroke. Gaseus-contrast transcranial doppler (cTCD) is a useful method for determination RLS. The aim of this study is to describe utility of cTCD before and during efficacy Valsalva maneuver in the diagnosis of RLS in young patients with cryptogenic stroke.

Methods: We conducted an observational, prospective cTCD examination of consecutive young adults with cryptogenic stroke. We used the database register of the neurology ultrasonology laboratory. There were 485 RLS studies of 13589 database registers between April 2009 and December 2018.

Results: During normal breathing, massive RLS was detected in 37 (7.6%), nonmassive RLS in 121 (25%) and absence of RLS in 327 (67.4%). During the efficacy standardized Valsalva maneuver, which could not be performed by 15 patients, massive RLS was detected in 97 (20.7%), nonmassive RLS in 111 (23.6%) and absence of RLS in 262 (55.7%). Efficacy Valsalva maneuver increased the detection rate of RLS by 11.7%.

Conclusion: Our results show utility of cTCD for determination RLS. With an efficacy Valsalva maneuver during the examination, there is a significant increment of RLS detection rate. Evaluation of cryptogenic stroke in young adults should include a cTCD for RLS detection.

Disclosure: Nothing to disclose

EPO3059

Rare ischemic stroke mechanisms in 4,154 consecutive patients: causes, predictors, treatment and outcome

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Background and aims: There are few systematic analyses of rare mechanisms of stroke (RMS) in acute ischemic stroke (AIS). Our aim was to define the frequency, etiologies, predictors and outcome of RMS in a large consecutive single center series of AIS.

Methods: Data from consecutive patients arriving within 24 hours from 2003-2016 were extracted from the Acute STroke Registry and Analysis of Lausanne. Frequency of subcategories of RMS were calculated. Multiple variables of RMS were compared with strokes of all other mechanisms. Long-term outcome was assessed with 3-months-Rankin-shift and 12-months-mortality/recurrence rates.

Results: 222 of 4154 AIS (5.3%) were found to have a RMS (42.3% female, median age 66 years). The most frequent RMS etiologies were related to medical interventions (26%), active cancer (22%) and vasculitis (12%). In multivariate analysis, RMS patients were younger, had more preceding and bilateral strokes, and higher admission temperature.

They were associated with less traditional risk factors and more systemic disease (such as AIDS, coagulopathy, and cancer). RMS had more early changes on plain CT, less revascularization treatments but more symptomatic hemorrhagic transformations.

RMS had significantly higher 3-months disability (Rankin-shift-OR adj 1.74), 12-months recurrence rate (OR adj 1.99) and 12-months mortality rate (OR adj 2.41).

Conclusion: RMS occurred in 5.3% of a large consecutive AIS population and are most frequently related to medical interventions, cancer and vasculitis. Such patients have less traditional risk factors but more systemic comorbidities, hemorrhagic transformations, recurrences, and a worse long-term outcome. Identification of RMS has direct implications on early treatment and long-term outcome.

Disclosure: Nothing to disclose

EPO3060

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL): “Retrospective study in the National Health Service of Ciudad Real (Spain)”

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Background and aims: CADASIL is an autosomal dominantly inherited angiopathy caused by mutations in the NOTCH3 gene. The estimated prevalence is 0.8 to 5 per 100.000 individuals. Clinical features comprise migraine, ischemic stroke and transient ischemic attacks (TIA's), cognitive deficits and neuropsychiatric symptoms. Recent studies concluded that substantial proportion of CADASIL adults experience clinical deterioration over a period of three years (incident stroke, dementia, progressive disability or death).

Methods: All clinical records of patients with genetically confirmed CADASIL diagnosis at the population area of reference (250.000 individuals) were retrospectively reviewed. Signalment, signs and symptoms were tabulated for analysis.

Results: 9 patients were diagnosed in the past 12 years, resulting in a prevalence of 3.6 patients /100.000 individuals. The age of diagnosis ranged between 40 and 72 years (average: 56 years old). The average follow-up time was 5.4 years (1-12 years). The initial clinical symptoms/signs of ischemic stroke or TIA's were present in 8 of the patients. 4 of the patients suffered migraine at diagnosis. 5 of the patients showed clinical symptoms of mild cognitive deterioration, although only 2 of them developed dementia. White matter hyperintensities on MRI were seen in all, and three cases had cerebral microbleeds.

Conclusion: We would like to comment the low incidence of progression to dementia from the initial diagnosis. The other signs and symptoms, and prevalence did fit with previously published data. We just want to highlight the case of a 54 years-old patient with neuro-psychiatric clinical symptoms at onset, which showed an unusual fast progression over a two-year period.

Disclosure: Nothing to disclose

EPO3061

Blood pressure variability during mechanical thrombectomy and outcomes, is there a connection?

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Background and aims: Optimal values of blood pressure during mechanical thrombectomy (MT) are not well known. Blood pressure (BP) variability during MT is a direct response of autonomic nervous function, and its dysregulation can affect cerebral autoregulation. BP and BP variability can have an effect on outcome after MT. The aim of this study was to assess the association of BP variability during MT with different outcomes in patients with acute ischemic stroke (AIS).

Methods: Patients with AIS and confirmed occlusion of middle cerebral artery or basilar artery were included. Mean arterial pressure (MAP) was recorded during MT. BP variability was expressed through few variables: generalized ARV, mean MAP, MAP SD, CV MAP and Δ MAP. Outcomes were defined as: mTICI score 2b/3, no early dramatic response (NEDR), as well as unfavorable neurological outcome (UNO, mRS after 90 days >3).

Results: Anterior circulation occlusion had 80% of patients. NEDR had 73%, while 56% had UNO. Patients with NEDR had higher MAP SD (mean \pm SD) 7.3 \pm 3.3 (vs. 5.3 \pm 1.4), $p < 0.05$. Mean MAP during thrombectomy was higher 100.4 \pm 14.3 (vs. 90.6 \pm 11.9), while Δ MAP was lower 7.9 \pm 20.5 (vs. 19.9 \pm 18.1) in group of patients with UNO, which was significant ($p < 0.05$). Other BP variability variables were not significantly different between outcome groups.

Conclusion: BP variability during mechanical thrombectomy is associated with unfavorable outcomes. Mean arterial pressure and its variability during thrombectomy can affect outcomes.

Disclosure: Nothing to disclose

EPO3062

Biomarkers of inflammation, hypoxia and dyslipidemia in the acute period of cerebral stroke

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Background and aims: Inflammation, impaired systemic oxygenation, dyslipidemia are some of the key points in the development of acute cerebrovascular pathology.

To determine the relationship of inflammation, lipid metabolism disorders, tissue oxygenation with the clinical manifestations of acute stroke (AS).

Methods: 36 people with AS were examined at the age of 68.5 (68; 75.7) years; comparison group – 18 volunteers aged 65.0 (62.0; 66.8) years. Patients were assessed using the NIHSS, Rivermead Mobility Index (RMI), the modified Rankin scale (mRS) and the presence of comorbidity. On the 1st day after AS, blood cholesterol, low density lipoproteins (LDL), apolipoprotein A-I (ApoA1), C-reactive protein (CRP) levels, pCO₂, pO₂, pH and serum IL-6 (ELISA) were determined.

Results: Neurological status of patients: NIHSS 7.5 (5.3; 12.5), mRS 4 (3.0; 4.0), RMI 3 (1.0; 5); heart failure was observed in 44% of patients. A decrease blood pO₂ to 56.8 (50.6; 71.23) mmHg was revealed and correlated with the presence of heart failure and the serum IL-6. A decrease blood LDL (3.1 (2.5; 3.8) mmol/l) and ApoA1 (1.59 (0.8; 1.4) g/l) was revealed. The correlation of LDL and ApoA1 with serum IL-6 was found ($r = -0.380$, $p < 0.05$ and $r = -0.433$, $p < 0.01$, respectively).

Conclusion: A violation of tissue oxygenation, the development of systemic inflammation and a decrease of transport atherogenic and antiatherogenic lipoproteins in patients with the acute phase of cerebral stroke was observed.

Disclosure: Nothing to disclose

EPO3063

Neurosonological findings in female patients with hypertension

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Background and aims: There are no clearly defined neurosonological criteria for the diagnosis of fibromuscular dysplasia. Due to subtle changes of blood vessel most patients remain unrecognized.

The aim of the study was to determine neurosonological findings in carotid and vertebral arteries in younger hypertensive women.

Methods: The study included 50 female patients, BMI<25 with hypertension and no obvious vascular risk factors, referred to ultrasound laboratory. Neurosonological findings were divided into 6 categories. 1. Carotid markers (diffuse or localized increase IMT>0,70mm); 2. Focal or multifocal, obvious or subtle, stenosis of carotid or vertebral arteries with appearance of string of breads; 3. Tortuosity (S shape, kinking, coiling); 4. Intracranial aneurysm; 5. Fibrous septum; 6. Carotid web.

Results: Among 50 female patient (mean age 47±2), thirteen (26%) had thyroid gland abnormalities. Most patients, 45 (90%), had neurosonological changes. 6 patients (8%) had only initial changes, carotid markers, and IMT increase was found in 33 (66%) patients. Strings of breads were found in 5 (10%) patients. Tortuosity were most common changes, in 19 patientes (26%). Most common combination was tortuosity of carotid arteries with carotid markers in 15 patients (39%). Carotid web was found in 5 (10 %) patients.

Conclusion: Most female patients with hypertension and no other vascular risk factors had at least one pathological finding on either the carotid or vertebral artery.

Disclosure: Nothing to disclose

EPO3064

High on- treatment platelet reactivity predicts recurrent vascular events- 3 years follow-up study.

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Background and aims: The aim of this prospective, 3 years follow-up study, was to establish the role of high on-treatment platelet reactivity (HTPR) in predicting both early and late recurrence of vascular events in patients after cerebral ischemia.

Methods: The study included 101 subjects with non-embolic cerebral ischemia - 69 patients who met the AHA/ASA criteria for the diagnosis of ischemic stroke and 32 patients with transient ischemic attack treated with 150mg of acetylsalicylic acid a day. Platelet reactivity was performed in the 1st 24 hours after cerebral ischemia onset by impedance aggregometry (ASPI-test). Recurrent vascular events, including recurrent ischemic stroke, transient ischemic attack, myocardial infarction, systemic embolism or sudden death of vascular reason, were assessed 36 months after cerebral ischemia onset.

Results: Recurrent vascular events occurred in 8.5% of all subjects, in HTPR subgroup in 17.9%, in non-HPRT subgroup in 4.6%. Aspirin resistant subjects have significant higher risk of recurrent vascular events than aspirin sensitive (OR=4.57, 95% CI 1.00-20.64; p= 0.0486) (Fig.1). Cox proportional hazards models showed that large vessels disease (HR 12.04, 95% CI 2.43-59.72; p= 0.0023) and high on-treatment platelet reactivity (HR 4.28, 95% CI 1.02-17.93; p=0.0465) are independent predictors of recurrent vascular events.

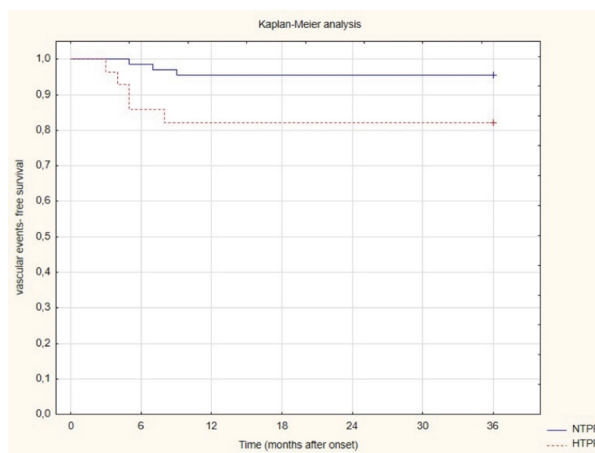


Fig.1

Conclusion: High on-treatment platelet reactivity in acute phase of cerebral ischemia and large vessels etiology of cerebro-vascular incidents are associated with higher risk of recurrent vascular events, both early and late.

Disclosure: Nothing to disclose

EPO3065

Aspirin resistance is associated with worse clinical condition in stroke due large vessel disease.

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Background and aims: The aim of the study was to assess the relationship between platelet reactivity and clinical and functional condition in patients with ischemic stroke, with particular emphasis on the role of stroke etiopathogenesis.

Methods: The study involved 69 patients with ischemic stroke, including 20 subjects with large vessel disease. The assessment of platelet reactivity was made using 2 aggregometric methods: impedance and optical, while the clinical condition was assessed using the NIHSS scale and the functional state using the mRS scale on the 1st and 8th day (early prognosis) and the 90th day of stroke.

Results: The initial platelet reactivity was found to be higher in patients with severe neurological deficit on the 90th day after stroke, than in the group with mild or moderate neurological deficit ($p=0.033$). In the subgroup of patients with large vessels disease a significant correlation between the platelet reactivity and the functional condition on the 1st day of stroke was found ($r=0.4526$; $p=0.0451$), platelet reactivity was higher in the subgroup of patients with severe than mild neurological deficit on the 1st day of the disease ($p=0.0372$), and patients resistant to aspirin have significantly greater possibility of a severe neurological deficit on the 1st day of stroke compared to those sensitive to aspirin (OR=14.00, 95% CI 1.25-156.12, $p=0.0322$).

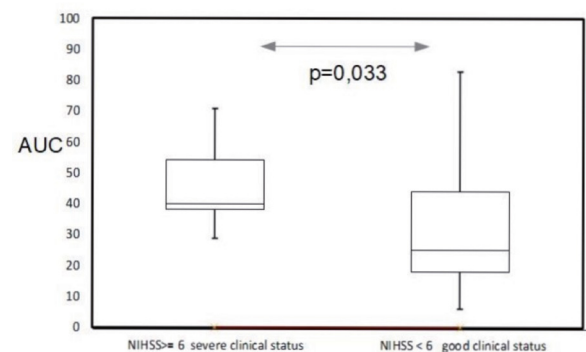


Figure 1. Comparison of platelet reactivity with the Multiplate method in subgroups of patients with mild and moderate/severe neurological deficit on the 90th day.

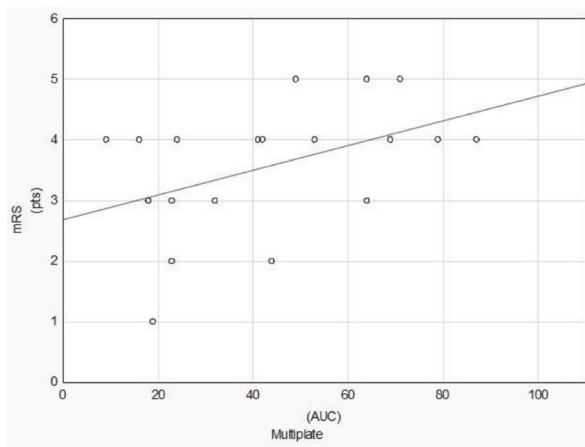


Figure 2. Dependence of platelet reactivity assessed by the Multiplate method and functional status (mRS score on the 1st day of stroke) in the subgroup of patients with the pathology of large vessels.

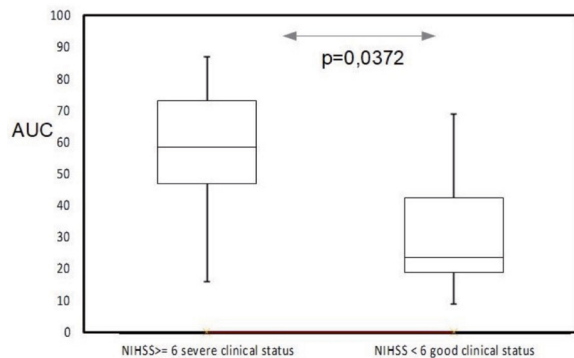


Figure 3. Comparison of platelet reactivity with the Multiplate method in subgroups of patients with the pathology of large vessels with mild and moderate/severe neurological deficit on the 1st day of stroke.

Conclusion: Aspirin resistance is associated with worse late prognosis overall and in the subgroup with large vessels disease with worse early prognosis and clinical condition.

Disclosure: Nothing to disclose

EPO3066

Recurrence Ischemic Stroke and Bleeding Complications Among Thai Octogenarians with Nonvalvular Atrial fibrillation Using Warfarin and Novel Oral Anticoagulants, A Retrospective Comparative study

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Background and aims: Stroke prevention with oral anticoagulants (OACs) is gold standard for management of nonvalvular atrial fibrillation (NVAF). Data using non-vitamin K antagonists (NOACs) among patients aged over 80 are limited. This study investigated efficacy and safety of NOACs compare with warfarin in extreme aged population.

Methods: A retrospective comparative study in octogenarians with NVAF initiating OACs was conducted in tertiary care hospital in Thailand. Patients who received apixaban, dabigatran, rivaroxaban or warfarin for stroke prevention from 2013 to 2018 were recruited. Primary outcome was recurrence of ischemic stroke in 90 days. Recurrence of ischemic stroke, major bleeding and non-major bleeding in 180 days were evaluated as secondary outcomes.

Results: A total of 205 patients were enrolled, 135 patients (65.9%) were OACs-naïve. 39 patients received NOACs which most of them were apixaban. Mean age was 84.5 years old. Median CHA₂DS₂VASc scores and HAS-BLED scores were 6 and 4. Patients in warfarin group had higher CHA₂DS₂VASc and HAS-BLED scores. 24 patients (62%) were prescribed dose of NOACs appropriately based on their renal function. During 90 days, rate of ischemic stroke in NOACs group were lower than warfarin (1.6% vs. 4.3%, p=0.52). Rate of ischemic stroke and non-major bleeding in 180 days were similar in both group. However, rate of major bleeding in 180 days was significantly higher in NOACs group (1.8% vs. 0.6%, p=0.007).

Conclusion: NOACs and warfarin demonstrated similar rate of recurrence ischemic stroke in 90 and 180 days among octogenarians with NVAF. However, major bleeding occurred higher in NOACs group despite receiving appropriate dosing.

Disclosure: Nothing to disclose

EPO3067

The reasons for not providing thrombolytic therapy to acute ischemic stroke patients: A stroke centre experience in Turkey

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Background and aims: Intravenous thrombolysis with recombinant tissue plasminogen activator (tPA) remains the only effective and approved treatment for acute ischemic stroke (AIS). Despite scientific evidence, its use has not become widespread as desired. We aimed to investigate the reasons for not providing tPA to AIS patients in our center. **Methods:** The study was conducted between January 1, 2019 and December 31, 2019 at a Training and Research Hospital which is a comprehensive stroke center in Istanbul. AIS patients who did not receive thrombolytic therapy although they were admitted to the emergency department within 4.5 hours of symptom onset, were included in the study. Patients' demographic characteristics, comorbidities, onset-to-door time, NIH stroke scale (NIHSS) scores at admission and brain imaging findings were recorded. The reasons for not providing tPA to AIS patients were determined.

Results: Of 294 patients with AIS, 103 (35%) did not receive tPA. The most common reason that associated with treatment failure was mild stroke (NIHSS<5) without large vessel occlusion (25%). 22 patients (21%) were using oral anticoagulant agents. History of intracranial hemorrhage, recent major surgery, presence of cerebral aneurysm or brain metastases, failure to obtain informed consent, resistant high blood pressure at admission, low ASPECT score and intrahospital delays were some of the other reasons. Some of other controversial factors including age, severe stroke, dementia, prior ischemic stroke and cerebral microbleeds did not affect our decision.

Conclusion: The reasons for the low utilization are multifactorial. Further investigations and educational programs are needed to clarify the clinician's uncertainty in the treatment of AIS.

Disclosure: Nothing to disclose

EPO3068

Tissue-type plasminogen activator-associated macro- and microstructural changes in patients with cerebral small vessel disease

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Background and aims: White matter hyperintensity (WMH) is the main neuroimaging marker of cerebral small vessel disease (cSVD), leading to cognitive impairments, increased risk of stroke and disability. Tissue-type plasminogen activator (tPA) is secreted by endothelial cells and involved in key mechanisms of cSVD: inflammation, blood-brain barrier (BBB) disruption, endothelial dysfunction.

Aim: To estimate association between t-PA and macro- and microstructural changes in patients with cSVD

Methods: 71 patients with cSVD (48 f., 60.5±6.8) according to STRIVE and 21 age- and sex-matched healthy controls (15 f., 57.3±5.2) were included in study. Patients and control group underwent conventional and DTI MRI (3T) and laboratory testing for t-PA level. Macrostructural changes were assessed by the Fazekas (F) scale. As a marker of microstructural changes were used fractional anisotropy (FA) and mean diffusivity (MD) in WMH and normal-appearing white matter (NAWM) in different white matter regions. ANOVA ($p < 0.05$) and Pearson correlation analyses were used

Results: WMH was corresponded to F1 stage in 17, F2–24, F3–30 patients. Significantly higher level of t-PA was determined between patients with F3 compare to control ($p = 0.000$) and F1, F2 groups ($p = 0.003$, $p = 0.002$). Significant negative correlation was revealed between decrease in FA in WMH of anterior frontal lobe with t-PA increasing ($r = -0.310$). Significant positive relationship was determined between increase in MD in NAWM of frontal lobes ($r = 0.388$), temporo-parietal lobes ($r = 0.428$) and increase in t-PA

Conclusion: We demonstrated an important role of t-PA in pathogenesis of white matter lesions and microstructural integrity changes in cSVD. Correlation with MD may suggest involvement of t-PA in BBB dysfunction.

Disclosure: Nothing to disclose

EPO3069

Proteomic changes in ischemic stroke

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Background and aims: The search for biomarkers of cardiovascular diseases is a promising scientific field in medicine, which is important in the screening, diagnosis, prognosis and monitoring of the effectiveness of the therapy. Among all possible technologies for the search for new disease biomarkers, proteomic ones are the most promising. Of particular interest is the study of the protein composition of human brain tissue in cerebral infarction

Methods: Autopsy brain samples were obtained within 6 hours after the death of patients with ischemic stroke (n=4): the cortex and white subcortical substance in the infarction zone with the corresponding sites of the opposite brain hemisphere. 2-dimensional O'Farrell electrophoresis was used for fractionation. Peptide sets were studied by MALDI-TOF MS and MS/MS mass spectrometry. The quantitative content of proteins was calculated using the ImageMaster 2D Platinum version 7 software package.

Results: In the infarction zone a fraction of the isoform of 18.5kDa of the myelin basic protein (MBP) was found. A significant amount of MBP is preserved in the form of discrete, diminished forms only by amino acid residues of arginine, which turned it into citrulline. As a result, the preserved part of MBP shifted to the acid side of the pH gradient, and began to be detected with the equilibrium 2DE variant at the level of hemoglobin fractions.

Conclusion: Determination of arginine-deiminated forms of the MBP is a promising method for the diagnosis of the acute stage of cerebral stroke.

Disclosure: Nothing to disclose

EPO3070

Seizures in cerebral venous thrombosis: is it a predictor of poor prognosis?

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Background and aims: Cerebral venous thrombosis (CVT) is a rare disease with potentially serious consequences, usually affecting young to middle-aged patients. Headaches, although frequently neglected, are the most common presentation of CVT. Therefore, seizures are often an alarming sign that urges the consultation.

We aimed to assess the predictors of CVT associated seizures and compare these patients with seizure-free patients (SFP).

Methods: A retrospective study was conducted over 10 years [2009-2019] including patients who attended our department of Neurology and were diagnosed with CVT. All patients had a neurological examination and were explored with a CT-scan and venous MRI(MRV).

Results: A total of 56 patients were enrolled with a sex-ratio M/F=19/37 and a mean age of 41,55 years (range:10-77). Among them, 17 patients (30%) had seizures as a revealing symptom and most of them were generalized (64%). Half of the patients with seizures (SP) had also focal motor deficits and altered consciousness. MRV showed an extensive CVT affecting multiple sinuses (58%) and venous infarction (64%) mostly frontoparietal. The majority of patients were seizure-free as soon as the anticoagulation and an antiepileptic monotherapy were initiated. Only one patient had recurrent seizures after CVT recovery leading to long-term antiepileptic therapy.

Compared to SFP, symptoms were remarkably more severe in SP (motor or sensitive deficit, altered consciousness) (58% vs. 20% and 47% vs. 12% respectively) and cerebral infarcts were more frequent in SP (82% vs. 29%). However, the outcome is nearly the same after treatment.

Conclusion: We concluded that the occurrence of seizure is predicting severe CVT cases but had no impact on long-term prognosis.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 2

EPO3071

Could Telemedicine improve detection and diagnosis of Neurocognitive disorders in Nursing homes?

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Background and aims: There is a lack of detection of neurocognitive disorders (NCD) in nursing homes (NH) in Europe. Obstacles include general practitioner's (GP) limited time, unawareness of diagnosis guidelines and tools, and difficulties to refer disabled patients to NCD specialist doctors. Telemedicine (TLM) could improve this situation.

Methods: During the "Act On Dementia" European Joint Action, 3 countries (Bulgaria, France, and Greece) tested TLM for NCD detection/diagnosis in 6 NH (1 in Bulgaria; 3 in Greece; 2 in France) from April to June 2018.

NCD detection tools were shared as well as satisfaction and dementia attitude questionnaires for NH staffs.

Results: The 6 NH were faced with various legal, ethical and practical requirements before TLM could be implemented. In Greece, NH staff followed a 30 hour teleeducational training about NCD. In France, there was current TLM for behavioral disorders, yet few requests for diagnosis, due to unawareness of diagnosis benefits for NH residents. In Bulgaria, NH staff training and 17 teleconsultations for NCD diagnosis took place.

All the NH teams were satisfied of TLM. The dementia attitude questionnaire results were similar between different NH, between countries, and between health professionals and other NH professionals.

Conclusion: This pilot helped identify facilitators to improve NCD diagnosis in NH, e.g. training about benefits of NCD etiological diagnosis for NH staff and GPs.

The main request for TLM for NCD in NH was for BPSD; NCD detection and diagnosis in NH could be improved by TLM when combined with BPSD evaluation.

Disclosure: Nothing to disclose

EPO3072

Management of an unusual presentation of spontaneous intracranial hypotension (SIH)

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Background and aims: A 49-year-old woman presented with a 9 month history of progressive cognitive decline, predominantly affecting memory and language, and worsening somnolence. In the few weeks prior to presentation her family reported occasional intermittent generalised headaches (although this was a minor feature), worsening postural instability, intermittent right hand tremors and urinary incontinence, with symptomatic improvement after lying flat.

Positive examination findings included: apathetic affect, vertical gaze restriction, persistent right-sided pill-rolling tremor, rigidity and bradykinesia, globally brisk reflexes and a markedly unsteady gait. Her ACE was 50/100.

Brain MRI showed features consistent with intracranial hypotension with suggestion of possible dural leak at C7. Initial Digital Subtraction Myelogram (DSM) was non-diagnostic, but repeat DSM identified a leak at C6-7 with a large irregular diverticulum.

Methods: Not applicable

Results: A blind blood patch at mid-thoracic level showed a temporary improvement in symptoms (ACE transiently increased to 75). An L-dopa challenge worsened her somnolence. Subsequently, a CT-guided fibrin patch was injected at C6/7 which again only yielded a transient improvement. Finally, definitive surgical repair of the diverticulum effected a dramatic and permanent improvement in both her cognitive and motor symptoms (ACE 85 on discharge).

Conclusion: SIH presenting with cognitive decline and parkinsonism is a challenge to diagnose and manage. DSM – which may require multiple attempts – is an ideal aid in diagnosing CSF leaks. Cognitive presentations can be challenging to manage with percutaneous procedures, and definitive management often requires open surgery.

Disclosure: Nothing to disclose

EPO3073

Profile of behavioural and psychological symptoms in vascular parkinsonism with dementia

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Background and aims: The clinical profile in vascular parkinsonism with dementia (VPD) is not well described in the literature, especially with regard to behavioural and psychological symptoms (BPS). Our goal is to evaluate the frequency of BPS in VPD.

Methods: This is an observational descriptive study that prospectively recorded data of 48 consecutive patients, who met vascular parkinsonism criteria proposed by Zijlmans plus dementia, in 2 outpatient neurological consultations in Salamanca, Spain. Mean age at onset was 74.3±7.9 years, mean duration of dementia 4.3±2.8 years, 45.8% were women, MMSE score 15.9±6.3. 85.4% exhibit hypertension, 41.7% diabetes, 66.7% dyslipemia, 41.7% cigarettes and 25% alcohol consumption. 17.1% reported previous transient ischemic attack, 75% ischemic stroke, 4.2% hemorrhagic stroke and 55.1% recurrent cerebrovascular events. The Neuropsychiatric Inventory (NPI) was used to assess BPS.

Results: At least one BPS occurred in 97.9% of VPD participants; the median NPI score was 46 (range:0-132), with a median number of 5 symptoms per patient. The most frequent symptoms were depression (70.8%) apathy (70.8%), sleep disturbances (64.6%) and irritability (64.6%), followed by agitation (54.2%), anxiety (54.2%), delusions (52.1%), hallucinations (41.7%), appetite/eating abnormalities (33.3%), disinhibition (27.1%), aberrant motor behaviour (18.8%) and euphoria (8.3%). 52.1% received antidepressants, 43.8% antipsychotics, 35.4% anxiolytics and 25% hypnotics. It is remarkable that 8 of 16 patients with appetite/eating abnormalities showed hyperphagia.

Conclusion: BPS are frequent in VPD. New investigations are required to better evaluate the relationship between neuroimaging evidence of cerebrovascular disease in VPD and different BPS profiles.

Disclosure: Nothing to disclose

EPO3074

Cognitive Impairment in early stages of White Matter diseases

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Background and aims: We tried to clarify the differences in White Matter diseases analyzing 2 leucoencephalopathies: Multiple Sclerosis (MS) and CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy).

Methods: We enrolled 15 patients with MS and 14 ones with CADASIL. All participants were right-handed and showed no sign of cognitive impairment or campimetric deficit. They assessed the Poffemberger test, that inspects reaction times analyzing 4 different conditions (LVF-LH left visual field-left hand, LVF-RH left visual field-right hand, RVF-LH right visual field-left hand, RVF-RH right visual field-right hand) and the BRB-NT (Brief Repeatable Battery Neuropsychological test or RAO battery).

Results: Considering the Poffemberger test, we found a statistical difference between the groups in LVF-LH $p=0.05$ and CUD (Crossed Uncrossed Difference) $p=0.026$, with negative marks in the 2nd group. The comparison of the mean values of BRB reached a significative difference in WLG (Word List Generation) test ($p=0.03$), with lower scores in CADASIL patients. A comparison of proportion in single domain showed lower scores in PASAT (Paced Auditory Serial Addition task) in MS patients ($p=0.01$). We completed the analysis with a Spearmann Rank Correlation, that pointed out no correlation within reaction times, age and education.

Conclusion: Our results could be interpreted as a major lobar lesion load in vascular leucoencephalopathy. Moreover since the early stages of the diagnosis, verbal fluence (tested by WLG) has been compromised in patients with CADASIL. Finally, we might say that executive functions represent the weakest domain in MS, and they get worse over the years.

Disclosure: Nothing to disclose

EPO3075

Therapy of post-stroke dementia on the example of memantine

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Background and aims: According to various studies, post-stroke cognitive impairment of varying severity is detected in 40-70% of stroke patients, on average, in about half of patients.

To study the effectiveness of memantine in the treatment of post-stroke dementia.

Methods: The study was conducted on 30 patients with ischemic stroke hemispheric localization in retro ventricular projection. The age of patients 60 to 75 years. Patients were divided into groups: 1st-main (15 people) receiving basic therapy and memantine); 2nd - control (15 people) who received only basic therapy, without memantine. Assessment of cognitive function was performed on the MMSE scale.

Results: Cognitive impairment was studied in 30 patients on the MMSE scale on the 1st day of hospitalization in the clinic, among them 17 patients (56.7%) showed a mild degree of disorders - 21-27 (average 24) points, in 8 patients (26, 7%) the average degree is 11-18 (14.5) points; in 5 patients (16.6%), the severe degree is 3-10 (6.5) points.

A 2nd study was conducted after 1 month on an outpatient basis. In group 1, in 6 patients, cognitive disorders were not detected (40%); 5 patients (33.3%) have a mild degree of disorders; 4 patients (26.7%) had an average degree of disorders. In the 2nd group: in 7 patients (51.7%) a mild degree of cognitive impairment was revealed; 5 patients (33.3%) - moderate; 3 patients (15%) have a severe degree of disorders.

Conclusion: This study showed that memantine effectively affects behavioral disorders, patient aggressiveness, thought processes, and the memory of patients with post-stroke dementia.

Disclosure: Nothing to disclose

EPO3076

Withdrawn

EPO3077

Recovery of cognitive and neurological functions in patients with ischemic stroke.

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Background and aims: To study the degree and dynamics of restoration of cognitive and neurological functions in patients with acute ischemic stroke (AIS) in vertebral basilar basin (VBB) and in right middle cerebral artery basin (RMCAB).

Methods: The research was conducted at Central Clinical Health Department. 182 patients (95 women & 87 men) between 39-82 years were studied in acute(1 & 10 days) period with AIS in VBB and RMCAB. In addition to studies of neurological status and routine research methods, we used MMSE and MOCA-test.

Results: The average age of patients with AIS in VBB was 60.79±11.14 (women 64.11±10.13, men 57.80±11.40), patients with AIS in RMCAB was 65.46±12.28 years old (women 65±10.11, men 64.40±16.47). In course of the data analysis, reliable results (p<0.05) were obtained that in the most acute(1 day) period of AIS patients with localization in RMCAB had more pronounced cognitive disturbances in comparison with patients with AIS in VBB, and more pronounced dynamics of recovery in acute period (10 days). Also statistically significant (p<0.05) were results of evaluation of neurological deficit and dynamics of its recovery in 2 groups of patients. Patients with AIS in RMCAB had more pronounced neurological deficit compared to patients with AIS in VBB, both in 1 and 10 days.

Conclusion: Patients who had AIS in RMCAB had more pronounced cognitive impairment and lower recovery rates than patients with AIS in VBB. Patients with AIS in RMCAB had more neurological deficits than patients with AIS in VBB. Also, the dynamics of neurological function recovery in AIS patients in RMCAB is less pronounced than in AIS patients in VBB.

Disclosure: Nothing to disclose

EPO3078

Associations of separate working memory parameters with COMT genotypes in Western Siberia

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Background and aims: To evaluate the associations between working memory parameters and Val158Met (rs4680) polymorphism of the COMT gene in young adults.

Methods: 371 young adults of both sexes 25-44 years old were recruited from population sample of Novosibirsk. The study included 199 (53,6%) men (average age was 36,54±5,67 years) and 172 (46,4%) women (average age was 36,84±5,75 years). Cognitive function were determined by standardized screening methods. Luria's 10-words test, letter cancellation test (modified Bourdon's test), and test of excluded of incorrect words (verbal version of the test) with fixing the time for its implementation, as well as animal naming test were used. Genomic DNA was isolated from venous blood by the phenol-chloroform extraction. Genotyping of the Val158Met polymorphism (rs4680) of the COMT gene was performed using PCR with RFLP.

Results: Statistically significant associations ($p < 0.05$) between quantity of the animals who are correctly called in 1 minute, with time which was spent for exclusion of incorrect words, as well as with the 1st reproduction of the words memorized immediately in Luria test and Val158Met (rs4680) polymorphism of the COMT gene in young adults were revealed. Moreover the quantity of the complaints about the forgetfulness of used phone numbers had significantly higher in the presence of 1 or 2 A alleles of the Val158Met polymorphism of the COMT gene.

Conclusion: The allele A of the Val158Met (rs4680) polymorphism of the COMT gene, especially in the homozygous state, has a significant association with the working memory parameters of Novosibirsk residents.

Disclosure: Nothing to disclose

EPO3079

Associations of separate working memory parameters with apolipoprotein E gene polymorphism at the Siberian adolescents: the population-based study

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Background and aims: To investigate the associations between apolipoprotein E (APOE) gene polymorphism and its influence on a verbal memory in adolescence population of Novosibirsk city (the largest scientific and industrial centre of West Siberia).

Methods: Cross-sectional population-based survey of randomly representative sample of school students aged 14-17 of both sexes in Novosibirsk was implemented (totally enrolled 549 persons). Cognitive domains were determined by standardized screening methods. Letter cancellation test (modified Bourdon's test), Luria's 10-words test and test of excluded of incorrect words were used. Genomic DNA was isolated from venous blood by the phenol-chloroform extraction. General linear models (GLM) were used to test the association between variation in the APOE polymorphism (e4 presence vs. absence) and memory measures.

Results: APOE gene polymorphism was tested at 290 persons (117 male, 173 female). The main effect of e4 allele presence in GLM on the mean quantity of errors at reproduction of the words memorized immediately in Luria's test is significant, $F(1,285)=4.49$, $p < 0.05$. From the estimated marginal means, it can be seen that the subjects made significantly more errors with e4 allele presence ($M=2.21$), than without e4 allele ($M=1.85$). The main effects of age and sex are not significant ($F(1,285)=1.15$, $p > 0.05$, and $F(1,285)=2.27$, $p > 0.05$, respectively). The age*sex interaction is not significant, $F(1,285)=1.57$, $p > 0.05$.

Conclusion: The allele e4 of the apolipoprotein E gene has a significant association with the working memory parameters in adolescence population of Novosibirsk city.

Disclosure: Nothing to disclose

EPO3080

Excessive daytime sleepiness prevalence and associated psychosocial problems in Siberian urban adolescents: the school-based study

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Background and aims: Excessive daytime sleepiness (EDS) is 1 of the most common sleep disorders in adolescents associated with social behaviors patterns and school performance. The Strengths and Difficulties Questionnaire (SDQ) was developed by R. Goodman [1] as a brief psychopathological screening tool that has been recommended for the detection and classification of psychosocial problems in adolescents. Data regarding the SDQ assessment in adolescent with sleep disturbances are limited.

Methods: 3022 urban Siberian (Krasnoyarsk) school-based adolescents (aged 12-18; boys/girl ratio 1393/1629) were tested with self-report version of SDQ questionnaire and Pediatric Daytime Sleepiness Scale (PDSS [2]); cutoff for EDS was 15 points, as was proposed [2]. Chi-square test was used.

Results: The prevalence EDS was 28.0%. The prevalence of EDS was significantly higher among girls (35.1%) compared to boys (20.4%, $p < 0.001$) and among older (aged 15-18, 24.0%) compared to younger (aged 12-14, 32.7%, $p < 0.001$) adolescents. Significant positive associations were detected between SDQ and PDSS scores and (Kruskal-Wallis test < 0.001 ; Fig. 1).

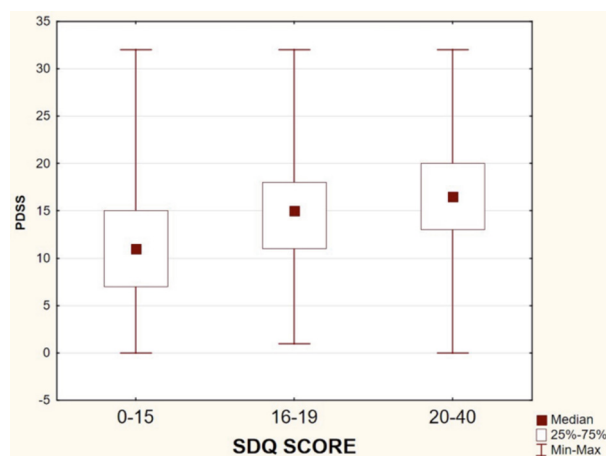


Figure 1. PDSS scores in adolescents with different SDQ scores.

Conclusion: The prevalence of EDS with PDSS cutoff 15 points in Central Siberia urban adolescents is very high (35.1%). EDS is closely associated with adolescence psychosocial problems.

References: Goodman R. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child*

Adolesc Psychiatry 2001; 40(11): 1337-45. Drake C. The pediatric daytime sleepiness scale (PDSS): sleep habits and school outcomes in middle school children. *SLEEP* 2003; 26(4):455-458. Meyer C. Proposal of cutoff points for pediatric daytime sleepiness scale to identify excessive daytime sleepiness. *Chronobiology International* 2018; 35(3): 303-11.

Disclosure: Nothing to disclose

EPO3081

A Rare Case of Transient Global Amnesia Caused by A Brain TumorB.G. Turk¹, A.F. Özdemir², C. Işler²¹Istanbul, Turkey, ²Department of Neurosurgery, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

Background and aims: Transient global amnesia (TGA) is defined as a period of an anterograde and retrograde amnesia that lasts up to 24 hours. The exact etiological mechanism has not been known yet. Among the other reasons; the co-occurrence of brain tumor and TGA is extremely rare, happening to have approximately 20 cases reported in the literature. Here we present a case with TGA whom to have a brain tumor.

Methods: 55-year-old right-handed woman was referred to the neurology outpatient clinic. She had a complaint of memory loss for 3 hours. During this period she was able to recognize who she is, where she is. Only she kept asking repetitive questions about what happening within just. After 3 hours; spontaneously her symptoms recovered completely. Magnetic resonance (MR) brain imaging showed a lesion at the right frontal lobe (Figure-1). The imaging findings were thought most likely to indicate low-grade neoplasia. Surgical resection of the lesion was offered to her, but she preferred not to. She is under clinical and radiological follow up for last 3 months.

Results: There are cases of TGA associated with brain tumors in the various locations. In our case the tumor was locating at the non-dominant frontal lobe and it's known that frontal lobe has a role in the temporal processing of the memory.

Conclusion: The evidence suggests that the concurrence of brain tumor and TGA is extremely rare. However; on the basis of the location of the tumor we interpreted that TGA is relevant with the tumor itself.

Disclosure: Nothing to disclose

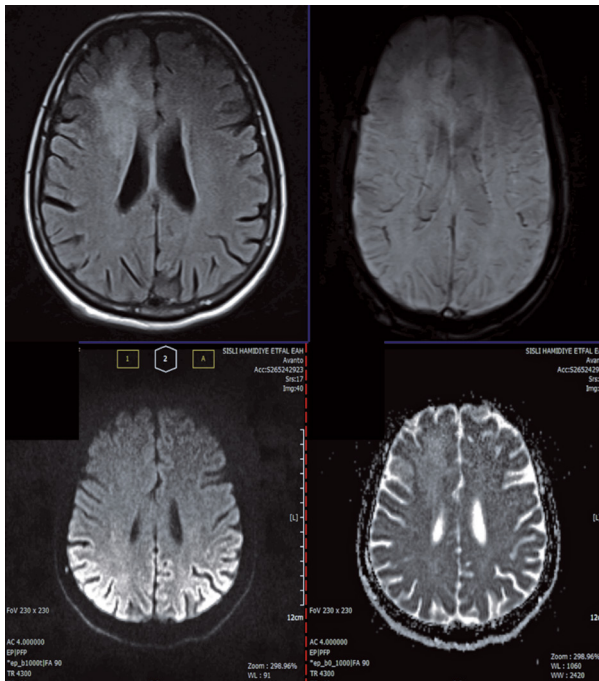


Figure-1: Cranial MRI of the patient

EPO3082

The Average Reaction Time and the Speed of the Fine Motor Skills in the Patients with Arterial Hypertension and Vascular Mild Cognitive Impairment

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Background and aims: The assessment of the average reaction time (ART) and the fine motor skills performance in the patients with arterial hypertension (AH) and vascular mild cognitive impairment (VaMCI).

Methods: The study subjects were 150 patients with VaMCI (n=65) and those without VaMCI (n=85) in AH (Table 1). Cognitive performance tests included MoCA scale and Shulte's tables. Fine motor skills were assessed by the Nine Hole Peg Test (NHPT), by the 10 sequential finger tapping (FT) and by the computerized testing (while patients were to hit the center of the repeatedly appearing target square with the cursor and to tap mouse button). ART (from the moment of appearing square to the moment of moving the mouse) and average time before clicking (ATC-from the moment of appearing square to the mouse clicking the square) were automatically calculated.

Table 1 – Characteristics of the patients included

patients with AH (not achieving target blood pressure)	150
grade I hypertension n (%)	72 (48%)
grade II hypertension n (%)	78 (52%)
male/female (n)	67/83
age (mean±SD)	55,4±9,1

Table 1 – Characteristics of the patients included

Results: It was found that the ART (427.0±61.1 vs 385.6±65.4ms, p<0.001) and ATC (2349.3±359.2 vs 1944.0±313.4ms, p<0.001) as well as the NHPT time (23.5±2.9 vs 21.7±2.6sec, p<0.001) and FT time (20.5±4.9 vs 15.3±2.3sec, p<0.001) were significantly higher in VaMCI patients compared to the patients without VaMCI. MoCA total score and Shulte's tables time significantly correlated with ART (R=-0.37, p<0.001 and R=0.42, p<0.001), ATC (R=-0.52, p<0.001 and R=0.48, p<0.001), NHPT time (R=-0.48, p<0.001 and R=0.35, p<0.001), FT time (R=-0.54, p<0.001 and R=0.48, p<0.001).

Conclusion: The increase of the ART, ATC as well as NHPT time and FT time may be suggested as early markers of psychomotor slowing and may be valuable in earlier diagnosing VaMCI in the patients with AH.

Disclosure: Nothing to disclose

EPO3083

The Subclinical Statokinetic Instability in the Patients with Arterial Hypertension and Vascular Mild Cognitive Impairment

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Background and aims: The aim of the study was detecting early diagnostic markers of statokinetic instability (SI) by static stabilography data in the patients with arterial hypertension (AH) and vascular mild cognitive impairment (VaMCI).

Methods: The study subjects were 150 patients with grades I and II of AH (male/female - 67/83, age 55.4±9.1) not achieving target blood pressure and 30 healthy controls. Patients with other risk factors for cerebrovascular disease (excepting AH) were excluded. Cognitive performance examination used Montreal Cognitive Assessment (MoCA). Patients with AH were categorised as having VaMCI and without VaMCI according to Petersen's criteria. Postural function was assessed by the computerized static stabiloplatfrom ("Stabilan 01" Russia) using the parameters: the ellipse area (EA), the quality of balance function (QBF), the average speed of pressure center movement (ASPCM).

Results: It was found that more pronounced SI in the patients with VaMCI in AH was evidenced by larger EA and ASPCM as well as the decrease of QBF compared to the subjects without VaMCI in AH and healthy controls. There was no significant difference in postural stability in the patients without VaMCI in AH and the healthy controls (Table 1). The significant negative correlation between MoCA total score and EA (R=-0.30; p<0.001) and ASPCM (R=-0.31; p<0.001) as well as positive correlation with QBF (R=0.33; p<0.001) were found.

Parameters	Patients with AH and VaMCI n=65 median [IQR]	Patients with AH without VaMCI n=85 median [IQR]	Healthy controls n=30 median [IQR]	Kruskal-Wallis H-test
	1	2	3	
EA (mm ²)	163,1 [104,8; 278,0] Z _{1,3} =3,79; p _{1,3} <0,001 Z _{1,2} =2,49; p _{1,2} =0,041	121,3 [79,8; 235,7] Z _{2,3} =2,09; p _{2,3} =0,108	103,0 [77,4; 139,8]	H=15,1 p<0,001
QBF (%)	71,6 [59,9; 80,6] Z _{1,3} =4,48; p _{1,3} <0,001 Z _{1,2} =3,02; p _{1,2} =0,008	79,7 [69,8; 86,7] Z _{2,3} =2,21; p _{2,3} =0,083	84,8 [80,2; 88,1]	H=21,7 p<0,001
ASPCM (mm/s)	12,1 [9,7; 15,9] Z _{1,3} =4,46; p _{1,3} <0,001 Z _{1,2} =3,04; p _{1,2} =0,007	10,1 [7,7; 12,4] Z _{2,3} =2,18; p _{2,3} =0,088	8,6 [7,5; 9,8]	H=21,6 p<0,001

Table 1. - Parameters of static stabilography in the patients with AH and VaMCI, the patients with AH without VaMCI and the healthy control subjects

Conclusion: VaMCI in the patients with AH was associated with the subclinical SI detected by static stabiloplatform. Assessment of stabilography parameters (EA, QBF, ASPCM) may be suggested as an early markers of SI in the patients with VaMCI in AH.

Disclosure: Nothing to disclose

EPO3084

Psychoemotional distress in parents of patients with Autism Spectrum Disorders: a cohort study

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Background and aims: Treatment of children with ASD should not be singly related to patients themselves. The prolonged emotional stress experienced by the parents of a child with autism forms certain features of their personality, such as increased sensitivity and anxiety, insecurity, internal contradictions. Such an emotional state, coupled with anxiety, uncertainty in itself, in turn, adversely affects the emotional and personal development of the child.

The social demand of parents of ASD children for a qualitative and timely examination, diagnosis, systematic medical and psychological and pedagogical assistance does not always correspond to the realities of life. Faced with a disease, the family can be isolated because of misunderstanding or rejection by society.

Methods: After baseline examination, 358 parents of patients with ASD (F84.0) (mean age 32.2y., range 21-46y.) were examined using Autism Spectrum Questionnaire (ASQ), Family Quality of Life Survey (FQoLS-2006), Analysis of Family Relations- Eidemiller version (AFR), Internet Addiction Test (IAT), General Health Questionnaire (GHQ-28).

Results: Parents of ASD children have increased levels of anxiety, social dysfunction, psychological instability that is primary (commonly occurring problems in the perinatal period, parents of mostly older age) and the secondary (constant psycho-emotional stress associated with the increased care and supervision after ASD child). They have more autistic traits than average, moderate-level of Internet addiction.

Conclusion: The system of interaction with the child isn't formed enough and most often manifests itself in the form of disharmonious education strategies. Interaction is mandatory between parents of ASD children and neurologists, psychologists, speech therapists involved in family-based rehabilitation.

Disclosure: Nothing to disclose

EPO3085

A clinical case report of a probable Heidenhain Variant of Creutzfeldt-Jakob DiseaseB. Vuchkova¹, J. Samuel², M. Dimitrova³¹*N.I. Pirogov, Sofia, Bulgaria*, ²*Sofia, Bulgaria*, ³*Neurology, UMHATEM "N.I.Pirogov", Sofia, Bulgaria*

Background and aims: Creutzfeldt-Jakob Disease (CJD) is a rapidly progressive, rare, transmissible, fatal, neurodegenerative condition caused by defects in prion proteins. It has been classified into sporadic, hereditary, acquired and variant types, and clinically presents with rapidly progressing dementia, ataxia, myoclonus and psychiatric symptoms. The Heidenhain variant is characterized by isolated visual disturbances at disease onset

Methods: A 65-year-old man presented with complaints of progressive loss of vision, visual field restriction, disturbed color perception, behavioral and personality changes along with difficulty recognizing relatives that evolved over a period of 2 months. The patient underwent physical and neurological examinations (NE), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the Brain, Electroencephalography (EEG), ophthalmological tests, screening for autoimmune encephalitis, Cerebrospinal Fluid (CSF) and serological tests for infections.

Results: NE on admission revealed bilateral amaurosis, optical apraxia, psychomotor slowing, executive function impairment and extrapyramidal symptoms of bradykinesia and rigidity. EEG recordings showed periodic sharp-wave complexes, paroxysmal discharges, and diffuse non-specific slowing. Brain MRI with contrast showed no significant pathological changes. Screening for autoimmune encephalitis, serological and CSF tests for viral, bacterial, as well as toxic-metabolic etiologies were negative. Genetic tests for mutations in the PRNP gene were negative. The CSF biomarker analysis of protein 14-3-3 was positive. Within a couple of weeks, the patient's condition worsened into severe dementia with loss of speech and mobility.

Conclusion: The patient had a fatal outcome within four months of disease onset. We present a clinical case of a probable Heidenhain variant of CJD with an extremely rapid disease progression.

Disclosure: Nothing to disclose

EPO3086

Saliva THz Analysis in Alzheimer's Disease, Relatives and CaregiversI. Zhukova¹, E. Kolupaeva¹, N. Zhukova¹, O. Izhboldina¹, D. Vrazhnov², M. Popova³¹*Department of Neurology and Neurosurgery, Siberian State Medical University, Tomsk, Russian Federation*, ²*Tomsk, Russian Federation*, ³*Laboratory of Biophotonics, Tomsk State University, Tomsk, Russian Federation*

Background and aims: The current diagnostic methods of the Alzheimer's disease (AD) are inefficient, expensive, and unsuccessful at making diagnoses during the earliest stages of the disease progression. Patients with AD usually need a high level of care in all types of everyday life, most of which are provided by family members, friends, or caregivers. Caregivers must cope with both age-related conditions and dementia-related factors. The burden of care could be a reason of cognitive impairment and negative outcomes on a quality of life in family members and informal care. Recent works show promising approach by saliva analysis via Raman Hyperspectroscopy. Several works demonstrate ability to diagnose AD by terahertz spectroscopy (THz) of the brain tissue by the low level of tryptophan and beta-amyloid plaque buildup within grey matter.

The aim of study is search of the potential markers of neurodegenerative process in saliva in patients with AD, relatives and caregivers.

Methods: In our work the THz time-domain spectroscopy (THz-TDS) was used to compare defrosted and dried saliva samples from AD patients, relatives and caregivers. Further analysis was made by machine learning methods. Principal component analysis and unsupervised learning methods were used to visualize and study latent relations in the initial data.

Results: The aforementioned methods was applied to 3 subject groups: 12 adults with the AD, their 8 healthy relatives, and 9 healthy caregivers. The obtained results show difference between groups by THz-TDS.

Conclusion: THz-TDS is a promising technique for early diagnosis of neurodegenerative process.

Disclosure: Nothing to disclose

Epilepsy 4

EPO3087

Paediatric epilepsy monitoring unit: 8 years experience

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Background and aims: Adult epilepsy monitoring units (EMU) are primarily dedicated to surgical evaluation of known epilepsies. When evaluating children, the study of paroxysmal events is the most important indication. Our aim was to characterize the population of children admitted to the paediatric EMU.

Methods: Observational, retrospective study to characterize clinical, imaging and neurophysiologic features of patients admitted to the paediatric EMU between January 2010 and November 2018.

Results: We analysed 329 Video-EEG exams. 56% were males, with a mean age of 6 years. Differential diagnosis was the most common (46%) indication for the exam. 196 children (59%) did not have an epilepsy diagnosis. 109 (33%) had a normal MRI, 56 (17%) had a single lesion and 69 (21%) multiple lesions. Patients were monitored for a mean of 30 hours. 66 (20%) had at least one seizure, 153 (46,5%) had interictal EEG activity and in 124 (38%) interictal dysfunction was detected in the EEG. 43 (13%) had a diagnosis of an epileptic encephalopathy and in 30 a genetic mutation/Cromossomopathy was detected.

Conclusion: This series shows our centre's 8 years experience with paediatric EMU. This is a vital exam for its value in diagnosing and managing epileptic and non epileptic cases. We also highlight the short duration of the Video-EEG needed to capture the abnormal events, making it an efficient tool in this population.

Disclosure: Nothing to disclose

EPO3088

Women's issues in epilepsy: a cross-sectional survey of community pharmacists' knowledge in the West Bank of the occupied Palestinian territories

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Background and aims: Community pharmacists are key providers of healthcare services for patients with chronic diseases including women with epilepsy. This study was conducted to assess pharmacist's knowledge of women's issues in epilepsy in the West Bank of the occupied Palestinian territories.

Methods: This study was conducted using a cross-sectional observational design. The study participants were community pharmacists of both genders. A total of 500 community pharmacists were approached in person in their places of work and invited to take part in the study. After collecting their sociodemographic and practice details, the participants responded to a validated and reliable 12-item KOWIE-II knowledge questionnaire of women's issues in epilepsy.

Results: The questionnaire was completed by 408 pharmacists, giving a response rate of 81.6%. On the 12-item questionnaire, the median correct score was only 53.8% with an IQR of 30.8. Pharmacists who interacted with ≥ 10 patients with epilepsy per month were 1.61 (95% CI of 1.04-2.49) more likely to score $\geq 60\%$ in the test than those who interacted with < 10 patients with epilepsy per month. Nearly 91% of the pharmacists answered correctly the question on the role of folic acid in reducing teratogenesis and only 46% answered correctly the question on exposure to valproic acid and the risk of giving birth to a child with autism.

Conclusion: Although pharmacists could be knowledgeable and in key position to provide essential information to patients with chronic diseases, in this study pharmacists were fairly knowledgeable of issues pertaining to women's general health issues.

Disclosure: Nothing to disclose

EPO3089

A Multicenter Retrospective Study evaluating Brivaracetam in the treatment of epilepsies in clinical practice.

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Background and aims: Introduction: Brivaracetam (BRV) is the latest approved antiepileptic drug and acts as a synaptic vesicle protein 2A ligand. The aim of the present study was to evaluate the efficacy and tolerability of BRV in every day clinical practice.

Methods: In this retrospective, observational, multicentre study, data from epilepsy patients receiving BRV anytime from January 2018 to July 2019 were collected. Patients with age ≥ 16 who had at least one follow up were included.

Results: 156 consecutive patients were included in the study (82 males, 74 females). The mean age was 40 (16-84 yrs), the mean duration of epilepsy was 21 yrs and 39% of them suffered from drug resistant epilepsy. Of the 156 patients, 81% were diagnosed with focal onset epilepsy, 16% with generalized seizures while 3% suffered from unclassified seizures. The mean cosponsored drugs with the BRV treatment were 2.28 at baseline. 9 patients received BRV as monotherapy. After BRV treatment, the rate of $\geq 50\%$ responder was 36%. Seizure freedom was achieved in 56 (39%) patients, while 15% remained unchanged. 6 patients (4%) were recorded with increased seizure frequency, while the remaining 9% had a responder less than 50%.

26 patients (17%) showed clinically significant adverse events. 16 patients discontinued BRV after the 1st follow up. The reasons for discontinuation were lack of efficacy (2 patients) and adverse events (10 patients) or both (4 patients).

Conclusion: Brivaracetam seems to be an effective, easy to use and safe antiepileptic drug in clinical setting

Disclosure: This research was funded by UCB

EPO3090

The peculiarities of epileptic process in MS patients

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Background and aims: Seizures are a rare manifestation of MS, however, a number of studies have shown that the risk of seizures and epilepsy in MS patients is 3-6 times higher than in the general population. The aim of this work was to clarify the links in the pathogenesis of MS, which lead to the development of symptomatic epilepsy, and the features of its course.

Methods: Material and methods. The study examined 22 MS patients, burdened with epileptic seizures.

We used clinical-anamnestic method, MRI, PET with 18Fdeoxyglucose, video-EEG monitoring (VEM).

Results: The structure of seizures is dominated by secondary generalized tonic-clonic seizures (57.14%), a high percentage (38.1%) of vegetative seizures. 33.33% of patients had a series of seizures, 3 patients (14.29%) had epileptic status. On MRI, cortical-juxtacortical lesions were observed in 45.45% of patients. Epileptiform patterns were mainly localized in temporal and frontal leads on VEM. According to the results of the PET study, data were obtained that confirm the data of VEM on the localization of epileptic foci, however, the area of epileptic lesions is more extensive.

Conclusion: Clinical and radiological manifestations of the inflammatory process (white and gray matter) in MS patients can lead to the activation of the latent focus of epileptic activity due to concomitant chronic inflammatory metabolic disorders and changes in the cerebral micro-environment. We have shown that the clinical manifestations of epilepsy in MS patients are determined not by the number, but by the activity of foci of the inflammatory process, with predominant localization in the fronto-temporal regions.

Disclosure: Nothing to disclose

EPO3091

Invasive EEG monitoring for presurgical evaluation in patients with drug resistant form of epilepsy

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Background and aims: Resective epilepsy surgery based on an invasive EEG (iEEG), performed with subdural grids or depth electrodes is considered to be the best option towards achieving seizure-free state in drug-resistant epilepsy.

Methods: prospective analysis of 79 patients with drug-resistant epilepsy who underwent iEEG monitoring for the presurgical evaluation before resective surgery.

Results: 31 patients (39%) - MRI negative, 48 (61%) - MRI positive. During sEEG in 55 patients (69%) seizure onset zone (SOZ) was bilateral. In 24 (31%) patients results of MRI and sEEG were not concordance. In patients with bilateral SOZ by sEEG, on iEEG we found: 6 (13%) patients had bilateral SOZ and in 49 (87%) seizure began in one side. In patients, with non-concordance MRI/scalp EEG: 3 patients (9%) didn't have epileptiform activity on sEEG, but had it on iEEG; in 3 patients (9%) - sEEG was not concordance with iEEG and in 18 patients SOZ were detected only by iEEG. For all patients were made resective surgery. Outcomes after 12 months after surgery in 60 patients (76%): 32 patients (53%) became seizure free: 26 patients (43%) - Engel Ia, 2 - Engel Ic, 4 - Engel Id. Eleven (18%) - Engel II: 1 - Engel IIa, 7 - Engel IIb, 1 - Engel IIc, 2 - Engel IId. The unsatisfactory result of treatment were noted at 13 patient (21%): 3 - Engel IIIa, one - Engel Iva, 9 - Engel IVb. There was no mortality in our group. The complications developed in 7 (11%) patients: 2 - intracerebral hematoma in the area of electrode placement (without indications for surgery), 4 - status epilepticus and 1 - wound liquorrhea.

Conclusion: Our results confirmed efficiency and safety of iEEG as presurgical procedure in patients with drug resistant form of epilepsy. 53% patients become «seizure free» 12 months after surgery.

Disclosure: Nothing to disclose

EPO3092

VNS – second chance after failed resective epilepsy surgery

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Background and aims: To evaluate the effectiveness of vagus nerve stimulator (VNS) after failed resective epilepsy surgery.

Methods: All the patients who had persistent seizures after resective surgery who subsequently VNS placement at our institution from 2016 to 2019 were included in the study. 21 consecutive patient (14 women) were enrolled and followed for the outcome. Seizure outcomes were based on modified Engel classification (I: seizure-free/rare simple partial seizures; II: >90% seizure reduction (SR), III: 50-90% SR, IV: <50% SR; classes I to III (>50% SR) = favorable outcome).

Results: the average age was - 31.15 (±2.3) y, the mean duration of the epilepsy was 17.6 years. Temporal lobe epilepsy was diagnosed in 5 patients, temporal plus (temporal+frontal) - 8 patients, 6 patients had bilateral lesions and 2 multifocal. All patients in this group previously had resective surgery: 20 patients - anterior medial temporal lobectomy (AMTLE) and 1 patient - AMTLE plus extTLE. Ten patients (47%) were evaluated 12 months after surgery: 2 (20%) had a modified Engel class I outcome, 4 (40%) had class II, 4 (40%) had class III. The pathohystology was: FCD Ia-2, FCD Ic-4, FCD IIa - 1, FCD IIIa-10, FCD IIIId-4. There was no surgical mortality. Side effects of VNS were: hoarseness-10 (47%) patients, cough during stimulation-3 (14%)

Conclusion: In our series, patients who failed surgical therapies, VNS improved seizure control in all 100% patients. We confirmed its efficacy and safety: 20 % patients become “seizure free”, 40% - had >90% seizure reduction and 40% - 50-90% SR 12 months after surgical treatment.

Disclosure: Nothing to disclose

EPO3093

Types of epileptogenic lesions in patients with drug-resistant forms of epilepsy.

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Background and aims: To evaluate pathomorphological types of epileptogenic lesions in patients with drug-resistant epilepsy.

Methods: Prospective analysis of 270 patients with drug-resistant epilepsy, who had undergone resective surgery in University Clinic of Moscow State University of Medicine and Dentistry between 01.01.2014 and 12.12.2019.

Results: According to MRI data 49 (18%) patients were MRI negative and 221 patients (82%) – MRI positive. Data of the pathohistological results were: FCD Ia – 14 patients, FCD Ic – 37, FCD IIa – 34, FCD IIb – 3, FCD IIIa – 117, FCD IIIb – 11, FCD IIIc – 5, FCD IIId – 28, LGG – 10, HS – 3, AVM – 4, HH – 3, LGG+HS – 1. Based on the histology data, the main type of pathology was FCD IIIa – 117 patients (43%). In group of patients with FCD IIIa, the accompanying pathology with HS was: FCD Ia – in 12 patients, FCD Ib – 2, FCD Ic – 32, FCD IIa – 52, FCD IIb – 19. In analysis patients with MRI positive and negative forms the following results were obtained: in MRI positive forms the main type of epileptogenic lesion was FCD IIIa – 50%, in MRI negative – FCD Ic – 32% and FCD IIId – 26%. No statistically important relationship between outcomes of surgical treatment and pathomorphology was found in our study.

Conclusion: The results obtained in our series revealed that the main type of epileptogenic lesions were FCD – 43% and in MRI positive forms - FCD IIIa – 50%, in MRI negative – FCD Ic – 32% and FCD IIId – 26%.

Disclosure: Nothing to disclose

EPO3094

Quality of life in patients with epilepsy – experience from a tertiary epilepsy centre in Croatia

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Background and aims: Many factors influence quality of life (QoL) of patients with epilepsy. The aim of this study was to evaluate the relationship between epilepsy, anti-epileptic drugs (AEDs) and QoL.

Methods: Quality of life in epilepsy-31 (QOLIE-31) was used for evaluation of QoL, Arizona Sexual Experiences Scale (ASEX) for SD and Hamilton Rating Scale for depression (HAM-D17).

Results: 108 patients with epilepsy were enrolled (68 (63%) women, 40 (37%) men; mean age 39.54±15.91; 16 (14.8%) focal, 38 (35.2%) generalized and 44 (40.7%) combined type of epilepsy). Mean result on QOLIE-31 was 62.88±17.21 (women 63.31±16.51, men 62.18±18.51). No significant differences were found regarding gender, type of epilepsy and age, except in regard to the domain ‘Overall QoL’, where the age group 35-55 years was found to have statistically significantly lower QoL in comparison to those younger than 35 years. Patients taking both types of AEDs were found to have significantly lower QoL compared to those on newer AEDs. Lower QoL was found to be associated with more pronounced symptoms of SD ($r=-0.34$, $p=0.001$) and depression ($r=-0.71$, $p=0.000$). Out of 44 patients with drug-resistant epilepsy, 27 were treated with vagus nerve stimulation (VNS), with statistically significant differences found between the 2 groups ($p=0.041$).

Conclusion: Patients with epilepsy taking both types of AEDs were found to have lower QoL in comparison to those on newer AEDs. Furthermore, QoL and mood were found to improve following VNS implantation in patients with drug-resistant epilepsy.

Disclosure: Nothing to disclose

EPO3095

EEG seizure onset patterns in status epilepticus

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Introduction: Seizure-onset (SON) patterns have been studied especially in isolated seizures in epilepsy surgery candidates. EEG studies characterizing the SON patterns in status epilepticus (SE) are lacking.

Methods: Consecutive EEG recorded from adult patients admitted for focal SE, from January 2015 to August 2019 were reviewed. 5 SON patterns were identified (Tanaka et al. 2018): (1) paroxysmal rhythmic slow activity at <13Hz; (2) paroxysmal rhythmic fast activity at ≥13Hz; (3) repetitive epileptiform discharge; (4) suppression of background activity to ≤10μV; and (5) artifacts. For each patient 1 to 5 seizures were analyzed, and each seizure's duration was registered.

Results: 307 seizures were analyzed in 100 consecutive patients (mean age 70 yrs); the most frequent SON pattern was pattern 3 (39 patients) followed by pattern 1 (34 patients) and pattern 2 (14 patients); pattern 4 and 5 were observed 1 and 3 patients respectively. 9 patients presented with multiple SON. Seizures with SON pattern 3 showed longest duration ($p<0.05$). No statistical difference in demographics, SE etiology, semeiology and treatment response was observed among the different SON, while a higher 28-day mortality was observed in SON pattern 3 ($p=0.02$; HR 3.00; 95% CI 1.13-7.97).

Conclusion: In SE the pattern characterized by repetitive epileptiform discharges (# 3, spike and waves) was the most frequent, with the longest mean seizures duration, and associated to highest short-term mortality. Analysis of SON patterns could improve our understanding on SE mechanism and could become a useful EEG biomarker.

Disclosure: Nothing to disclose

EPO3096

Periodic Leg Movements in Sleep May Influence Severity of Epilepsy

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Background and aims: Sleep disorders are important risk factors for patients with epilepsy (PWE). Abnormal sleep-interrupting phenomena could influence the course of epilepsy. Periodic leg movements (PLM) in sleep (PLMS) are a hidden but frequent encounter in general population which could also play a role in PWE being associated with arousals. Our aim was to evaluate relationship between abnormal EEG discharges and PLMS among PWE.

Methods: 85 PWE had polysomnography (PSG) plus EEG studies. PSG was performed and scored according to accepted standards. PLMS index (PLMI)≥10/h was considered abnormal. 12 PSG-EEG recordings from 10 PWE (F-50%, mean age-39.6) with high PLMI and abnormal EEG were selected. EEG was inspected visually and epileptiform discharges were marked manually. Special EEG-LM/PLM association events were attributed and counted. Yearly seizure frequency (YSF) was obtained.

Results: On average we registered 145 (29-614) EEG events per recording and mean EEG event index in sleep was 24.75h. Leg movement (LM) data: LM index (LMI)-31.8h, PLMI-22.6h. REM-PLMI-4.7h was lower than NREM-PLMI-29h, similarly REM-EEG event index-12.4h was lower than NREM-EEG event index-28.1h. We found no correlation of EEG events with LMI and PLMI. There was a strong positive correlation between LM-linked EEG events and YSF ($r=0.9$ $p<0.001$). Independent EEG events did not show this association ($r=0.45$ $p=0.3$). PLM sequence-associated ($r=0.5$ $p=0.1$) and independent EEG events ($r=0.17$ $p=0.6$) did not correlate with YSF.

Conclusion: Although, we found no relationship between EEG abnormalities and LMI/PLMI, the LM-linked EEG epileptiform discharges were in strong correlation with YSF. This is the first report of such association.

Disclosure: Nothing to disclose

EPO3097

The role of assessment of cognitive dysfunction in the differential diagnosis of pharmacoresistant epileptic and psychogenic non-epileptic seizures.

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Background and aims: Epileptic seizures and psychogenic non-epileptic seizures (PNES) often should be differentiated. The main diagnostic method is video-EEG. It is not always available and allows to assess only clinical event during the study. The most difficult situation is a combination of epileptic seizures and PNES in one patient.

Methods: 116 patients: 32 men and 84 women, mean age 31.5±11.3 years. 1 group (n=60) – pharmacoresistant epilepsy (PRE), 2 (n=23) – combination of epileptic seizures and PNES, 3 (n=28) – PNES. Cognitive status, emotional-volitional sphere, personality profile were analysed. Cognitive status was assessed using the diagnostic tool developed by us, which contains 34 items, adequate for the study of aphasia, gnosis, praxis and other higher mental functions. Emotional-volitional sphere – using STAI, BDI, MFI-20, personality profile – MMPI.

Results: The most characteristic and significant differences between groups:

1 group – asthenic syndrome, decrease of cognitive functions, decrease of all subtests of modal-specific memory impairments;

2 group – asthenic syndrome, normal cognitive status, mono-impairment: regulatory apraxia, tactile inattention;

3 group – high rates of anxiety and depression, conversion/somatiform personality profile, normal cognitive status, mono-impairment: tactile alexia, auditory agnosia, auditory and motor inattention.

Conclusion: Conversion features of the personality profile were characteristic only in the 3rd group. Group 1 and 2 differed mainly in terms of cognitive status. The presence of the abovementioned mono-impairments in groups 2 and 3 can be caused by functional reactions, characteristic for dissociative disorders. The results demonstrate the role of assessment of cognitive status in the diagnosis of PRE and PNES.

Disclosure: Nothing to disclose

EPO3098

A retrospective, multicentre study of perampanel efficacy and tolerability in pharmacoresistant focal epilepsy.

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Background and aims: To study the efficacy and tolerability of Perampanel (PER) as an additional antiepileptic drug (AED) in patients with pharmacoresistant focal epilepsy. The study design: multicenter retrospective.

Methods: The study included 164 patients over 12 years old. The average age 37.7±15.2 years, men – 49.4%, disease duration over 10 years - 68.7%, structural temporal lobe epilepsy - 53.4%, structural frontal - 39.1%. For the majority of patients, PER was prescribed in addition to 2 AEDs 50.9% and after 3 previous lines of therapy 26.6%. The maximum duration of the study was 12 months.

Results: The average dose of PER was 8mg. The retention rate on therapy for 12 months was 80.7% (95% CI: 72.3%-89.1%). The absence of all types of seizures was achieved in 22.7%, responders (>50%) in 52.8%. The absence of focal to bilateral tonic-clonic seizures (FBTCS) was achieved in 60.8%, FBTCS responders accounted for 27.8%. Adverse events (AEs) were observed in 31.3% of patients: drowsiness - 10.4%, aggression - 9.8%, irritability - 6.7%, gait shakiness - 6.1%, other AEs were observed extremely rarely (<3% each).

Conclusion: PER has shown high efficacy mainly in FBTCS seizures and a predicted safety profile in a group of patients with focal pharmacoresistant epilepsy. The average dose of PER was 8mg. PER dosage above 4 mg to prevent AE should be increased more slowly and AE should be monitored.

Disclosure: Nothing to disclose

EPO3099

Anti-epileptic drugs consumption in the primary health care in Albania, 2004-2018L. Kakariqi¹, G. Vyshka¹, J. Kruja²¹University of Medicine in Tirana, Biomedical and Experimental Department, Faculty of Medicine, Tirana, Albania, ²University Hospital Center "Mother Theresa" and Faculty of Medicine, University of Medicine in Tirana, Service of Neurology, Tirana, Albania**Background and aims:** Authors discuss the use of anti-epileptic drugs (AEDs) in Albania, with focus on the consumption of AEDs at the primary health care level; and differences of prescription patterns over a period of 15 years. The relation between the consumption data of AEDs and the level of epilepsy morbidity is also considered for the period 2004-2018.**Methods:** The data were assembled from Health Insurance Institute in Tirana, Albania and analysed for the period 2004-2018. The consumption of drugs was expressed as a number of Defined Daily Dose (DDD)/1000 inhabitants/day. We also analysed the data of imported and domestically produced drugs, which represent the total consumption of AEDs in the country.**Results:** The consumption of AEDs was 1.82-2.30 DDD/1000 inhabitants/day; as for the minimum and maximal figures registered during 2004-2018. The most prescribed AEDs are the classic or the old-generation drugs with values of 1.77-1.69 DDD/1000 inhabitants/day. New-generation AEDs included in the reimbursement scheme are lamotrigine, gabapentin, levetiracetam and topiramate, with values of consumption resulting 0.06-0.61 DDD/1000 inhabitants/day.**Conclusion:** The consumption values of anti-epileptic drugs in Albania is comparatively low. We noted an annual decrease in the time-trend consumption of classic antiepileptic drugs, compensated with higher consumption of new-generation drugs. An important part of the anti-epileptic drugs flows out from the reimbursement scheme. Epilepsy morbidity data indicated an existing significant correlation between the disease and the trend of consumption of AEDs. A comparative analysis in the consumption of AEDs between Albania and other countries suggested also important differences in the overall consumption figures.**Disclosure:** Nothing to disclose

EPO3100

Effects of deep brain stimulation on PTZ-induced seizure and sleep disruptionY.L. Yang¹, P.-L. Yi², F.-C. Chang¹¹National Taiwan University, Taipei, Taiwan, Chinese Taipei, ²Department of Sport Management, Aletheia University, Taipei, Taiwan, Chinese Taipei**Background and aims:** Deep brain stimulation (DBS) can effectively suppress epilepsy. However, the mechanism of DBS is still unclear. One of hypothesis of DBS mechanism is to affect epileptogenesis, which is an important process in epilepsy development.**Methods:** A low-dose pentylenetetrazole (PTZ) was Intraperitoneal (IP) injected every 2 days, for a total of 6 injections, to achieve the effect of kindling, and the DBS was stimulated 10 minutes before the PTZ injection and lasted 20 minutes after the injection. We recorded the entire process using an electroencephalogram (EEG) to analyze frequency of seizures and sleep changes.**Results:** The seizure duration after the 6th injection of PTZ was 68.49% lower in the DBS treatment group comparing with the PTZ group ($P < 0.05$). After the 1st injection of PTZ, duration of NREM in the DBS-treated group higher than that in the PTZ group ($P < 0.05$). After the 6th injection of PTZ, it was found that sleep duration of NREM sleep was decreased, but the DBS blocked the PTZ-induced NREM sleep decreases ($P < 0.01$). In the interictal section, the DBS treatment lower the epileptic spikes.**Conclusion:** DBS does improve PTZ-induced seizures and has an effect on the epileptogenesis and sleep duration.**Disclosure:** Nothing to disclose

EPO3101

Deep brain stimulation (DBS) increases epilepsy threshold by altering REM sleep and delta powers during NREM sleepP.-L. Yi¹, H.-T. Tseng², F.-C. Chang²¹*Department of Sport Management, Aletheia University, Taipei, Taiwan, Chinese Taipei,* ²*National Taiwan University, Taipei, Taiwan, Chinese Taipei*

Background and aims: Epilepsy and sleep reciprocally influence each other. Our previous result elucidates that unilateral deep brain stimulation (DBS) of anterior nucleus of thalamus (ANT) suppresses epilepsy recurrence. In present study, we tried to further determine whether DBS changes sleep and delta powers during non-rapid eye movement (NREM) sleep to suppress spontaneous recurrence of epilepsy.

Methods: We intraperitoneally injected pentylenetetrazol (PTZ) for consecutive 14 days to induce spontaneous epilepsy in rats, and a 30-minute or a 3-hour DBS of unilateral ANT was applied to suppress epilepsy. The frequency of DBS stimulation was 200Hz and the electrical currents consisted of biphasic square pulses with an intensity of 50 μ A, an 100 μ s pulse width and a 4.1ms stimulation interval. Sleep and epileptiform electroencephalograms (EEGs) were recorded for 24 hours.

Results: Unilateral ANT DBS prolonged the onset latency of the ictal epilepsy, decreased the spontaneous seizure duration, and increased the survival rate. Unilateral ANT DBS increased the amounts of REM sleep. Our result also indicated that power intensities of all frequencies were enhanced during the PTZ-induced ictal period and subsequent spontaneous epilepsy. 39 of ANT DBS suppressed the augmentation of low-frequency (<10Hz) intensities during spontaneous epilepsy. Consecutive injections of PTZ progressively increased the enhancement of the delta powers during NREM sleep, whereas ANT DBS inhibited this progressive enhancement.

Conclusion: These results elucidated that unilateral ANT DNS enhanced the seizure threshold by increasing REM sleep and decreasing the progressive enhancement of delta power during NREM sleep to suppress spontaneous seizure recurrences.

Disclosure: Nothing to disclose

EPO3102

Symptomatic epilepsy in stroke

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Background and aims: Stroke is one of the leading causes of disease and death in older population. The risk of developing epilepsy after stroke is seven times higher compared to normal population. The development of PSE is caused by stroke at a younger age, the size of stroke, cortical presentation, early seizures, cerebral hemorrhage.

Methods: This prospective study analyzed patients with the first stroke with ischemic and hemorrhagic genesis. The research was conducted at the Clinic of Neurology Nis and it lasted for a year. The same group of patients was monitored for the following 2 years, focusing on the development of symptomatic epilepsy.

Results: The control group was composed of 246 patients without symptomatic epilepsy after 1st stroke and the other group of 21 patients, with epileptic seizures after 1st stroke. The lesions were classified into deep lesions and those with cortical localization. The depth of the lesions had a statistically significant influence on the development of seizures. The lesions are classified into big and small. The small lesions included changes that were ≤ 3 cm whereas big lesions included changes > 3 cm. A statistical significance between the size of the lesion and seizures was not determined although twice as more patients with a big lesion were observed in PSE group.

Conclusion: The frequency of PSE in the examined group was 7.86%. Big lesions were more commonly found in the PSE group. The PSE group more often had stroke in the MCA territory. The number of patients with cortical and subcortical lesion was significantly higher.

Disclosure: Nothing to disclose

Headache and pain 3

EPO3103

Effect of cervical proprioception disorders on balance function in patients with chronic migraine

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Background and aims: One of the causes of imbalance may be comorbidity of migraine with vestibular dysfunction (VD) and proprioception disorder of the cervical spine muscles (CSM).

Aim: to evaluate statokinetic stability (SS) in patients with migraine in a period between headache attacks.

Methods: 32 patients (females) were examined, mean age 38 ± 9.4 , diagnosis of migraine according to ICD-3 beta. SS was evaluated by stabilometry ("Stabilan-01-2") using Romberg test with open eyes, closed eyes, and with head turns. Ellipse area (EA, m^2), balance function quality (QBF, %), movement speed of the pressure center (MSPC, mm/s) were evaluated. Trigger points (TP) in CSM were determined by manual testing.

Results: While comparing the results with closed eyes to the results with open eyes, a significant decrease in QBF was revealed from $87.5[84.2;94.2]\%$ to $81.4[75.7;88.8]\%$; an increase in EA from $78[34.0;111.9]mm^2$ to $108.4[44.5;279.6]mm^2$; an increase in MSPC from $6.1[5.3;9.03]mm/s$ to $8.1[7.1;12.4]mm/s$, (Wilcoxon, $p < 0.05$). While "Head turn" test MSPC increased significantly to $6.4[5.0;9.7]mm/s$ while right turn, and to $7.0[5.45;9.5]mm/s$ while left turn. TP were detected in the trapezoid muscles in 32 patients, and in the splenius cervicis muscles in 8.

Conclusion: Stabilography allowed to quantify VD in patients with migraine. Statistically significant deterioration of SS while visual deprivation and head rotations indicates contribution of altered afferentation from trigger points in CSM on the condition of balance in patients with migraine.

Disclosure: Nothing to disclose

EPO3104

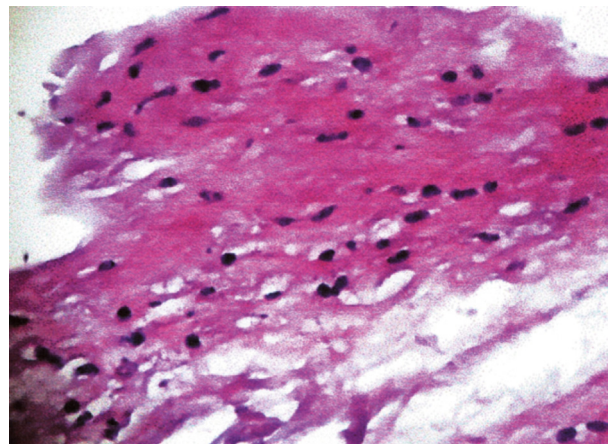
Prevalence of Arachnoiditis in patients with Paroxistic Trigeminal Neuralgia with Continuous Persistent Pain

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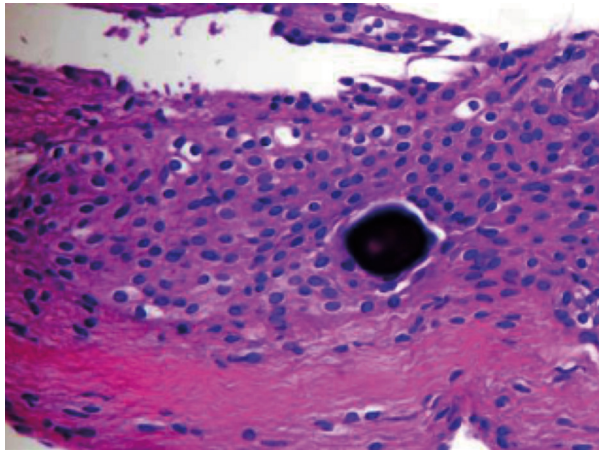
Background and aims: Trigeminal Neuralgia (TN) can be classified based on its clinical presentation in paroxistic or paroxistic with continuous persistent pain, previously known as atypical trigeminal neuralgia. There is no explanation as to why some patients develop this clinical presentation. The objective of this study was to describe the presence of inflammatory findings on biopsies of arachnoid in patients with atypical TN.

Methods: 43 patients with atypical TN seen at our center between January 2014 and December 2018 selected for Microvascular Decompression (MVD) were included for our study. Biopsies of arachnoid were obtained in every case and analyzed with a hematoxylin-eosin stain. Follow-up was at three- and twelve-months post-surgery.

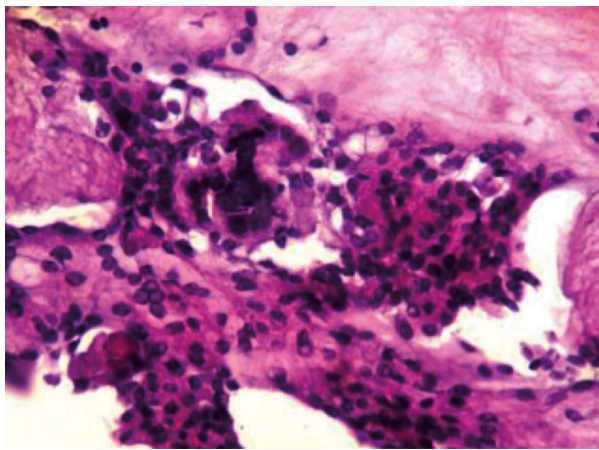
Results: Analysis of the biopsies revealed components of chronic arachnoiditis: mild fibrosis (n=17), moderate fibrosis (n=6) and severe fibrosis (n=3), dystrophic microcalcifications (n=9) and hyperplasia of neuroepithelial cells (n=6). Average time of disease evolution was 7.75 years. 7 patients developed a contralateral neuralgia after being operated of MVD. The surgery had a success rate of 67.44% (n=29). 23.26% (n=10) of patients had persistence of pain after surgery and 9.30% (n=4) patients had recurrence of pain between 12-60 months.



Fibrosis and Microcalcifications



Microcalcification in the Arachnoid



Hyperplasia of neuroepithelial cells

Conclusion: The pathology results suggest that there is a chronic inflammatory process accompanying the TN with paroxistic and continuous persistent pain. These inflammatory changes probably occur after a prolonged neurovascular contact. This hypothesis may offer an explanation to the atypical clinical presentation of TN and new ideas regarding the treatment and management of this disease.

Disclosure: Nothing to disclose

EPO3105

Pooled Analysis of Cardiovascular Safety of Fremanezumab in Patients ≥60 Years of Age With Migraine: Pooled Results of 3 Randomised, Double-blind, Placebo-controlled Phase 3 Studies

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Background and aims: Although migraine prevalence declines with age, treatment may be challenging in older patients as some preventive medications may cause cognitive and cardiac side effects in this population. Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for the preventive treatment of migraine in adults. Overall adverse events (AEs) and cardiovascular (CV) AEs with fremanezumab were evaluated in a subgroup of patients ≥60 years of age in this pooled analysis.

Methods: This analysis in patients ≥60 years of age with episodic migraine (EM) or chronic migraine (CM) included data from three phase 3 trials (HALO EM, HALO CM, and FOCUS), in which patients were randomised 1:1:1 to receive subcutaneous quarterly or monthly fremanezumab or matched monthly placebo over 12 weeks. Overall AEs and CV AEs were summarised for these patients.

Results: Overall, 246 patients ≥60 years of age were included in these pooled analyses. A total of 73 (30%) patients had CV medical history. AEs were reported for similar proportions of patients across treatment groups; the most common AEs were injection-site induration, pain, and erythema (Table 1). In patients with CV medical history, 4 individual CV AEs were reported across treatment groups. In patients without CV medical history, 2 individual CV AEs were reported (Table 2).

Table 1. Overall AEs Occurring in ≥1 Patient ≥60 Years of Age in Any Treatment Group

AEs, n (%)	Placebo (n=80)	Quarterly fremanezumab		Monthly fremanezumab	
		675mg/placebo/placebo (n=74)	675/225/225mg (n=46)	225/225/225mg (n=46)	
Patients with ≥1 AE	44 (55)	48 (65)	29 (63)	24 (52)	
Injection-site induration	14 (18)	11 (15)	10 (22)	13 (28)	
Injection-site pain	10 (13)	13 (18)	9 (20)	10 (22)	
Injection-site erythema	13 (16)	8 (11)	7 (15)	3 (7)	

AE, adverse event; SAE, serious adverse event.

Table 2. CV AEs in Patients ≥60 Years of Age With and Without CV Medical History

CV AEs, n (%)	Placebo (n=23)	Quarterly fremanezumab		Monthly fremanezumab	
		675mg/placebo/placebo (n=6)	675/225/225mg (n=14)	225/225/225mg (n=30)	
Patients with CV medical history					
Patients with ≥1 CV AE	1 (4)	1 (3)	2 (14)	0	
Palpitations	1 (4)	0	1 (7)	0	
Supraventricular tachycardia	0	1 (3)	0	0	
Hypertensive crisis	0	0	1 (7)	0	
Patients without CV medical history					
Patients with ≥1 CV AE	0	0	2 (6)	0	
Hot flush	0	0	1 (3)	0	
Hypertension	0	0	1 (3)	0	

CV, cardiovascular; AE, adverse event.

Conclusion: This pooled analysis demonstrates that fremanezumab treatment over 12 weeks was well tolerated in patients ≥ 60 years of age, with CV AEs occurring in similar proportions of patients with or without a CV medical history.

Disclosure: This study was funded by Teva Pharmaceuticals.

EPO3106

Dialysis headache: 4 cases of a tertiary headache centre

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Background and aims: Dialysis headache (DH) is a secondary headache, occurs during hemodialysis (HD) and resolves up to 72h after HD ends. Its pathophysiology is not established, and it is a rare headache in the outpatient clinic. We aimed to characterize DH in a patient sample consulted in the headache outpatient clinic.

Methods: A retrospective analysis of headache outpatient registries fulfilling DH criteria. Variables collected: demographic and clinical data (time-to-onset (TTO) since HD and TTO during HD, localization and type of headache, headache duration, accompanying symptoms, pharmacotherapy, response to therapeutics, previous headache diagnosis).

Results: 4 patients (3 men), 51-72 years-old, were identified, with headache starting 0-4 years since commencing HD. Localization was variable, but bilateral in all patients. Pain was described as dull (n=2), pulsatile (1) or both, and lasted up to 48h, starting 2-3h after HD. 3 patients presented associated symptoms: nausea, vomiting, phonophobia, photophobia, and kinesiophobia. 3 patients took symptomatic treatment, with partial relief in 2 (paracetamol, metamizole, zolmitriptan), and total resolution in 1 (eletriptan). 2 patients had a previous migraine diagnosis, 1 of them with an associated medication-overuse headache.

Conclusion: There is not a specific pattern for DH, besides its temporal profile and its relation to HD. Response to triptans in one suggests a migraine-type pathophysiology.

Disclosure: Nothing to disclose

EPO3107

Pharmacological treatment of trigeminal neuralgia in a secondary hospital.

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Background and aims: Trigeminal neuralgia is a relatively common cause of headache. Usually there is a good response to pharmacological treatment, but according to some series, up to 25% of the patients are refractory, having tried at least one drug at maximal dosage. In these cases, other therapies should be tested in order to try to avoid side effects of polytherapy.

Methods: We analysed all patients diagnosed with trigeminal neuralgia during 2018 in our centre, focusing on magnetic resonance imaging and pharmacological treatment.

Results: We diagnosed a total of 60 patients, with a mean age of 67 years. 80% women and a medium disease duration of 8 years. Nearly 75% of patients had no abnormalities in brain MRI (1.5T), being diagnosed with idiopathic trigeminal neuralgia. Only 12,5% showed neurovascular compression.

Regarding treatment, 40% of the patients were controlled with a single drug; 50% have tried at least 2 different drugs; and 18% had tried 3 or more. Pregabalin, gabapentin and amitriptyline were the more frequent add-on (table 1).

In our series, the most common side effects were drowsiness, nausea, dizziness, hypertransaminasemia and hyponatremia, presenting in 20% of patients treated in monotherapy, increasing up to 50% in polytherapy. Only 8,4% of patients were evaluated by a neurosurgeon, all of them with abnormal MRI

	CBZ	OXC	ESL	GBP	PGB	AMI	LAC
Carbamazepine (CBZ)	11			1	6	3	
Oxcarbazepine (OXC)		1		1			
Eslicarbazepine (ESL)			8	1	2	1	
Gabapentin (GBP)				4		2	
Pregabalin (PGB)					4	2	
Amitriptyline (AMI)				1	1	1	
Lacosamide (LAC)						1	2

Drugs used more frequently.

Conclusion: Although an extensive variety of drugs to treat trigeminal neuralgia exist, we found that up to 50% of patients can be considered refractory to medical treatment. Refractory patients should be referred promptly for neurosurgical evaluation to avoid polytherapy and unbearable side effects.

Disclosure: Nothing to disclose

EPO3108

Video Head impulse test in inter-ictal Vestibular Migraine

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Background and aims: To evaluate the vestibulo-ocular reflex (VOR) with the video head impulse test (vHIT) in patients with vestibular migraine (VM).

Methods: We studied 62 VM patients, 55 females, 7 males aged 18-63 years (mean 43) diagnosed according to the ICHD-3 beta diagnostic criteria and 35 healthy controls aged 18-86 years (mean 41). The vHIT was evaluated in 3 semicircular (SCC) planes: right lateral-left lateral, right anterior-left posterior and left posterior- left anterior using GN Otometrics apparatus.

Results: While mean VOR gains from each SCC were within normal limits, VOR gain was below normal from: one anterior SCC in 29 patients; one posterior SCC in 26 patients; one lateral SCC of 35 patients; both posterior SCCs in 19 patients, both anterior SCCs in 8 patients and both lateral SCCs in 11 patients. Even with normal VOR gain overt catch-up saccades (CUS) were present from both lateral SCCs in 14 patients and from both posterior SCCs in one patient and overt CUS were present from one lateral SCC in 1 patient and from one posterior SCC in 3 patients. 2 patients with covert CUS in posterior SCC also had low VOR gain.

Conclusion: VM patients had normal mean VOR gain, but half the patients had low gain from one or more individual semicircular SCCs. Our study confirms that VOR impairment – either with low VOR gain or with catch-up saccades, or with both seems to be a regular feature of interictal VM.

Disclosure: Nothing to disclose

EPO3109

Generalisability of the CONQUER trial results to routine clinical practice: galcanezumab versus placebo in patients with inadequately controlled migraine

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Background and aims: Healthcare decision makers are often concerned about the external validity of randomised controlled trials (RCTs) (i.e., results may not apply to all patients who are intended to receive treatment in the ‘real-world’ [RW]). CONQUER is a RCT of galcanezumab in patients who experienced ≥ 4 migraine headache days/month and for whom 2–4 prior preventive treatment categories had failed. This analysis aimed to generalise results from CONQUER to the RW French migraine population.

Methods: The InovPain migraine database is a RW cohort of all French patients with migraine followed in a large tertiary headache centre (Pain Department, CHU Nice). This analysis was conducted in steps:

Step 1: Individual patient-level data from CONQUER were weighted to match aggregated InovPain data regarding the subgroup of French patients with migraine and ≥ 2 preventive treatment failures using the Signorovitch method (2010). Matched patient characteristics were gender, age, migraine type and duration, number of migraine headache days and number of headache days at baseline.

Step 2: The primary endpoint of CONQUER was reanalysed using the weighted CONQUER patient data using a priori defined methodology.

Results: Table 1 shows patient characteristics before and after weighting. Results of the weighted analysis were similar to those of the primary CONQUER analysis, with a statistically significant greater mean reduction in the number of monthly migraine headache days for galcanezumab versus placebo (Table 2).

Table 1. Baseline patient characteristics before and after weighting

	InovPain (N=130)	CONQUER (N=462)	Weighted CONQUER IPD with InovPain characteristics (ESS=320)
Age, years	45.8 ± 12.3	45.8 ± 11.8	45.8 ± 11.9
Females	109 (83.8)	397 (85.9)	(83.8)
Years since migraine diagnosis	25.3 ± 13.9	23.2 ± 13.5	25.3 ± 14.2
Number of monthly MHDs	14.6 ± 7.0	13.2 ± 5.9	14.6 ± 6.3
Number of monthly headache days	17.7 ± 8.8	15.0 ± 6.2	17.7 ± 6.9
Episodic migraine	65 (50.0)	269 (58.2)	(50.0)
HFEM	53 (40.8)	198 (42.9)	(40.8)
LFEM	12 (9.2)	71 (15.4)	(9.2)
Chronic Migraine ^a	65 (50.0)	193 (41.8)	(50.0)
Acute medication overuse ^b	73 (56.2)	207 (44.8)	(53.6)
Failure of 2 previous preventive treatments ^c	64 (49.2)	159 (34.4) ^d	(33.2)
Failure of 3 previous preventive treatments ^c	43 (33.1)	127 (27.5) ^d	(27.7)
Failure of 4 previous preventive treatments ^c	14 (10.8)	82 (17.8) ^d	(17.2)
Failure of >4 previous preventive treatments ^c	9 (6.9)	93 (20.1) ^d	(21.7)

Data shown are mean ± standard deviation or n (%) of patients. Data were matched using the corresponding variables of the values shown in bold in the last column.
^aCapped at about 40% of the study population in CONQUER.
^bData collection may have differed between the two sources.
^cIn InovPain, all beta-blockers were considered as a single treatment.
^dFailure during lifetime.
 ESS, effective sample size = $\frac{(\sum_{i=1}^n weight_i)^2}{\sum_{i=1}^n weight_i^2}$; HADS, Hospital Anxiety and Depression Scale; HFEM, high frequency episodic migraine (8 to 14 MHD/month); IPD, individual patient data; LFEM, low frequency episodic migraine (<8 MHD/month); MHD, migraine headache days.

Table 1. Baseline patient characteristics before and after weighting

Table 2. Results of the primary CONQUER and weighted analyses: overall mean change from baseline in the number of monthly migraine headache days during the 3-month double-blind treatment phase for the total population with episodic or chronic migraine

	Placebo LSM (SE)	Galcanezumab LSM (SE)	Difference LSM (95% CI)	p-value
Primary CONQUER analysis	N=228	N=230	-3.12	<.0001
	-1.02 ± 0.32	-4.14 ± 0.32	(-3.92, -2.32)	
Weighted CONQUER IPD with InovPain characteristics	ESS=173	ESS=151	-3.13	<.0001
	-1.04 ± 0.36	-4.17 ± 0.36	(-4.02, -2.24)	

CI, confidence interval; ESS, effective sample size = $\frac{(\sum_{i=1}^n weight_i)^2}{\sum_{i=1}^n weight_i^2}$; IPD, individual patient data; LSM, least squares mean; SE, standard error.
 LSM and SE were obtained with a mixed model for repeated measures (MMRM) model including the following variables: treatment, pooled country, month, treatment*month, baseline, and baseline*month, and used an unstructured covariance structure.

Table 2. Results of the primary CONQUER and weighted analyses: overall mean change from baseline in the number of monthly migraine headache days during the 3-month double-blind treatment phase for the total population with episodic or chronic migraine

Conclusion: There is no evidence to suggest that the treatment effects observed in CONQUER would be different if the RCT population had been similar to the RW French InovPain cohort.

Disclosure: This study was sponsored by Eli Lilly and Company. M-AP, AT-H, MB and FC are employees and minor shareholders of Eli Lilly and Company; ML-M has received honoraria for advisory boards, speaker panels or investigation studies from Amgen, Astellas, ATI, Boston Scientific, Grunenthal, Lilly, Medtronic, Menarini, Novartis, Pfizer, ReckittBenckiser, Saint-Jude, Sanofi-Aventis, Teva, and Zambon in the past 5 years.

EPO3110

Could Medical Cannabis be an Effective Treatment for Migraine? A Literature Review

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Background and aims: Cannabis has been prescribed for headache alleviation by physicians since the time of the ancient Persians. The main chemical components of cannabis are: Cannabidiol (CBD) and Tetrahydrocannabinol (THC). Recently, studies have begun to show that these compounds can increase the bodies endogenous endocannabinoid systems levels. The endocannabinoid system is involved in the mediation of pain. The purpose of this review is to evaluate whether medical cannabis could be an effective treatment for the headache disorder migraine.

Methods: This review was carried out using papers across two web databases; PubMed and Web of Science.

Results: The papers reviewed highlight the fact that endocannabinoid system dysfunction is likely to contribute to chronic migraine. This is thought to be from reduced levels of endocannabinoids which result in increased CGRP and Nitric Oxide production leading to migraine. This is backed up by the reduced levels of certain endocannabinoids in the CSF of people with chronic migraine compared to controls. People with chronic migraine have also been shown to have increased CGRP and NO production. Human based studies primarily have been case-reports, but these also given intriguing results. Not only has cannabis been reported to be effective in the abortion of migraine attacks but there is some evidence that it reduces the frequency of migraine attacks as well.

Conclusion: Medical Cannabis appears to be a promising treatment for migraine, especially with its potential ability to reduce migraine frequency. More research is required into which forms of medical cannabis are the most efficient in combating migraine.

Disclosure: Nothing to disclose

EPO3111

Post-operative pain following lumbar spine surgery: risk factors of chronic pain and quality of life outcomes

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Background and aims: Chronic pain (CP) after lumbar spine surgery (LSS) is distinguished by high prevalence and socio-economic burden. Study aimed to investigate risk factors of CP after LSS and impact of CP on quality of life.

Methods: Prospective cohort observational study recruited adults after L4-L5 or L5-S1 microdiscectomy. Patients were divided into 3 groups - with CP, episodic pain (EP) and without pain (control group). All patients were tested prospectively and retrospectively with Numeric and Verbal rating scales, DN4 questionnaire, prospectively with Oswestry Disability Index, Holmes-Rahe Life Stress, Beck's Depression, Spielberger State-Trait Anxiety Inventories.

Results: Altogether 29 patients (15/29 females, median age 48 years old (IQR 45-51), median time after surgery 7.5 months (IQR 6-10)) were enrolled; 8/29 patients had CP, 7/29 - EP, 14/29 - no pain. There was no difference in characteristics of pain before surgery. Patients with CP had more points in DN4 as compared to EP (Figure 1). Before surgery patients with pain had higher body mass index (BMI), length of conservative therapy was longer among individuals with CP (Figure 2). Group with CP had higher functional disability, depression and anxiety after surgery, EP resulted to higher functional disability and anxiety as compared to control group, both CP and EP patients were characterized by higher stress in previous 12 months (Figure 3).

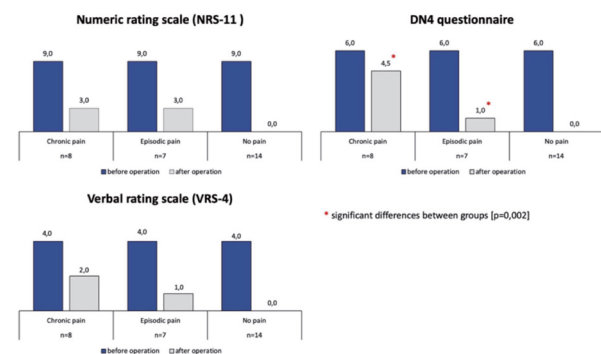


Figure 1. Dynamics of pain after the operation.

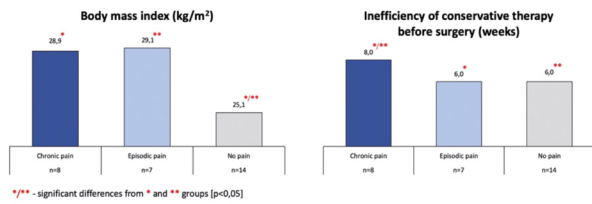


Figure 2. Body mass index, inefficiency of conservative therapy before the operation.

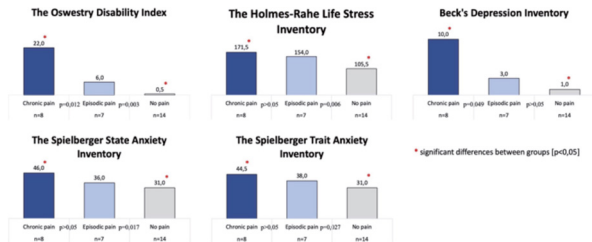


Figure 3. Comparison of indicators of anxiety, depression, disability, stress after the operation.

Conclusion: High BMI, stress and prolonged conservative therapy before LSS can be predictors of CP emergence. Post-operative CP is often neuropathic and can result to high functional disability, depression and anxiety.

Disclosure: Nothing to disclose

EPO3112

MRI and evoked potentials in postoperative estimation of trigeminal neuralgia

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Background and aims: It is accepted, constant artery pulsation leads to damage of nerve sheath and formation of demyelination area. The estimation of trigeminal nerve (TN) somatosensory evoked potentials (tnSEP) is 1 of functional methods for diagnosis of TN root demyelination. We can estimate the anatomical damage of TN using diffuse-tensor MRI, comparing the difference between fractional anisotropy (FA) parameters on damaged and contralateral sides.

We estimated the sensibility of tnSEP and FA in the setting of clinical improvement during 7-10 days after microvascular decompression (MVD) of TN root.

Methods: MVD of TN root was performed for 10 patients (7 male and 3 female, age from 47 till 76) suffered from with classical trigeminal drug-resistant neuralgia. Pain intensity at VAS was not less than 6. Preoperatively diffuse-tensor MRI of TN tracts with the estimation of FA parameters was performed for all patients. Estimation of tnSEP was performed at 6 patients resulting from pain syndrome provocation during electrodes placement on face skin. These diagnostic studies were repeated at in 7-10 days after operation.

Results: Clinical improvement was achieved in 100% postoperatively. No significant changes of FA parameters pre-and postoperatively. Initially we registered decreased speed transmission on symptomatic TN root at 2 patients while estimating tnSEP preoperatively. In 7 days after operation we observed symmetric signals from both TN at one of patients.

Conclusion: Such methods as tnSEP and diffuse-tensor MRI with FA parameters estimation not reflect preoperative and early postoperative changes of afferent conduction via TN branches and microstructural nerve changes even in case of clinical improvement.

Disclosure: Nothing to disclose

EPO3113

Posterior Reversible Encephalopathy Syndrome of unknown precipitating factor: A case report

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Background and aims: Posterior Reversible Encephalopathy Syndrome (PRES) is a complex condition caused from a loss of autoregulation and results in reversible subcortical vasogenic brain oedema. The most common precipitating factor is hypertension and other causes are renal failure, sepsis, autoimmune disorders, and use of immunosuppressive or cytotoxic drugs.

Methods: A 55-year-old female, with past medical history of osteosclerotic changes in Th11 and Th12, was admitted to our hospital due to persistent, throbbing headache with nausea and vomiting lasting for one week. No history of hypertension, previous immunosuppressive or cytotoxic drugs was found. Her family history was positive for seizures, arthritis and psoriasis.

Results: Examination revealed normal blood pressure and mild liver lesion. Urinalysis was unremarkable. Neurologic examination and funduscopic examination were within normal limits. The visual field was normal. Immunological laboratory tests were negative except for antimitochondrial antibody (AMA). The MRI scans demonstrated abnormal signal intensity involving bilateral occipital regions with cortical subarachnoid haemorrhage in the left frontal region consistent with the diagnosis of PRES. A brain MRI one month later demonstrated complete resolution of the initial cerebral lesions. Her headache resolves completely. After extensive work up, an internal medicine diseases was excluded as a cause of PRES.

Conclusion: PRES is reversible neurological disorder of unclear pathophysiological mechanism. Effective therapy includes treatment of underlying cause. Extensive workup did not reveal any precipitating factor of PRES. Even after months of monitoring, our patient did not fulfilled criteria for any disorder known as the cause of PRES which is a challenge in a treatment algorithm.

Disclosure: Nothing to disclose

EPO3114

Coping strategies for chronic low back pain in patients with anxiety and depressive symptoms – is behavior a decisive factor?

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Background and aims: Depression and anxiety in patients with chronic low back pain have an impact on coping strategies used by the sufferers. Passive coping strategies lead to the persistence of pain, increased level of disability and decreased social participation, while active positive behaviour would represent a core support in controlling pain.

Aim: To observe the coping strategies employed by patients suffering from chronic low back pain.

Methods: 31 (11 male/21 female) patients with chronic low back pain associated with anxiety and depression were included in the study. The Chronic Pain Coping Inventory-42, The Spielberger trait anxiety inventory measures, PHQ-9 Patient Health Questionnaire and visual analogic scale were used.

Results: Most of patients assumed passive methods of coping such as: guarding/avoiding physical activity (male - 3.58 ± 2.14 / female - 4.24 ± 1.21 , $p=0.36$); relaxation – avoidance of physical involvement (men - 2.96 ± 1.64 / women - 4.09 ± 2.23 , $p=0.15$); exercise (men - 3.04 ± 1.77 / women - 1.97 ± 1.29 , $p=0.06$). The least used strategy in both groups is persistence of task (male - 4.97 ± 2.00 , female - 1.82 ± 1.59 , $p<0.0001$). No statistically significant results were revealed comparing the types of coping strategies and pain intensity.

Conclusion: Determined trend of using passive coping strategies by patients with chronic low back pain and marked anxiety and depression confirm the need of active coping strategies implementation along education, that will bring a substantial benefit for management of persistent low back pain.

Disclosure: Nothing to disclose

EPO3115

Does fibromyalgia predict a poor response to Onabotulinumtoxin A in patients with chronic migraine?

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Background and aims: Patients with fibromyalgia were excluded from PREEMPT trials. Our aim was to evaluate the effectiveness of Onabotulinumtoxin A in a group of patients with chronic migraine (CM) and fibromyalgia.

Methods: This is an observational retrospective study that includes patients who suffered CM and had a previous diagnosis of fibromyalgia. The response to OnabotulinumtoxinA during follow-up visits was assessed.

Results: Data from 25 patients with CM and fibromyalgia were collected (100% females). 21 patients received Onabotulinumtoxin A at any point of follow-up. Mean age at first procedure was 50.38 ± 11.25 years (range 37–75 years). Depression (71.40%), other central sensitization syndromes (38.09%) and medication overuse headache (90.47%) were frequent comorbidities. 46,6% had failed ≥ 3 preventives previously. They received an average of 6.42 ± 4.11 injections cycles.

Response rate (at least 50% of reduction from baseline in headache days per month) was 52.94% at cycle 2, 50% at cycle 3 and 62.50% at cycle 4.

16 patients completed 1 year of treatment, with 12.28 ± 10.88 mean change from baseline in frequency of headache days and 43.75% patients reducing $\geq 70\%$ their headache frequency.

In 2 cases (9.52%) Onabotulinumtoxin A therapy was interrupted due to a lack of response. No adverse effects were recorded.

Conclusion: Response rate was 62.50% after 1 year of treatment. These results suggest that fibromyalgia does not predict a poor response to Onabotulinumtoxin A in CM.

Disclosure: Nothing to disclose

EPO3116

Onabotulinumtoxin A in high frequency episodic migraine: experience in a University Hospital.

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Background and aims: High frequency episodic migraine (HFEM) shares clinical features with chronic migraine (CM) regarding headache-related disability and impact on daily life. Our aim was to evaluate response to OnabotulinumtoxinA in HFEM.

Methods: An observational study was performed. We included patients diagnosed with HFEM attended in a headache unit. We analyzed data from medical records and evaluate treatment effectiveness.

Results: 24 patients were included. 96% were female, mean age was 44 ± 7 years (mean \pm SD). 17 patients received OnabotulinumtoxinA and 11 patients received oral medications (4 patients received both).

Patients receiving Onabotulinumtoxin A had failed a mean of 3.5 oral preventatives. 5 patients (27%) discontinued treatment due to a lack of response. 15 patients received ≥ 2 cycles of treatment, 13 patients ≥ 2 cycles and 8 patients ≥ 2 cycles. 81% and 73% reported subjective overall response (clinically significant reduction in frequency or intensity of attacks or response to acute treatment) after 1st and 3rd cycle, respectively. Mean reduction of monthly headache days was 3.4 after first cycle, 4.3 after second cycle and 4.4 after third cycle. 44% of patients experimented a reduction of $\geq 50\%$ in headache frequency.

Patients treated with oral medications had failed to a mean of 3 previous preventatives (35% had not received any preventive treatment). 54% of them had $\geq 50\%$ reduction in headache frequency after 6 months of treatment. Mean reduction on monthly headache frequency was 6 days.

Conclusion: Our results suggest that Onabotulinumtoxin A can be a therapeutic option in patients with HFEM who did not respond or tolerate oral treatments.

Disclosure: Nothing to disclose

Headache and pain 4

EPO3117

Visual Snow Syndrome: Quantification of symptoms over time

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Background and aims: Patients with 'visual snow syndrome' (VSS) describe a continuous disturbance of TV snow-like flickering dots in the entire visual field (visual snow, VS) with additional visual symptoms. This study aims at quantifying the severity of VS over time.

Methods: In 2019, we re-contacted 78 patients with definite VSS who had taken part in a previous interview in 2011. In addition to the distraction by VS, we assessed VS density, velocity, noticeability, and other characteristics. Parameters were measured using ordinal scales.

Results: We were able to interview 40 of 78 (51%) patients with a mean follow up time of 83.6±4.5 months. The distraction VS creates ameliorated in 10/40 (25%), whereas 6/40 (15%) reported worsening. Density of VS increased in 7/40 (17.5%) and decreased in 5/40 (12.5%), whereas movement of VS dots became more rapid in 10% (4/40) and slowed down in 10% (4/40). VS dots could be perceived on more surfaces in 4/40 (10%) and on less surfaces in 2/40 (5%). Morphologic characteristics (color and size of VS dots), duration of symptoms during the day and influence of different lightning conditions on VS were mainly unchanged. Fluorescent lightning was generally associated with a worsening of symptoms.

Conclusion: In VSS, visual snow itself remained stable in the majority patients. Distraction created by VS improved in one fourth.

Disclosure: The study was supported by the Baasch Medicus Foundation.

EPO3118

Synergic effect of anesthetic block and botulinum toxin in migraine in clinical practice.

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Background and aims: Onabotulinumtoxin A (OnabotA) is a therapy indicated in the treatment of chronic migraine. The anesthetic block (AB) with lidocaine or mepivacaine, appears as a second-line treatment in acute migraine attacks. Our goal is to evaluate the actual use of these techniques in a Headache Unit (HU), the frequency with which they are used and analyze the impact on the frequency of pain.

Methods: Retrospective analysis of patients treated for the first time in a HU between 2017-2018 who met migraine criteria according to those established in IHC-3 and on which techniques had been used (OnabotA, AB of both major occipital nerves (GON)). Pain frequency were analyzed after the use of these techniques. Response rate (frequency reduction of pain episodes ≥50%) was analyzed over 3 successive visits.

Results: 56 patients with migraine (79% chronic migraine) were included in which OnabotA was used. 78% of women. AB was additionally used in 12 of these patients. After 3 visits, a response rate of 70% was observed in patients in whom OnabotA was used exclusively and 83,3% in which additionally AB was performed in both GON

Age	41
Gender	78,6% women
Chronic migraine	78,6%
Aura	17,9%
Medication Overuse Headache	42,9%

Figure 1. Patients characteristics

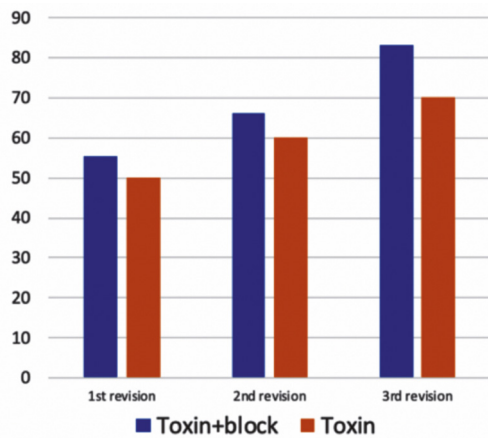


Figure 2: Percentage of response in patients infiltrated with toxin vs patients infiltrated with toxin + AB.

Conclusion: While the effectiveness of OnabotA as a preventive therapy in chronic migraine is known, the additional use of AB in consultation could have a synergistic effect on this preventive therapy.

Disclosure: Nothing to disclose

EPO3119

Effectiveness of Ayurveda for chronic migraine: a pragmatic, randomised, clinical trial.

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Background and aims: Ayurveda is the oldest holistic medical system and commonly practiced in India. To evaluate the effectiveness of Ayurveda in participants with chronic migraine, present study was undertaken.

Methods: Study was conducted as multicentre, pragmatic, randomised, clinical trial, 72 participants with chronic migraine were randomly assigned to Ayurveda or to usual care. Primary outcome measures were frequency of headache. Secondary outcome measures were severity of headache, disability and use of medication.

Results: After 16 weeks, a significantly larger reduction of headache frequency was found for the ayurveda group ($p < 0.01$). Disability and medication use showed significant differences in favour of the ayurveda group compared to usual care.

Conclusion: Ayurveda therapy could be more effective than usual care in the short-term in reducing symptoms of chronic migraines. Long term follow up is required.

Disclosure: Nothing to disclose

EPO3120

Effect of Vitamin D supplementation on symptoms in patients with migraine

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Background and aims: Migraine is the most common headache around the world including Korea. This study investigated whether vitamin D supplementation would be beneficial for patients with migraine

Methods: A randomized, double-blinded, placebo-controlled parallel trial was conducted in migraine patients (40 women and 20 men, 20-65 years of age). A 4-week baseline period was conducted before randomization to 48 weeks of treatment. The patients were divided into 2 groups: Group 1, which had low vitamin D levels and received vitamin D therapy (n=30, 22 women and 8 men, 300,000 IU cholecalciferol intramuscular injection per 6 months), Group 2, which had low vitamin D levels and did not receive vitamin D therapy (n=30, 18 women and 12 men). The response rate (i.e. experiencing a 50% or greater reduction in migraine frequency from baseline to week 48), change in migraine severity, duration and number of migraine days were recorded.

Results: The group 1 demonstrated a significant decrease ($p<0.001$) in migraine frequency from baseline to week 48 compared with the group 2. The number of headache days changed from 13.14 ± 3.60 in the group 1 and 12.8 ± 5.52 in the group 2 at baseline to 6.58 ± 3.24 and 11.7 ± 4.24 by the end of the trial, respectively. The incidence of aura, phonophobia/photophobia, allodynia, and resistance to medications were significantly decreased ($p<0.005$) in the group 1 than those with the group 2.

Conclusion: Vitamin D supplementation was significantly beneficial in decreasing duration, frequency, and severity of headache attacks.

Disclosure: Nothing to disclose

EPO3121

The opportunity of using tolperisone for treatment of tension-type headacheV. Shirokov¹, V. Gusev², O. Lvova², I. Evdokimova³

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Background and aims: Tension-type headache (TTH) is common and has a high socio-economic impact. The lack of effectiveness of existing therapeutic methods requires the study of alternative treatments for these patients.

Methods: We enrolled 48 patients met the diagnostic criteria for Chronic TTH (The International Classification of Headache Disorders, 3rd edition). Mean age 39 years; 31 women; signed informed form. Patients had one injection of 100mg tolperisone in different muscles of the head and neck according to "follow the pain" method (Blumenfeld AM, 2003). The number of points and muscles for injection was determined by the condition, the physique, the muscle size and the severity of pain in a particular area (m. masseter, m. temporalis, m. frontalis, m. pterygoideus lateralis, m. trapezius, m. sternocleidomastoideus). All patients were evaluated before, one day and one month after treatment using a visual analog scale (VAS), Verbal Rating Scale (VRS).

Results: VAS score significantly diminished from baseline to one day (5.12 ± 0.18 vs 2.55 ± 0.17 $p<0,05$) and one month after treatment (5.12 ± 0.18 vs 2.17 ± 0.18 , $p<0.05$). VRS score from baseline to one month after treatment decreased as well (1.88 ± 0.12 vs 1.07 ± 0.09 , $p<0.05$).

Conclusion: The data obtained may allow to use tolperisone injections as affordable alternative medicine to BTA in TTH patients due to its efficacy as well as possibility of more frequent injections.

Disclosure: Nothing to disclose

EPO3123

Is tolerability to onabotulinumtoxin A injection correlated with adverse events or clinical response? A prospective cohort study.

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Background and aims: Onabotulinumtoxin A (OnabotA) is an effective treatment for Chronic Migraine (CM), with a distinct Adverse Event (AE) profile. The procedure sometimes overwhelms patients. We aim to analyze if tolerability is associated with AE occurrence and clinical response.

Methods: Prospective cohort study including all consecutive patients with CM treated with OnabotA from January 2017 to December 2019 in a headache unit. All patients were asked to rate tolerability to onabotA injections in a 0-10 scale. We phoned patients 2 weeks afterwards and systematically asked about AE. We analyzed if 50% response was correlated with tolerability, headache intensity at the moment of injection or AE occurrence. We hereby present data obtained after first procedure.

Results: We included 97 patients, aged 43.7 (Sx=±10.9), with 44.4 (Sx=±58.4) months of CM. Headache at the moment of injection was referred in 72.1% of them, with a mean intensity of 3.58 (Sx=±2.9). Patients described tolerability to the injections as 7.6/10 (Sx=±1.8). 52.6% patients had a 50% response, with a mean reduction of 10.2 headache days compared with baseline. AEs was described in 70.1% of patients. Frequency of AE did not differ in the responder group compared with non-responders (67 vs 75%; p=0.34). We did not found association between tolerability and response

Conclusion: OnabotA tolerability was good in our series and it did not correlate with presence of adverse events or response.

EPO3124

Interferon-β produces analgesic effect through activating μ-opioid receptor

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Background and aims: Interferons (IFNs), such as type-I IFN (IFN-α) and type-II IFN (IFN-γ) are produced by immune cells to elicit antiviral effects. IFNs are also produced by glial cells in the CNS to regulate brain functions. As a proinflammatory cytokine, IFN-γ drives neuropathic pain by inducing microglial activation in the spinal cord. However, little is known about the role of IFN-β in regulating pain sensitivity in spinal cord. Thus, we will study the role of IFN-β in regulating pain sensitivity and mechanism of antinociception in this study.

Methods: To produce persistent inflammatory pain, complete Freund's adjuvant was injected into a hindpaw. Intrathecal IFN-β injection (10000u) was also made to provide antinociceptive effect for acute inflammatory pain. After behavior test, the spinal cords were dissected for immunohistochemistry staining and western blot.

Results: Spinal (intrathecal) administration of IFN-β increased pain threshold in naïve rats and reduced complete Freund's adjuvant (CFA)-induced inflammatory pain, whereas removal of endogenous IFN-β by a neutralizing antibody induced hyperalgesia in naïve rats. Intrathecal injection of naloxone reversed the antinociceptive effect of IFN-β on CFA-induced mechanical allodynia. IFN-α/β receptor (type-I IFN receptor) was expressed in the superficial dorsal horn and co-expressed with the μ-opioid receptor. Intrathecal injection of IFN-β induced phosphorylation of μ-opioid receptor evidenced by the increased expression of phospho-μ-opioid receptor after injection of IFN-β.

Conclusion: IFN-β binds to IFN-α/β receptor expressed in superficial dorsal horn of spinal cord and partially activates μ-opioid receptor to induce antinociceptive effect. Methods of boosting IFN-β release may open a new avenue for pain management.

Disclosure: Nothing to disclose

EPO3125

Patient attitudes and valuation of preventive migraine treatments: A focus group study

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Background and aims: This study aimed to understand patients' attitudes towards and valuation of injectable preventive migraine treatments, including preferred characteristics of administration devices.

Methods: 9 face-to-face focus groups were conducted among participants (n=47) with episodic (n=28) or chronic (n=19) migraine in the United States, the United Kingdom and Germany. The semi-structured focus groups consisted of open discussions about symptoms, impacts on quality of life, treatment expectations, hands-on testing of 5 administration devices (i.e. 2 prefilled syringes and 3 auto-injectors) and an interactive ranking of treatment aspects. Transcripts were analysed using content analysis and online questionnaires were analysed using descriptive statistics.

Results: Participants were on average 46.8 (SD: 13.0) years, mostly female (85.1%) and naïve to self-injectable treatments (74.5%). While most participants (85.1%) had experience with beta-blockers, antidepressants or anticonvulsants, participants emphasized a need for efficacious and safe/tolerable migraine prevention treatments due to dissatisfaction with current treatments. The ranking exercise indicated that patients' valuation of such treatments is largely driven by decreasing migraine frequency, reduction in migraine severity and concerns about thinking/memory problems. Patients' treatment valuation was also driven by frequency of administration and administration device characteristics, including device type (prefilled syringe and auto-injector), ease of use (needle auto-retraction, injection angle and shape), sense of control, dose confirmation (visual and audio) and injection time.

Conclusion: Patients reported a need for efficacious and safe/tolerable treatments for migraine prevention. While their valuation of injectable preventive treatments mostly depend on the overall benefit-risk profile, patients' treatment valuation was affected by attributes of the administration device.

Disclosure: The study was funded by Eli Lilly and Company.

EPO3126

Epidemiology of pain: a long way to effective pain management

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Background and aims: Despite the ubiquity and burden of pain, whether acute, chronic or intermittent, patients still have to go a long way to get the right diagnosis and treatment, frequently getting unnecessary medications and procedures.

The aim was to evaluate the prevalence of different pain syndromes in patients of the pain department and their journey to effective treatment.

Methods: The cross-sectional study included 2521 patients who came to the appointment in a pain department and had completed a questionnaire. The questionnaire was designed to assess the intensity and quality of pain and previous patient's experience. It included demographic data, questions about preceding doctor's visits and former treatment and Visual Analogue Scale (VAS).

Results: Back pain (46.5%), headaches (22.6%) and joint pain (21.4%) were the most widely represented. Before the appointment in the pain department, almost 50% of patients had been consulted by more than 3 specialists, 38.9% - by 4-10 doctors, 10.2% - more than 10. Patients mostly went to neurologists (36.8%), general physicians (25.2%) and surgeons (16.7%). Due to intensive pain, 1 in 5 patients (19.1%) had called an ambulance at least once during the last year. The most common treatments prescribed to patients were medications, massage, manual therapy and physical exercise and were mostly not followed. Previous medications included nonsteroidal anti-inflammatory pills (41.2%), non-specific vascular-metabolic drugs (25.6%) and muscle relaxants (20.4%).

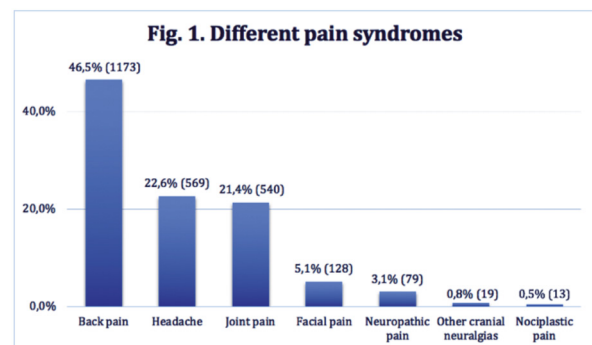


Fig. 1

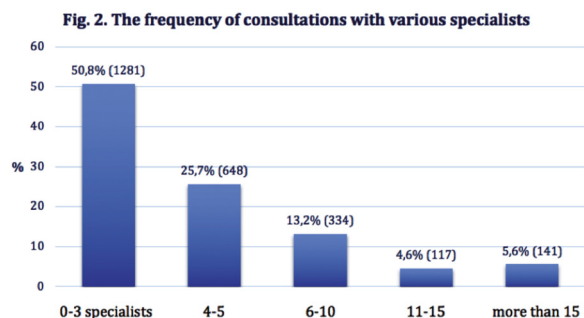


Fig. 2

Conclusion: Consultations by various specialists and non-adherence to therapy lead to ineffective pain management and more years with chronic pain.

Disclosure: Nothing to disclose

EPO3127

Epidemiology of pain: the intensity of everyday pain.

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Background and aims: Dealing with chronic diseases, patients often have to struggle with everyday pain, which can affect their working ability and social life.

The aim was to evaluate the duration and intensity of pain in out-patients of pain department and factors that may be associated with it.

Methods: The cross-sectional study included 2521 out-patients who had completed a questionnaire. The questionnaire was designed to assess the duration, intensity and quality of pain during the disease, the whole life-time and every-day pain with Visual Analogue Scale (VAS).

Results: There were more male (60.4%), working-age (76.4%) and highly educated (60.9%) patients. 88.1% of patients had chronic pain (>3 months). 76% indicated the most severe pain during the present disease as 5 or higher on VAS and 40.2% - as 8 or higher. More than 95% reported everyday pain, the intensity of which was ≥ 5 on VAS in 59.5% of cases. The average intensity of everyday pain depended on the duration of the illness: the longer the patient is in pain, the higher the intensity descriptors of his daily pain; e.g. the intensity of daily pain was 0.8 points higher in patients with a disease duration >3 months and 1 point higher if the disease lasts more than a year. Unemployed and widowed patients had more intense pain ($p < 0.05$).

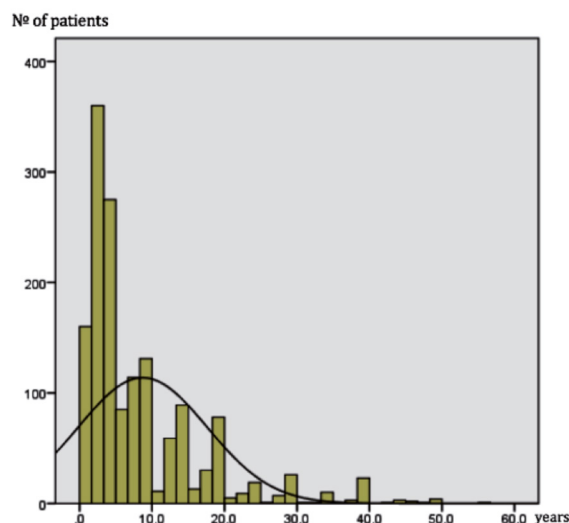


Fig.1. Pain duration in years

Fig.1. The duration of pain in years

Conclusion: Marital status, employment and duration of pain can affect the intensity of everyday pain in patients with chronic pain. There was no correlation of intensity with gender and education level.

Disclosure: Nothing to disclose

EPO3128

Epidemiology of pain and social consequences

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Background and aims: Pain seriously affects the patient's quality of life, since pain disorders are one of the main reasons for absence at work and increased number of years lived with disability.

The study aimed to evaluate the duration and intensity of pain, comorbidity as well as its repercussions in the workplace, and on the family and social environment.

Methods: The study enrolled patients who 1st came to the pain department and had completed a questionnaire. The questionnaire was designed to assess the intensity and quality of pain, comorbid diseases and the social impact of pain on the patient's life. It included Visual Analogue Scale (VAS) and DN4 questionnaire for neuropathic pain as well.

Results: There were 90 patients, 41.6% of which suffer from pain ≥ 5 years. 88.8% described their worst pain during the current disease as 6 or higher on VAS. One third (34.9%) of patients had neuropathic pain, mainly the patients who had pain for more than 3 years. Sleep disturbance and essential arterial hypertension were the most often comorbid diseases (Fig. 1). 92.3% of patients reported that pain limits their social activity. 76.9% and 75.6% also reported the limitation in working ability and family life, respectively.

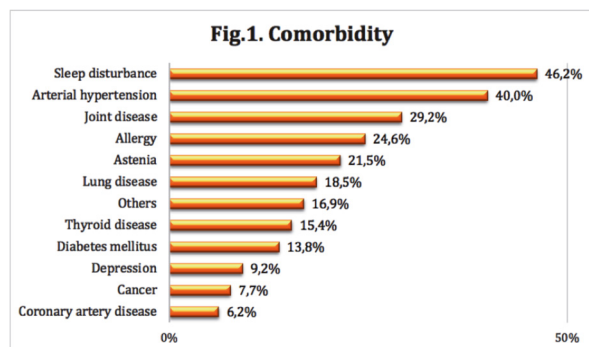


Fig. 1. Comorbidity

Conclusion: Comorbid sleeping disorders in almost half of the cases with high pain intensity during the disease limit the social and family-life activity of patients. Thus, we want to emphasize on the need to implement a multidisciplinary approach to treatment to achieve more comprehensive improvements for patients in familial and social contexts.

Disclosure: Nothing to disclose

EPO3129

Treating chronic SUNCT with a nerve blockade in an anticoagulated patient

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Background and aims: In chronic short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), attacks occur for more than 1 year without remission, or remission last less than 3 months. A migrainous biology has been associated with the pain between attacks and peripheral nerve blockades are efficacious.

Methods: Case report.

Results: This was a 73-year-old male with vascular risk factors, atrial fibrillation on rivaroxaban and recurrent cervical abscesses.

In 2010, he developed episodes of left facial sharp pain, occurring fortnightly and rated 8/10 in the pain Visual Analogue Scale (pVAS). Attacks appeared 50-100times/day, lasted for 30 seconds and extended from V2 to the fronto-temporal area. Triggers included touching, chewing or talking and were associated with bilateral photosensitivity, phonophobia, cranial allodynia, conjunctival injection, lacrimation, rhinorrhoea and facial flushing, without refractory period. Lamotrigine, carbamazepine, indomethacin, amitriptyline and melatonin were not effective. In 2015, after commencing gabapentin, the frequency diminished to 10attacks/day, although he developed a constant, bruising sensation (pVAS=5/10), that in 2019 became a multi-stabbing sensation (pVAS=7/10) and a daily, severe lancinating pain (pVAS=10/10) that lasted for 1 hour.

A supraorbital nerve (SON) blockade (methylprednisolone 30mg and 2% lidocaine 0.75mL) was performed. A 30G needle was used and pressure applied for 15 minutes, without adverse events. 2 weeks after the injection the background pain and the severe stabbings disappeared.

Conclusion: SON blockade may be an effective treatment for SUNCT and may even be considered in anticoagulated patients. The presence of migrainous features may predict a better outcome of peripheral blockades for SUNCT.

Disclosure: Nothing to disclose

EPO3130

Lasmiditan in Patients with Common Migraine Comorbidities: A Post hoc, Safety, and Efficacy Analysis of Two Phase 3 Randomized Clinical Trials

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Background and aims: Determine whether common comorbidities affect safety and efficacy of lasmiditan, a 5-HT_{1F} receptor agonist approved in the US, as an acute treatment for migraine. SAMURAI and SPARTAN were Phase 3 clinical trials of migraine patients, randomized to oral lasmiditan 50 (SPARTAN only), 100, 200mg, or placebo. Lasmiditan increased the proportion of pain-free and most bothersome symptom (MBS)-free patients at 2 hours after dose versus placebo. Common treatment-emergent adverse events (TEAEs) were dizziness, paresthesia, somnolence, fatigue, nausea, muscular weakness, and hypoesthesia.

Methods: Based upon literature review of common migraine comorbidities, anxiety, allergy, bronchial, cardiac, depression, fatigue, gastrointestinal, hormonal, musculoskeletal and pain, neurological, obesity, sleep, and vascular groups were created. Using pooled data, 2-hr pain freedom, 2-hr MBS freedom, and TEAEs were compared in patients with or without migraine comorbidity. P-values were calculated for treatment-by-subgroup interaction, based on logistic regression with treatment-by-Comorbidity Condition Status (Yes/No) as the interaction term; study, treatment group, and Comorbidity Condition Status (Yes/No) were covariates. Differential treatment effect was examined.

Results: No consistent statistical differences were observed between subgroups for 2-hr pain or MBS freedom. Similarly, no significant differential treatment by subgroup effects were identified with regards to TEAEs.

Conclusion: No consistent significant differences in efficacy were observed between patients with and without common comorbidities. Comorbidity status had no significant differential treatment by subgroup effects on the incidence of individual TEAEs. Therefore, the safety and efficacy of lasmiditan for treating single migraine attacks appears independent of comorbid conditions.

Disclosure: All the authors are employees and stockholders of Eli Lilly and Company.

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EPO3131

Which factors predict the success of Opicapone? Defining the optimal patient profile

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Background and aims: Opicapone (OPC) is a catechol O-methyltransferase inhibitor indicated as an adjunct treatment to levodopa in Parkinson's disease (PD).

Our objective is to evaluate the prognostic factors of OPC as an add-on therapy in PD fluctuator patients.

Methods: Descriptive retrospective study of PD patients treated with OPC in our hospital from 2018-2019. The primary efficacy variable was the difference in absolute OFF-time (OT) based on diaries, and secondary variables were the subjective reduction of fluctuations and the appearance of adverse effects (AE). Early fluctuators (EF) and switchers from Entacapone were evaluated by an independent subgroup analysis.

Results: 126 PD patients were enrolled (57.8% male, 42.2% female, 55.8 years old, s11.6).

We found an absolute OT reduction of 1,4h/day, and a decrease of fluctuations in 67% patients.

Age of disease onset ($p<0.005$), Hoehn and Yahr (HyY) ($p<0.001$), and Schwab and England (SE) ($p<0.0001$) were significantly related with OT reduction and fluctuation decrease. A shorter course of PD was related with a higher reduction of fluctuations.

38% of patient withdraw OPC; dyskinesia or hallucinations were the main reasons. HyY, SE, having hallucination previously or cognitive impairment were significantly related with withdrawal.

Only 18 patient were EF, efficacy differences could not be demonstrated, however they developed less hallucinations and dyskinesia.

In switchers from Entacapone subgroup analysis, the only differences found were equivalent dose of Levodopa pre- (1055mg vs 872, $p<0.008$) and post- OPC (997mg vs 827mg, $p=0.01$).

Conclusion: Early stages of the disease with less time of evolution, low score on HyY and high on SE seem to be related with more efficacy of OPC and less AE.

Disclosure: Nothing to disclose

EPO3132

Can clinical features help to differentiate Holmes tremor from post-thalamic stroke tremor?: a review of 13 cases.

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Background and aims: Holmes Tremor (HT), previously called Rubral tremor, is a debilitating movement disorder with unique characteristics and involves the midbrain and its connections, but has a poorly understood pathophysiology. Some of its clinical features can resemble post-thalamic stroke tremor and differentiation requires careful clinical examination. We report a case-series of 13 patients highlighting their clinical and radiological findings with a focus on distinguishing HT from the post-thalamic stroke tremor clinically.

Methods: A retrospective review of 13 patients with a HT type presentation was conducted. The tremor characteristics, as well as associated clinical and radiological findings were analysed.

Results: 9 of the patients had a myorhythmic tremor at rest which increased in amplitude on posture and further on goal directed movement, without any additional features beyond mild dystonic posturing distally. These were classified as HT. 4 patients had complex involuntary movement of the limbs, with a slow, large amplitude tremor proximally with choreathetoid movements distally and associated proprioceptive sensory loss, representing the entity of post-thalamic stroke tremor. Haemorrhagic lesions (cavernoma, arteriovenous malformations, and traumatic brain injury) were the predominant causes of HT whereas ischaemia was more commonly associated with post-thalamic stroke tremor.

Conclusion: When examining patients with Holmes tremor, careful attention to the presence of other movement disorders and other neurological features such as sensory deficits can help the clinician in the accurate localisation of the causative lesion which can have significant implications on the clinical management.

Disclosure: Nothing to disclose

EPO3133

Non-motor burden grading may serve as a predictor of cognitive decline in Parkinson's disease

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Background and aims: The identification of risk factors, which may predict cognitive decline (CD), 1 of the most important non-motor (NM) features in Parkinson's disease (PD), is highly relevant for the improvement of clinical management. Subtyping PD, considering also NM symptoms, may be a useful strategy of understanding the PD's heterogeneity. The NM symptom scale (NMSS) has been validated and standardized in the evaluation of PD patients and could contribute to PD subtyping.

Methods: To investigate if specific differences in PD NM profiles predispose to the development of CD, we performed a longitudinal study on 541 non-demented PD patients taking part in the NM International Longitudinal Study, assessed among others with Mini Mental State Examination (MMSE), NMSS and scales for outcomes in PD -motor, -daily living (SCOPA-A, B) at baseline and last follow-up (median 3- year follow-up).

Results: We found that PD patients, who developed CD defined by MMSE ≤ 25 at last follow-up (N=107), had significantly more frequent and severe hallucinations/perceptual problems and deterioration of the attention/memory NMSS domain at baseline. These findings were independent of dopaminergic medication, presence of depression/anxiety, sleep disorders and disease duration, but we did notice that PD patients with CD were older, had more advanced H/Y stages and performed worse in SCOPA-A, -B and MMSE scores at baseline.

Conclusion: Our results complement previous findings but demonstrate, for the 1st time, that baseline NM profiles assessed through the NMSS could aid in predicting the development of CD in PD. These clinical features might comprise the phenotype of the cognitive subtype of PD.

Disclosure: Dr. P. Oikonomou does not report any conflicts of interest. The European Academy of Neurology Clinical Fellowship Programme 2019 supported Dr. P. Oikonomou.

EPO3134

Sudden-onset hemichorea-hemiballism as first manifestation of brain metastasis in a patient with colon cancer

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Background and aims: Hemichorea-hemiballism (HC-HB) has a strong association with lesions of the subthalamic nucleus (STN). Vascular lesions are the most frequent cause of HC-HB, but the differential diagnosis include granulomatous, neurodegenerative and demyelinating disorders, as well as some metabolic and infectious diseases. Acute onset HC-HB secondary to STN involvement by metastasis is rarely reported in the literature.

Methods: We report a case of a 71-year-old man with sudden-onset of difficulty controlling his left upper limb due to abrupt involuntary movements.

Results: Medical history included hypertension and ischemic cardiopathy, medicated with dual antiplatelet therapy, which he stopped 2 weeks prior due to gastrointestinal bleeding, and recent palliative immunotherapy with pembrolizumab due to stage IV colon adenocarcinoma. Examination revealed spontaneous, non-rhythmic, choreiform, involuntary movements of the left arm and hand associated with oromandibular dyskinesias (video). Vascular stroke of the basal ganglia was initially suspected. Non-contrast brain-CT showed 3 mildly hyperdense lesions in left thalamus, right corona radiata, and right subthalamic region. Additionally, brain-MRI showed perilesional oedema extending to the posterior limb of the internal capsule and cerebral peduncle on the right side, peripheral contrast enhancement and small foci of intralesional hemorrhage.

Conclusion: Sudden-onset focal neurological signs, including lateralized involuntary movements, are highly characteristic of an acute vascular lesion. Other causes of acute HC-HB can be found in the literature, the most frequent being nonketotic hyperglycemia. In our case, brain metastasis was the cause of the sudden-onset of HC-HB. Our case illustrates that sudden-onset involuntary movements can be the first and only manifestation of strategic brain metastasis.

Disclosure: Nothing to disclose

EPO3135

Frailty as clinical modulator of brain damage and progression in Parkinson's disease

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Background and aims: Frailty is a complex syndrome characterized by increased risk of disability in the elderly. No studies assessed frailty in patients with Parkinson's disease. Objective of the study was to evaluate the prevalence of frailty and correlation with motor and cognitive features symptoms in Parkinson's disease.

Methods: 162 consecutive outpatients with PD diagnosis (mean age 68.8 y, mean disease duration 8.3 years) entered the study. Each subject underwent a comprehensive motor and nonmotor evaluation and geriatric assessment using multidimensional prognostic index (MPI) and 104 patients underwent clinical follow-up at 2 years.

Results: Pre-Frailty assessed by MPI was presented by 38.5% of patients and correlated with age and disease duration and its prevalence increased along with Hoehn and Yahr staging. When stratified for H/Y staging, PD patients with frailty presented similar motor impairment but worse non-motor symptoms and cognitive performances. At 2-years follow-up, frailty predict worse cognitive and motor progression when adjusted for disease burden.

Conclusion: Frailty is a possible important modulator of pathology and brain vulnerability in Parkinson's disease and could explain different severity in motor and non-motor symptoms. Longitudinal larger studies are warranted to evaluate the impact of frailty in disease progression.

Disclosure: Nothing to disclose

EPO3136

Exploring the Use of Wearable Sensors in Parkinson's disease and the Detection of Early Morning Periods

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Background and aims: Early Morning Off (EMO) is a common feature found in Parkinson's disease (PD). It can be difficult to detect and often presents with a combination of motor and non-motor symptoms. Whilst EMO can be detected by patient interview, this method is unreliable. Wearable sensors offer an alternative method of identifying EMO. The Parkinson's Kinetigraph (PKG) is a wristwatch device which uses accelerometry to provide, objective ambulatory monitoring of PD throughout the day This is the 1st study to evaluate the use of wearable-sensors in EMO detection. The primary objective of this study was to examine if PKG recordings were relevant to the clinical description of EMO in a treated PD population. Secondary objectives were to find potential predictors for EMO.

Methods: Using data from the Non-motor Longitudinal International Study we performed a retrospective, cross-sectional study on 104 participants at King's College Hospital, London. To identify patients whose PD symptoms were morning worse (and thus likely suffering from EMO) a ratio was created using Bradykinesia data from the PKG (see attached figure).

Results: Our cohort's EMO prevalence was 38%. EMO patients had much higher levels of motor dysfunction. This was reflected by significantly higher SCOPA Motor dysfunction scores and more advanced HY scores. From our correlation, only higher SCOPA C scores were seen to be predictive of EMO presence.

Conclusion: Our results showed a strong correlation between higher levels of motor dysfunction and EMO presence. As prior clinical EMO descriptions mention a correlation between more advanced PD and EMO this result is not unexpected.

Disclosure: Nothing to disclose

EPO3137

The Upper Limb Cardiopulmonary Exercise Test in Friedreich Ataxia Patients

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Background and aims: In Friedreich Ataxia (FRDA) primary endpoints for phase IIb trials, or secondary functional endpoints are currently missing. Aim of our study was to explore the feasibility of upper limbs cardiopulmonary exercise testing (CPET) in FRDA patients and to compare the results with a cohort of matched Healthy Controls (HC).

Methods: CPET was performed using an upper limbs cycle ergometer. Patients followed a ramp protocol of 5W/min, HC of 10 W/min. We recorded: peak oxygen consumption (peak-V₂), anaerobic threshold (AT), ventilation per minute vs CO₂ production (VE/VCO₂). Variables were compared using an unpaired t test, or a χ^2 test when appropriate. Correlation was performed using the Pearson's correlation coefficient.

Results: We studied 55 FRDA and 54 HC. Age (35.3±13.8 vs 32.1±10.5; p=0.186), gender (p=0.851), and BMI (23.1±4.6 vs 23.5±3.5; p=0.557) did not differ between groups. In FRDA, peak-VO₂ showed a 31% reduction (15.2±5.7 vs 22.0±6.1 mL/Kg/min; p<0.001), and AT-VO₂ a 36% reduction (p<0.001) (Figure 1). In FRDA, peak-VO₂ correlated with clinical measures (Table 1). AT occurred at 33% of peak workload in FRDA and at 86% in HC (p<0.001) (Figure 2). In HC, time at AT correlated with workload (R=0.610; p<0.001) and O₂ consumption (R=0.586; p<0.001), but did not in FRDA. VE/VCO₂ slope was higher in FRDA (33.0±5.4 vs 27.1±4.9; p<0.001).

Variable	R	P value
BMI	-.333	0.014
Interventricular septum thickness	-.281	0.039
SARA	-.434	0.001
Disease duration	-.397	0.003
9HPT	-.437	0.001
ADL	.536	<0.001
IADL	.385	0.004

Correlations with peak VO₂ and clinical measures in FRDA

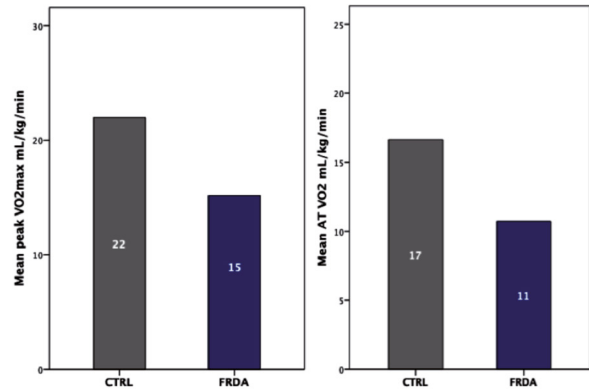


Figure 1. O₂ consumption at peak and at AT

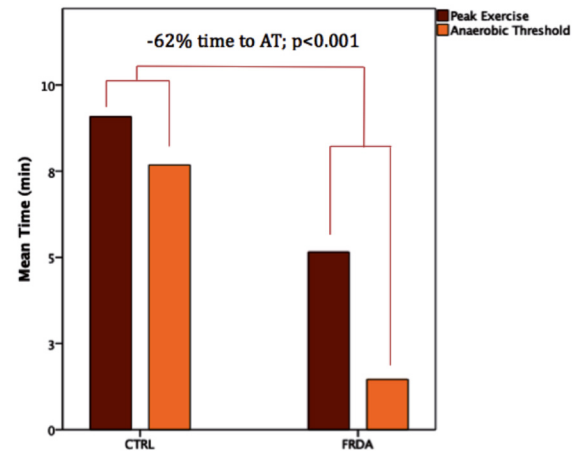


Figure 2. Time at peak and at AT: FRDA patients take in percentage 53% less time to reach peak workload and 63% less time to the AT relative to peak workload, as compared to HC (p<0.001).

Conclusion: FRDA patients showed reduced peak-VO₂ at the CPET compared to HC. Patients reached the AT very early during workload, indicating a dysfunctional mitochondrial energy production with a rapid shift to anaerobic metabolism. CPET could be successfully used as a primary endpoint in phase IIb studies.

Disclosure: Nothing to disclose

EPO3138

Is there evidence of bradykinesia in essential tremor?

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Background and aims: Essential tremor (ET) is a movement disorder primarily characterized by postural tremor of the upper limb. Although still under-investigated, bradykinesia may be part of the phenotypic spectrum of ET. We aimed to evaluate the bradykinesia features in ET by clinical examination and kinematic analysis of repetitive finger movements. We compared data collected in ET patients with those recorded in Parkinson's disease patients and healthy controls.

Methods: Overall, 258 subjects participated in the study (90 ET patients, 84 Parkinson's disease patients, and 84 healthy controls). Repetitive finger tapping was kinematically recorded using an optoelectronic motion analysis system. Movement velocity and amplitude, as well as decrement (sequence effect), were measured. We first compared the 3 groups by 1-way analysis of variance. We also performed a cluster analysis to better address the data variability observed in ET patients. Possible relationships between kinematic and clinical data were assessed in ET.

Results: ET patients were slower than healthy controls. Movement slowness in ET did not correlate with tremor severity. We also found that movement slowness in ET was not associated with sequence effect, which instead is a common feature in Parkinson's disease. Cluster analysis showed that a proportion of ET patients may have movement abnormalities as those showed in Parkinson's disease.

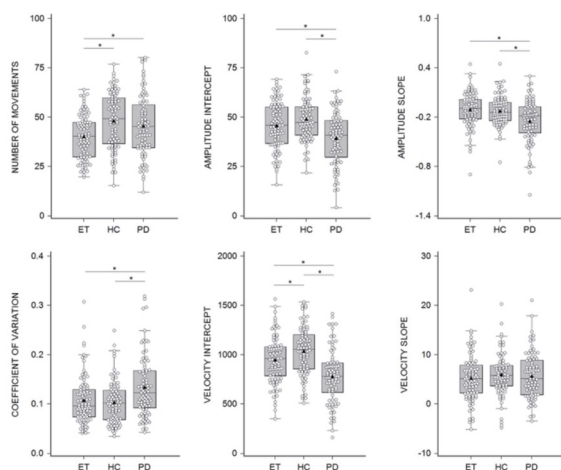


Figure 1: Kinematic variables of repetitive finger movements in ET, Parkinson's disease (PD) patients and healthy controls (HC). Triangles: mean values. Boxes: ± 1 standard error of the mean. Whiskers: ± 1 standard deviation of the mean. Circles indicate each individual value. Asterisks: $P < 0.05$ in the post hoc comparisons.

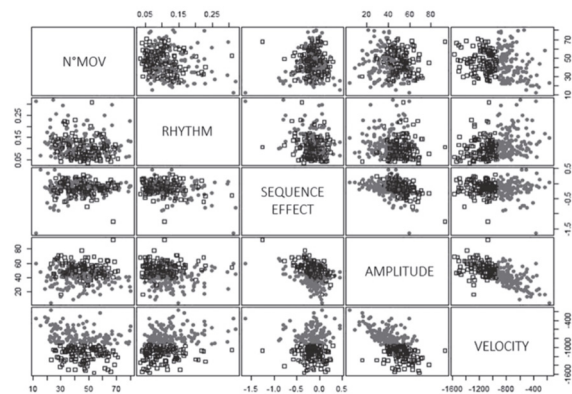


Figure 2: Cluster analysis. Kinematic variables of repetitive finger movements in subjects in cluster 1 (white squares) and cluster 2 (grey circles). Rhythm refers to the coefficient of variation (CV) of the inter-tap intervals. Sequence effect refers to amplitude slope.

Conclusion: Movement slowness without sequence effect is a common feature in ET patients that is likely mediated by prominent involvement of the cerebellum. The present findings are relevant when interpreted in the context of the new tremor classification system.

Disclosure: Nothing to disclose

EPO3139

The sooner, the better: early diagnosis and treatment in functional neurological disorders

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Background and aims: Functional neurological disorders (FND) are common and may present acutely. They are potentially disabling, but early diagnosis and treatment may improve outcome.

Methods: Retrospective analysis of patients with FND admitted in the emergency department of our tertiary hospital, with the intervention of a neurologist in the acute phase. A positive diagnosis of the FND was effectively communicated to the patient following current recommendations. Online material was also provided (www.neurosymptoms.org) for further information about diagnosis, and an early ambulatory appointment with the same specialist was programmed.

Results: 10 cases were included in the analysis (8 female, mean age 33,8 years; 21-58), from October 2018 to December 2019. Symptoms were functionally relevant for daily activities in all cases. A positive diagnosis was made on clinical grounds, although complementary tests were also performed, with normal results in all cases (head CT scan and blood tests in all cases; CT angiography, cranial MRI in 3). The mean time from onset to 1st consultation in the hospital was 2.56 weeks (0-10). All patients were reassessed ambulatory 1-4 weeks after the 1st hospital visit, and followed for a mean time of 13.1 weeks (2-54). Neurological symptoms disappeared in 90% of cases during the follow-up.

Conclusion: In our experience, the early diagnosis and intervention in FND with acute presentation was effective, with an early and sustained improvement of potentially disabling symptoms. Continuity of care with the same specialist and expertise in FND are likely to play a role in the positive outcomes.

Disclosure: Nothing to disclose

EPO3140

Trimetazidine Treatment in Parkinson's Disease: Is It a Real Problem or Just a Falme?

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Background and aims: Trimetazidine, a widely used second-line antianginal drug, is contraindicated in movement disorders, however, some recent data suggest that a considerable part of trimetazidine users is still patients with Parkinson's disease (PD). In the present study, we aimed to objectively determine the impact of trimetazidine on the severity of symptoms and the health-related quality of life of patients with PD by measuring changes after its withdrawal.

Methods: A consecutive series of 42 patients with PD using trimetazidine underwent detailed neurological and neuropsychological assessments at baseline and three months after the discontinuation of the drug.

Results: Clinically relevant improvements were achieved with discontinuation of trimetazidine according to changes in scores of each part of the Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale (Part I: -25.7%, $p < 0.001$; Part II: -23.8%, $p < 0.001$; Part III: -28.5%, $p < 0.001$; Part IV: -30.1%, $p = 0.004$) and total scores of the Non-Motor Symptoms Scale (-25.6%, $p = 0.004$) and the Montgomery-Asberg-Depression Rating Scale (-20.1%, $p = 0.001$). A remarkable improvement of axial symptoms, such as postural instability and gait disturbances, were detected. Benefits resulting from the withdrawal of the drug also manifested in the improvement of the health-related quality of life based on changes in the summary index of the 39-item Parkinson's Disease Questionnaire (-18.2%, $p = 0.031$). Discontinuation of trimetazidine did not lead to any cardiovascular events (e.g., acute ischaemic coronary syndrome and refractory angina pectoris) in the included patients during a 12-month follow-up.

Table 1. Changes in scores of the applied scales due to discontinuation of trimetazidine

	Baseline [means±SD or n (%)]	Follow-up ^a [means±SD or n (%)]	Change		p-value
			Absolute (means±SD)	Relative change (%) ^b (mean)	
MDS-UPDRS Part I	15.0±7.1	10.9±6.6	-4.0±4.4	-25.7	<0.001
MDS-UPDRS Part II	13.1±8.4	9.6±6.9	-3.5±4.7	-23.8	<0.001
MDS-UPDRS Part III	38.2±14.4	27.8±13.5	-10.4±6.7	-28.5	<0.001
MDS-UPDRS Part IV	3.4±3.2	2.2±2.4	-1.2±2.6	-30.1	0.004 ^c
PIGD score	10.6±6.2	7.5±5.2	-3.1±3.2	-27.9	<0.001
0	0 (0.0)	2 (4.8)			
1	1 (2.4)	3 (7.1)			
2	24 (57.1)	28 (66.7)			
3	9 (21.4)	4 (9.5)			
4	7 (16.7)	5 (11.9)			
5	1 (2.4)	0 (0.0)			
Change in HYS after TMZ	Improvement	16 (38.1)			
	No change	23 (54.8)			
	Worsening	3 (7.1)			0.008 ^d
NMSS					
Cardiovascular problems	3.5±3.7	2.4±3.2	-1.1±3.7	-28.6	0.053 ^e
Sleep problems	14.3±8.9	10.1±7.3	-4.1±7.3	-24.7	0.001
Mood problems	14.7±17.0	11.4±13.4	-3.3±13.5	-19.7	0.119
Hallucinations	1.7±3.9	1.8±5.3	0.1±5.3	5.1	0.931
Memory problems	6.7±7.7	4.8±5.9	-1.9±6.9	-23.6	0.085
Gastrointestinal problems	5.5±8.0	3.1±5.2	-2.4±6.7	-39.1	0.024
Urinary problems	12.2±10.0	9.6±8.7	-2.5±8.5	-20.5	0.060
Sexual problems	0.9±3.9	0.2±0.5	-0.7±3.9	-76.0	0.261 ^f
Miscellaneous	3.4±5.0	3.3±4.6	-0.2±4.0	-5.8	0.790 ^g
Total	62.8±49.9	46.6±35.3	-16.2±34.6	-25.6	0.004
MADRS	14.3±8.8	11.4±6.4	-3.0±5.4	-20.1	0.001
PDSS-2	17.5±10.9	15.1±11.4	-2.4±8.3	-13.8	0.068
ESS	6.4±4.7	5.5±4.7	-0.9±5.0	-9.3	0.246
MoCA	22.2±4.0	22.9±4.0	0.5±2.8	1.7	0.374
PDQ-39					
Mobility	30.2±29.5	24.3±23.6	-6.2±18.9	-20.7	0.043
Activities of daily living	20.7±23.7	15.2±16.4	-5.7±19.3	-27.2	0.067
Stigma	18.3±27.3	13.1±24.0	-5.6±16.5	-26.2	0.034
Emotional well-being	25.5±18.5	25.3±18.0	-0.2±13.0	-0.4	0.920
Social support	11.1±14.0	6.9±10.0	-4.5±13.9	-37.2	0.046
Cognition	19.6±16.3	19.1±13.4	-0.8±12.1	-3.7	0.692
Communication	14.7±22.5	12.6±21.3	-2.4±17.9	-15.1	0.388
Bodily discomfort	36.3±24.1	31.1±23.0	-5.3±22.1	-11.1	0.134
Summary index	21.9±16.5	18.3±13.9	-3.8±10.8	-18.2	0.031

^aFollow-up examinations were performed 95±25 days after the baseline visit.
^bTo calculate relative change the following formula was used: (Score_{Baseline}-Score_{Follow-up})/Score_{Baseline}*100
^cThe Wilcoxon signed rank test was used for the analysis of changes in these scores.
^dThe Chi-square test was utilized for the calculation of this value.
Abbreviations: ESS = Epworth Sleepiness Scale; EQ = EuroQoL instrument; HYS = Hoehn-Yahr Scale; MADRS = Montgomery-Asberg Depression Rating Scale; MDS-UPDRS = Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale; MoCA = Montreal Cognitive Assessment; NMSS = Non-Motor Symptoms Scale; PDSS-2 = Parkinson's Disease Sleep Scale 2nd version; PDQ-39 = 39-Item Parkinson's Disease Questionnaire; PIGD = postural instability and gait difficulty; TMZ = trimetazidine; VAS = visual analogue scale

Conclusion: Our results provide clinical rationale for strictly avoiding the use of trimetazidine in PD.

Disclosure: The examination discussed here is the own work of the authors with the help of government-based funds. This study was supported by the Hungarian Brain Research Program (2017-1.2.1-NKP-2017-00002), NKFIH EFOP-3.6.2-16-2017-00008, and NKFIH SNN125143 government-based funds. Our research was partly financed by the Higher Education Institutional Excellence Program of the Ministry of Human Capacities in Hungary, within the framework of the 5th thematic program of the University of Pécs, Hungary (20765/3/2018/FEKUSTRAT). Regarding this study, the authors did not receive any corporate funding.

EPO3141

Change in OFF-/ON-Time After Switching from Double-Blind Entacapone or Placebo to Open-Label Opicapone in Patients who Ended the 1-Year BIPARK-I Extension Study on Opicapone 50mg

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Background and aims: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients in two large multinational trials (BIPARK-I and II) [1,2].

Methods: Following completion of the double-blind phase of BIPARK-I, placebo (PLC)- and entacapone (ENT)-treated patients switched to OPC in a 1-year open-label extension (OLE) study. This exploratory post-hoc analysis evaluated the efficacy (change in absolute OFF-/ON-time) of OPC in levodopa-treated PD patients who switched from PLC or ENT to OPC and ended the 1-year OLE on OPC 50mg. Results were evaluated using analysis of covariance (ANCOVA).

Results: In the OLE study, 199 patients switched from PLC (n=99) or ENT (n=100) to OPC (Table 1). Overall, 44/98 (44.9%), 40/100 (40.0%) and 38/98 (38.8%) patients treated with PLC, ENT and OPC 50mg in the double-blind trial who entered the OLE study ended it on OPC 50mg, respectively (Full Analysis Set). For PLC or ENT switchers who ended the OLE study taking OPC 50mg, switching to OPC resulted in significant improvements in OFF-/ON-time (Table 2). Efficacy was maintained in patients originally allocated to OPC 50mg in the double-blind phase.

Table 1. Baseline characteristics (Safety Set)

Characteristic	DB PLC/OL OPC N=99	DB ENT/OL OPC N=100	DB OPC 50-mg/OL OPC N=98
At double-blind baseline			
Male gender, n (%)	61 (61.6)	64 (64.0)	61 (62.2)
Age, mean years	64.4	63.2	63.3
Disease duration, mean years	8.3	7.6	7.4
Daily OFF-time, mean hours	6.2	6.4	6.2
At OLE baseline			
Daily OFF-time, mean hours	5.1	4.9	4.3
Hoehn & Yahr stage (ON), mean	2.4	2.2	2.3
Presence of dyskinesia ^a – yes, n (%)	39 (39.4)	43 (43.0)	41 (41.8)
Daily levodopa dose, mean mg	661.2	606.0	675.2

^aFrom Unified Parkinson's Disease Rating Scale IV item 32
 DB, double-blind; ENT, entacapone; OL, open-label, OLE, open-label extension; OPC, opicapone; PLC, placebo

Table 1

Table 2. Change from OLE baseline to OLE endpoint in absolute OFF-/ON-time in patients who ended the OLE on OPC 50-mg (ANCOVA analysis; Full Analysis Set)

Characteristic	DB PLC/OL OPC N=44	DB ENT/OL OPC N=40	DB OPC 50-mg/OL OPC N=38
Absolute OFF-time, min			
LS mean change from baseline	-54.9	-68.2	-8.6
SEM	20.6	22.4	22.1
95% CI	-95.5, -14.4	-112.1, -24.2	-52.0, 34.8
p-value	0.0081	0.0025	0.6968
Absolute ON-time, min			
LS mean change from baseline	71.7	53.3	-4.5
SEM	21.0	22.7	22.4
95% CI	30.5, 112.9	8.6, 98.0	-48.6, 39.6
p-value	0.0007	0.0195	0.8412

ANCOVA, analysis of covariance; CI, confidence interval; DB, double-blind; ENT, entacapone; LS, least squares; OL, open-label, OLE, open-label extension; OPC, opicapone; PLC, placebo; SEM, standard error of the mean

Table 2

Conclusion: Significant improvements in OFF- and ON-time were achieved in patients switching from PLC or ENT to OPC and ending the BIPARK-I OLE study on OPC 50mg.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.

2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPO3142

Is CD56+ a possible laboratory biomarker of depressive symptoms at Parkinson Disorder (PD)?

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Background and aims: Patients with PD have signs of peripheral and central inflammation, including elevated levels of serum cytokines [1] and cerebrospinal fluid (CSF) [2], as well as activated microglia [3]. Analysis of peripheral blood lymphocyte subsets characterizes the lymphocytic immunity unit. To detect a possible correlations of peripheral blood lymphocyte subsets with the severity of depressive symptoms at PD patients was the aim of the study.

Methods: The study group consisted of 23 patients (m: f - 13: 10) with a diagnosis of PD according to the criteria of the Bank of the Brain of the Parkinson's Disease Society of the United Kingdom. The average age of the patients was 52.0 (43.5÷60.75) years, the duration of the disease was 6.5 (4.5÷7.5) years, the severity of the disease according to the Hen and Yar scale was 2.0 (2.0÷3.0) points. Hamilton Rating Scale for Depression was used for detection of the level of depressive symptoms. We used CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 and CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 ("BeckmanCoulter", USA) monoclonal antibodies panels for assessment of peripheral blood lymphocyte subsets. Statistical analysis based on counting Spearman's rank correlation coefficient.

Results: In patients with PD, there is a statistically significant correlation between the severity of depressive symptoms and levels of following peripheral blood lymphocyte subsets (CD56 +,% and CD, 56+ abs. Sc, * 10^{^6}) (p<0.05).

Conclusion: Our results indicate a relationship between the severity of depressive symptoms and the level of CD56 + (absolute and relative values) at blood of PD patients.

Disclosure: Nothing to disclose

EPO3143

Apomorphine in Multiple System Atrophy: a therapeutic tool?

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Background and aims: Multiple system atrophy (MSA) is a sporadic neurodegenerative disorder characterized by parkinsonism and/or cerebellar signs and autonomic failure. A poor levodopa response is one of the diagnostic criteria of MSA that helps differentiate it from Parkinson's disease (PD). Nevertheless, a transient response to levodopa may be observed in approximately 40% of patients during early disease stages.

Methods: We present 3 cases of MSA-P (MSA-parkinsonism) treated with apomorphine.

Results: The 1st patient is a 48-year-old male who presented with asymmetric parkinsonism, gait disturbance, dysarthria and orthostatic hypotension, diagnosed as MSA-p. He had clinical stability for 2 years after levodopa treatment. Treatment with continuous subcutaneous infusion was started, being responsive for 2 years.

The 2nd patient is a 68-year-old woman who presented with oromandibular dystonia, dysarthria, dysphagia, orthostatic hypotension and gait instability diagnosed as MSA-p. Treatment with levodopa improved partially her symptoms. Infusion of apomorphine was initiated to treat dystonia and non-motor symptoms, with improvement.

The 3rd patient is a 52-year-old male initially diagnosed as PD. He was treated with dopamine agonists with transitory improvement. He came up with urinary incontinence and erectile dysfunction after 2 years. Treatment with continuous subcutaneous infusion improved motor symptoms for 3 years.

Conclusion: We used apomorphine as a therapeutic trial in three patients diagnosed as MSA-p with good transitory response. No major side effects have been experienced (worsening of orthostatic hypotension). Subcutaneous administration may be an effective route of administration in patients who have gastroparesis as in MSA.

Disclosure: Nothing to disclose

EPO3144

Effects of sleep disorder on activities of daily living in patients with Parkinson's disease

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Background and aims: The paper aimed to examine the effects of excessive daytime sleepiness (EDS) and nocturnal sleep quality on activities of daily living (ADLs) as well as the effect of nocturnal sleep quality on EDS in Parkinson's disease (PD).

Methods: Study was cross-sectional and carried out at the Movement Disorder Outpatient Clinic. We examined a sample of 30 patients (12 female and 18 male) diagnosed with idiopathic PD. Demographic data were collected via a questionnaire. Nocturnal sleep disturbances were assessed using the Parkinson Disease Sleep Scale (PDSS). EDS was assessed using the Epworth Sleepiness Scale (ESS). ADLs were assessed using the Unified Parkinson Disease Rating Scale – Part II (UPDRS II).

Results: Average age, disease duration and test scores are shown in Table 1. No statistically significant differences were observed in UPDRS II scores of patient groups divided according to their ESS scores. Correlation of age, disease duration, ESS and PDSS scores with UPDRS II is shown in Table 2.: a statistically significant negative correlation was observed between PDSS and UPDRS II, while there was no correlation between other observed parameters and UPDRS II.

	Mean value	IQR/SD [§]
Age	72	63-77.25
Disease duration	5	2-6
ESS*	9.7	5.95 [§]
UPDRS II [#]	14.50	11.75 – 18.75
PDSS [§]	81.93	26.83 [§]

* Epworth Sleepiness Scale, [#]UPDRS – Unified Parkinson Disease Rating Scale part II, [§] Parkinson Disease Sleep Scale

Table 1. Mean age, disease duration and test scores

	Spearman correlation coefficient Rho	P value
Age	- 0,048	0,80
Disease duration	0,360	0,05
ESS*	0,222	0,24
PDSS [§]	- 0,593	0,001

* ESS – Epworth Sleepiness Scale; [§]PDSS – Parkinson Disease Sleep Scale

Table 2. Correlation of age, disease duration, ESS and PDSS scores with level of impairment in activities of daily living (UPDRS II)

Conclusion: The paper observed no effect of EDS on ADLs nor the effect of nocturnal sleep quality on EDS in patients with PD. Nocturnal sleep quality was found to have an effect on ADLs. Specifically, patients with comparatively pronounced disturbances exhibited greater difficulty in cutting food and handling utensils, dressing themselves, more frequent freezing of gait, gait disturbances and comparatively pronounced tremors.

Disclosure: Nothing to disclose

EPO3145

Beyond the ‘eye-of-tiger’: qualitative assessment of radiologic signs associated with preoperative motor clinical score and Deep Brain Stimulation outcome in PKAN patients

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Background and aims: PANK2 gene-associated-Neurodegeneration (PKAN) is the most common cause of Neurodegeneration with brain iron accumulation. The ‘eye-of-the-tiger’ is the classical MRI sign. To date, several small series have been published describing the outcome of Deep brain stimulation (DBS) in PKAN disease. The aim of this study was to identify potential MRI features guiding DBS surgery indication.

Methods: We conducted a retrospective review of all PKAN patients treated by pallidal DBS in our department, whose cerebral MRI was available for analysis. Qualitative assessment of pallidal, cerebellar and cortical atrophy, following a homemade scale, was analyzed by 2 independent clinicians. BFMDRS was used for motor clinical assessment.

Results: Among the 19 patients who underwent pallidal DBS surgery, MRI was available for 16. Median age at surgery was respectively 30 and 11 years for adults (n=6) and children (n=10). Median follow-up was 7 years (1-18). 7 patients died in the follow-up. Median BFMDRS motor was higher among patients with severe pallidal atrophy (72 (severe) versus 44 (mild/absent)). All patients but 1 showed an ‘eye-of-the-tiger’ sign. Later age of onset (>8 years) was associated with better clinical DBS outcome. Severe pallidal atrophy was found in 10 patients and diffuse cortical and cerebellar atrophy in respectively 7 and 7. All deceased patients had atrophy in at least 2 of these regions.

Conclusion: Pallidal, cerebellar and cortical atrophy were associated with higher motor scores and might be useful to predict the clinical outcome following DBS. Further studies are needed to confirm these results.

Disclosure: Nothing to disclose

EPO3146

How accurate is death certification in Parkinsonism? A Systematic Review and Meta-Analysis

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Background and aims: Death certification is often used in research studies to identify cases of, and deaths in parkinsonism. We systemically reviewed the literature on the accuracy of death certification in identifying different parkinsonian disorders.

Methods: Comprehensive searches were performed to identify studies that assessed the accuracy of death certification in parkinsonism. We extracted data on the proportion of patients with (i) any parkinsonian disorder mentioned on their death certificate and ii) the correct parkinsonian disorder on the death certificate. We included unpublished data from the Parkinsonism In the North East [PINE] incidence cohort in Aberdeen and performed random-effects meta-analysis. Two authors independently checked the data.

Results: 13 studies were included (9 Parkinson’s disease [PD], 3 progressive supranuclear palsy [PSP], 2 multiple systems atrophy [MSA], 4125 patients). In PD patients, meta-analysis showed sensitivity of 57% (95%CI 33-80%) for any parkinsonian condition mentioned on the death certificate and 60% (95%CI 52-67%) for PD being specifically named. In PSP the sensitivity was 69% (95%CI 61-77%) for any parkinsonian condition and 45% (95%CI 26-64%) for PSP. In MSA the sensitivity was 77% (95%CI 66-87%) for any parkinsonian condition and 31% (95%CI 0-67%) for MSA. There was substantial heterogeneity in each meta-analysis, in PSP and MSA this was in part attributable to one study. Regression analysis showed no evidence of improvement over time for PD.

Conclusion: Death certificates have low sensitivities for identification of parkinsonian syndromes. MSA and PSP were often incorrectly coded. Studies which use death certificates to identify cases will have substantial ascertainment bias.

Disclosure: Nothing to disclose

EPO3147

BouNDless: An active-controlled, randomised, double-blind, double-dummy trial of continuous subcutaneous infusion of levodopa/carbidopa with ND0612 in patients with Parkinson's disease experiencing motor complications

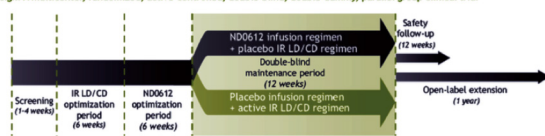
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Background and aims: The aim of this phase 3 study (NCT04006210) is to confirm the efficacy, safety, and tolerability of continuous levodopa infusion with ND0612 in comparison to oral immediate-release levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing motor complications. ND0612 is a proprietary drug-device combination delivering liquid levodopa/carbidopa (60/7.5mg/mL) via a subcutaneous (SC) infusion pump.

Methods: This is a randomised, active-controlled, parallel-group clinical trial including two 6-week open-label optimisation periods followed by a 12-week, double-blind, double-dummy maintenance period [Figure]. A total of 288 PD patients in Europe and the US will be enrolled (Hoehn and Yahr I-III) to reach 202 randomised patients on ≥ 4 doses/day of levodopa/carbidopa oral therapy (≥ 400 mg levodopa), experiencing ≥ 2.5 hours of daily OFF time.

Study design: A multicenter, randomized, active-controlled, double-blind, double-dummy, parallel group clinical trial



Results: The primary endpoint is the change in mean ON time without troublesome dyskinesia from Baseline to end of maintenance period (Week 12), based on patient-reported diary assessments. Secondary outcome measures include changes in: OFF time (key secondary), UPDRS (Parts II and III), Patient's and Clinician's Global Impressions of Change, ON time without dyskinesia, PDQ-39 and Parkinson's Disease Sleep Scale scores. Clinical assessments will be conducted by a blinded rater. Safety and tolerability will be assessed via adverse event reporting, including local skin safety assessment, rates of premature discontinuation, and treatment compliance.

Conclusion: BouNDless will be the 1st phase 3 randomized, active-controlled trial to evaluate the efficacy and safety of continuous subcutaneous levodopa/carbidopa delivery with ND0612 compared to oral immediate-release levodopa/carbidopa in patients with PD experiencing motor fluctuations.

Disclosure: Funded by NeuroDerm

EPO3148

Efficacy of Opicapone in Patients with Parkinson's Disease with Levodopa Dose Reduction: a Pooled Post-Hoc Analysis of BIPARK-I and II

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Background and aims: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved effective in treating end-of-dose motor fluctuations in Parkinson's Disease (PD) patients in 2 large multinational trials (BIPARK-I and II) [1,2]. This exploratory post-hoc analysis evaluated OPC 50mg as a potential levodopa-sparing agent by assessing its efficacy in levodopa-treated PD patients whose levodopa dose was reduced during the double-blind adjustment periods of BIPARK-I and II.

Methods: Data from matching treatment arms in BIPARK-I and II were combined in placebo (PLC) and OPC 50mg groups. Studies had similar designs and eligibility criteria [1,2]. Motor response (change in absolute OFF- and ON-time; Unified Parkinson's Disease Rating Scale parts II and III [UPDRS II and III]) and quality of life (Parkinson's Disease Questionnaire-39 [PDQ-39]) were assessed in patients who had levodopa dose reduction.

Results: Overall 41 patients treated with OPC 50mg had levodopa dose reduction, either due to dopaminergic adverse events (n=30) or proactively (n=11). These patients had longer disease duration and higher baseline levodopa dosing than the overall OPC 50mg population (Table 1). Although mean daily levodopa dose decreased by an average of 23.4%, these patients still experienced improvements from baseline in absolute OFF- and ON-time, UPDRS II and III scores, and PDQ-39 score (Table 2).

Table 1. Baseline characteristics (Safety Set)

Characteristic	OPC 50 mg N=265	OPC 50 mg with levodopa dose reduction N=41
Male gender, n (%)	160 (60.4)	24 (58.5)
Age, mean (SD) years	64.5 (8.8)	62.4 (9.4)
Disease duration, mean (SD) years	7.7 (4.3)	10.1 (4.6)
Daily OFF-time, mean (SD) hours	6.2 (2.0)	6.5 (1.8)
Levodopa dose, mean (SD) mg/day	698 (322)	842 (344)
Concurrent PD medications, n (%)		
Levodopa/carbidopa	155 (58.5)	28 (68.3)
Levodopa/benserazide	124 (46.8)	17 (41.5)
Pramipexole	96 (36.2)	19 (46.3)
Ropinirole	69 (26.0)	8 (19.5)
Amantadine	55 (20.8)	9 (22.0)
Rasagiline	39 (14.7)	5 (12.2)

OPC, opicapone; PD, Parkinson's disease; SD, standard deviation

Table 1

Table 2. Mean (SD) changes from baseline in motor response and quality of life in patients treated with OPC 50 mg who had levodopa dose reduction (Full Analysis Set)

Scale	OPC 50 mg with levodopa dose reduction N=41
Absolute OFF-time, min	-131.2 (171.8)
Absolute ON-time, min	125.4 (184.0)
UPDRS II score	-3.3 (4.6)
UPDRS III score	-1.7 (8.1)
PDQ-39 score	-2.8 (9.8)

OPC, opicapone; PDQ-39; Parkinson's Disease Rating Scale-39; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale

Table 2

Conclusion: These findings suggest that OPC could act as a levodopa-sparing agent while improving both the motor response and quality of life of levodopa-treated PD patients.

1. Ferreira JJ, et al., *Lancet Neurol.* 2016;15(2):154–165.

2. Lees AJ, et al., *JAMA Neurol.* 2017;74(2):197–206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPO3149

Rationale and design of SUCCESS study (an observational, prospective, multinational StUdy comparing the effeCtiveness of safinamide, rasagiline and “standard of care” as add-on to levodopa)

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Background and aims: Parkinson's disease (PD) is characterized by a wide range of symptoms with a significant impact on patients' quality of life (QoL). Whilst the range of problems has been documented, little effort has been made to assess such impacts directly from the individual's perspective.

Methods: The SUCCESS trial is a European, multicenter, real-world study directly comparing for the 1st time the effectiveness of safinamide vs. rasagiline and other standard of care (SoC) drugs in terms of QoL as measured by the PDQ-39. A total of 1235 patients already on treatment for no more than 2 months will be enrolled in 135 centers across Belgium, Germany, Italy, Spain and United Kingdom and will be followed for 1 year. Follow-up visits will be scheduled per standard routine practice, ideally after 6 and 12 months. The decision of starting treatment with safinamide, rasagiline or other SoC drugs must have been taken considering patients' medical need and routine clinical practice.

Secondary objectives are to evaluate how treatment affects motor symptoms, pain, use of concomitant analgesics and anti-PD drugs, healthcare resource consumption and number of lost working days.

Motor symptoms will be evaluated by the Investigators. Other information will be reported by the patients in a home-diary to be completed in the last five days of each month.

Results: The study is ongoing and results are expected by 2021.

Conclusion: Levodopa is the “gold standard” for the therapy however, additional treatments are needed to control the emergence of disabling complications and deterioration of QoL.

Disclosure: The study is sponsored by Zambon Pharma Group

Movement disorders 8

EPO3150

Outcome of Deep Brain Stimulation in Chorea-acanthocytosis

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Background and aims: Chorea-acanthocytosis is an autosomal recessive very disabling disease characterized by multiorgan involvement, including central and peripheral nervous system.

Methods: The available treatment is symptomatic.

Results: A 30-year-old man with familiar history of bipolar disease and consanguinity, presented with seizures at 25 years old. One year after orofacial movements and vocalizations appeared and Tourette's syndrome was considered. Later he started with lingual mutilation, weight loss and behaviour problems. Neurologic examination showed inattention, impulsivity, frequent vocalizations, dysarthria, sialorrhea, feeding dystonia, generalized choreic movements, bilateral bradykinesia and instable freezing gait. UHDRS-MS (motor score) 51/124, UHDRS-FCS (functional capacity score) 8/33 and UHDRS-IS (independence score) 50%. Blood analysis showed increased creatine kinase and acanthocytes. Brain and medullar MRI were unremarkable so as EMG. Genetic test revealed homozygosity to pathogenic change c.2-47>T (p-Gin783) in the VPS13A gene, confirming the diagnosis of chorea-acanthocytosis. The patient was partially dependent, with severe sleeping and eating impairment and poorly medicated with aripiprazol 10mg/d, naltrexone 50mg/d, lorazepam, eslicarbazepine 800mg/d, botulinum toxin and liquid diet. Pallidal deep brain stimulation was performed (left GPi (0-, Case+) 2.6V, 130Hz, 60mcs and right GPi (8-, Case+) 2.6V, 130Hz, 60mcs). 3 months after the surgery he had a marked improvement of the attention, gait, swallowing, weight and chorea, becoming almost independent, despite worsening of dysarthria. Evaluation scores were: UHDRS-MS 14/124, UHDRS-FCS 20/33 and UHDRS-IS 70%.

Conclusion: Functional surgery can be useful to improve motor symptoms in patients with chorea-acanthocytosis, however, the eligibility should be individualized considering the benefit-risk profile

Disclosure: Nothing to disclose

EPO3151

Gloves: the trick in guitarist dystonia

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Background and aims: Musicians' hand dystonia has been reported with several instruments, including the guitar.

Methods: Sensory tricks may reduce the dystonic symptoms of focal task-specific dystonias (FTSD).

Results: A 30-year-old man, guitar player, presented, at the age of 28, with discoordination while playing the guitar, at 1st more evident in the 3rd finger of the right hand, and, some months later, also noted in the 4th finger of the left hand, with abnormal postures in flexion, causing impairment and playing errors. No other tasks or body segments were involved nor other features as tremor, Parkinsonism or myoclonus. Blood analysis with copper and ceruloplasmin were negative. Brain and cervical MRI were unremarkable. Genetic test to Dyt1 and Dyt6 were negative. Once this was very disabling Artane, tritrate to 6mg, was initiated with poor response and no tolerance due to secondary effects. At this stage the use of gloves as a sensitive trick was suggested. At first he noticed lack of precision but, after cutting the fingers of the gloves, he noticed a marked improvement which allow him to maintain his professional activity.

Conclusion: FTSD are characterized by aberrant motor overactivation during the performance of a specific, often over-practised activity. The triggering activity can be associated with 1's occupation, and it can impact 1's livelihood. The aim of this report is to emphasize the gloves as a symptomatic relief option in guitarists and maybe other focal hand dystonia. Cutting the gloves fingers tip may be a piece of good advice when more precision is needed.

Disclosure: Nothing to disclose

EPO3152

Swimming disability as first symptom of motor impairment in Parkinson's diseaseM. Relja¹, V. Miletić²¹Department Neurology, Medical School Zagreb University, Zagreb, Croatia, ²Neurology, University Hospital Centre Zagreb, Zagreb, Croatia

Background and aims: Parkinson's disease (PD) is generally thought of as movement abnormalities with motor symptoms such as tremor, rigidity and bradykinesia. But non-mot affects one side of or symptoms (NMS) are common and some of them like depression, sleep problems and loss of smell could develop years before patients get a PD. Consequently, contrary to motor symptoms, NMS are considered as pre-symptomatic signs of PD. But PD often affects 1 side of body more than another and it may become more difficult to use extremities to perform some motor task even in the early stage of disease. Experimental research showed that swim test is a direct correlation with striatal dopamine content in MPTP animal model of PD.

To investigate the presence of swimming disability as 1 of the 1st motor symptom in the early stage of PD.

Methods: Development of swimming disability was investigated in 230 Parkinson patients retrospectively using structured interview and NMS questionnaire (NMSQ, self-completed screening tool designed to draw attention to the presence on NMS).

Results Discussion: Structured interview and NMSQ were performed in 230 Parkinson patients (age 65.7±7.3 years, mean±SD) with disease duration range 1/13 years. 46 (20%) patients experienced depression as 1st symptom that brought them to physician (before any motor task abnormalities). However, more than 50% of patients (130) reported swimming difficulties as 1st symptom they experienced in physical activity that was the reason for seeking medical examination.

Conclusion: Parkinson patients easier recognize motor symptoms and question of swimming disabilities should be included in 1st neurological examination.

Disclosure: Nothing to disclose

EPO3153

Utility of skin biopsy to detect phosphorylated α -synuclein deposits in the diagnosis of progressive supranuclear palsy and corticobasal syndrome

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Background and aims: Previous studies reported skin α -syn deposits in Parkinson's disease (PD) patients but not in patients with parkinsonism due to tauopathies, although data on the latter are few.

Aim of this study is to perform skin biopsy in patients with clinical diagnosis of tauopathy, i.e progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS).

Methods: We consecutively recruited 26 patients, 18 PSP and eight CBS, 26 patients with PD and 26 healthy controls. All subjects underwent skin biopsy to search for deposits of p-syn by immunofluorescence. 2 experts in immunofluorescent analysis blinded to the clinical classification analyzed the biopsies.

Results: All PSP/CBS patients except 2 had not skin α -syn deposits, as well as all the controls. Conversely, all PD patients showed p-syn deposition.

The 2 α -syn positive patients in the group of tauopathies were 1 diagnosed with PSP and 1 with CBS. Although clinical and MRI findings in support of these diagnoses, both patients had some atypical features for PSP/CBS and more typical of synucleinopathy. The PSP patient developed visual hallucinations and orthostatic hypotension with low doses of levodopa. The CBS patient had a slow parkinsonism progression, moderate levodopa response, and cardiac denervation at 123I-meta-iodobenzylguanidine scintigraphy.

Conclusion: The detection of skin α -syn deposits may help in the differential diagnosis of parkinsonism. Indeed, all PD patients and only 2 out of 26 with clinical diagnosis of PSP/CBS had skin α -syn deposits. Furthermore, these 2 patients showed clinical features that can suggest an atypical presentation of a synucleinopathy rather than false positive results.

Disclosure: Nothing to disclose

EPO3154

Long-term mortality of patients with Parkinson's Disease treated with Deep Brain Stimulation

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Background and aims: Parkinson's disease (PD) is a common neurodegenerative disorder, with a higher risk of death than general population. Deep Brain Stimulation (DBS) has been used to treat PD for more than 2 decades, but few studies exist concerning mortality in this subset of patients. Our goal is to analyse mortality in PD patients treated with DBS in our center.

Methods: Retrospective evaluation of clinical files of patients with PD who underwent DBS surgery consecutively between October 2002 and May 2019.

Results: We included 346 patients in the analysis, 60% male, with a mean age at disease onset of 48±8 years-old (18-64), mean age at surgery of 60.7 years-old (33-75), and mean disease until surgery of 14.6 years (3-52). Mean follow-up after surgery was 7.4 years (range 1-17). Overall mortality rate was 17.9% and mean age at time of death was 71.6 years-old. The main causes of death were pneumonia, dementia and acute myocardial infarction. In our series, male gender and disease duration until surgery were the only predictors of mortality in multivariate analysis.

Conclusion: Our study showed a long term survival higher than previously described, and suggest that the treatment of patients with shorter disease evolution might have a survival benefit. Death in PD patients treated with DBS seem to be unrelated to surgical treatment, as the main causes of death are comparable to non-DBS patients.

Disclosure: Nothing to disclose

EPO3155

Frontotemporal Lobar Degeneration: broadening the clinical spectrum.

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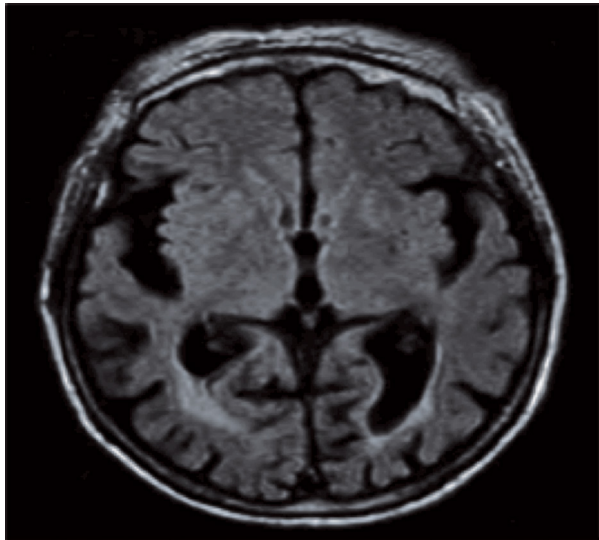
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Background and aims: Frontotemporal dementia (FTD) encompasses a group of clinically, genetically and neuropathologically heterogeneous neurodegenerative disorders. Clinical features include changes in social behaviour and personality, language impairment and, in some patients, additional motor symptoms, with variable survival.

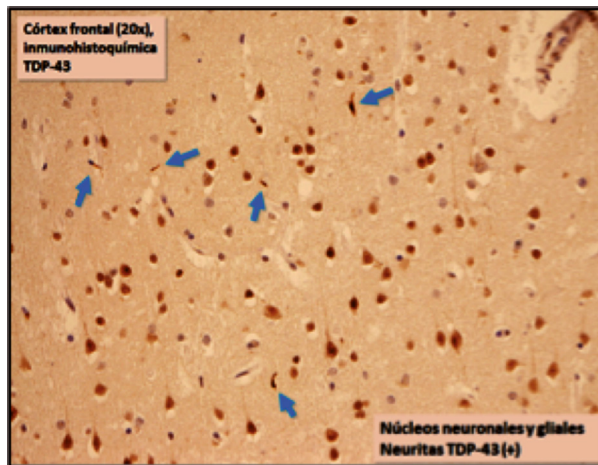
Methods: Case report.

Results: A 53-year-old previously healthy woman with no relevant family history, presented with a subacute gait disorder and repetitive falls.

The neurological examination revealed hypomimia, generalized bradykinesia with greater involvement of left limbs, hyperreflexia and bilateral Babinski. She progressively developed language impairment that finally led to anarthria, left-sided and oromandibular dystonia, supranuclear gaze palsy and gestural dyspraxia, without cognitive impairment. Brain MRI showed bilateral right-sided predominant cortical and subcortical atrophy. Electromyography, blood test, transcranial ultrasonography and cervical-MRI were normal. There was no response to dopaminergic therapies. She died 29 years after symptoms onset. Neuropathology showed frontal brain atrophy with cortical vacuolization, gliosis and TDP-43 positive pathology. Immunostaining was negative for TAU, Beta A4, and alpha-synuclein. Hippocampus was intact. The absence of p62 + inclusions in cerebellum would exclude the presence of C9ORF72 mutation and supports a sporadic TDP 43 frontotemporal lobar degeneration diagnosis.



Brain MRI: bilateral right-sided predominant cortical and subcortical atrophy.



Neuropathology: gliosis and TDP-43 positive pathology

Conclusion: We present an FTD TDP-43 positive case with a focal cortical frontal involvement and an atypical phenotype, with predominant motor symptoms in the corticobasal syndrome spectrum (TAU negative), no behavioural disturbances and long survival. It shows the complexity regarding the correlation between clinical phenotypes, genetics and neuropathology in neurodegenerative disorders, as well as pathology remains essential to accomplish a definite diagnosis.

Disclosure: Nothing to disclose

EPO3156

2 clinical cases of secondary parkinsonism due to cerebral glioblastoma

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Background and aims: Idiopathic Parkinson's disease (IPD) is the most common cause of parkinsonism. Other causes are: atypical Parkinsonisms and Secondary Parkinsonism (SP), due to structural, toxic-metabolic, infectious, or cerebrovascular disorders. We report 2 clinical cases of SP due to cerebral glioblastoma.

Methods: Case 1, 63-year-old woman with micrographia from 4 months and right hand rigidity and bradykinesia in examination. Case 2, 72-year-old man with left hand rest tremor, left knee pain and postural instability from 2 months, plus left bradykinesia in examination. Both started pharmacological treatment without clinical improvement and neuroimaging was performed.

Results: Case 1, MRI: tumoration at left basal ganglia extending to external capsula, insula and temporal lobe, with aedema and mass effect. Extension study was negative and brain biopsy showed high grade glioma. She was treated with temozolamide and radiotherapy, dying 2 years after diagnosis. Case 2, MRI: right frontal expansive process with vasogenic aedema, mass effect and peripheral ring enhancement, compatible with glioblastoma. He underwent total surgical resection and posterior temozolamide plus radiotherapy, with persistence of parkinsonism.

Conclusion: Intracranial tumours (specially those in basal ganglia) are a rare cause of SP. Glioblastomas are exceptionally reported being meningiomas the most frequent. IPD mustn't be excluded unless parkinsonism disappears after total resection, however, it's important to know that supratentorial tumours sparing extrapyramidal system also can produce parkinsonism due to damage of these structures secondary to mass effect, neural pathways disruption or blood flow impairment. We enhance the importance of neuroimaging for diagnosis of parkinsonism, specially in patients without pharmacological response.

Disclosure: Nothing to disclose

EPO3157

Prevalence of polyneuropathy in patients with Parkinson's disease in Germany

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Background and aims: The prevalence of the peripheral neuropathy (PN) is of 4.2-8% in those over 65yo [2-6]. In patients with the Parkinson's disease (PD) a much higher PN-prevalence of 34.2-55% was reported [8-10]. Low vitamin B12-blood level was reported in 13% of PD patients [12]. There is a higher prevalence of PN in levodopa-treated patients (36.1%) than in naive (12.1%) and in healthy controls (8.1%). The present study examines the prevalence of PN in patients with PD in Germany.

Methods: We examined 601 patients with PD. Of them, 407 patients underwent electrophysiological examination.

Results: 444 (73.9%) had clinically PN (Fig. 1). Of 407 patients who underwent electrophysiological investigations, in 361 (88.7%) PN was confirmed. The most common was axonal (304 patients; 84.2%), sensory (282; 78.1%) and slight (78; 21.6%) or moderate (164; 45.4%) PN (Tab. 1). Of 471 patients receiving levodopa, 369 (78.34%) had clinical PN, compared to 75 (56.8%) of 132 levodopa-naive patients (p<0.01).

At the T1-time-point of first-diagnosis of polyneuropathy, 179 patients (40.3%) of 444 with PN had a vitamin B12-deficiency. In 585 of patients, 38 (33.3%) of 114 levodopa-naive PD patients had vitamin B12-deficiency at the T1, compared to 129 (27.1%) of 471 levodopa-treated PD patients (p=0.2).

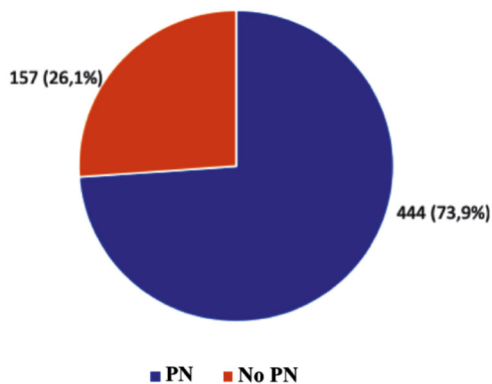


Fig. 1. Clinical polyneuropathy's prevalence in PD. PN – peripheral polyneuropathy

Total electrophysiology	PP confirmed	Type PNP				Intensity PP			PP		
		axonal	demyelinating	mixed	slight	moderate	heavy	Sensory	Motor	Sensomotor	
407 (100%)	361 (88,7%)	304 (84,2%)	37 (10,2%)	20 (5,6%)	78 (21,6%)	164 (45,4%)	119 (33%)	282 (78,1%)	3 (0,8%)	76 (21,1%)	

Tab. 1. Characteristics of polyneuropathy detected in PD patients.

Conclusion: In our group of PD patients the prevalence of a clinical polyneuropathic syndrome was very high and in almost 90% of cases it was confirmed electrophysiologically. 40% of patients with PN had a vitamin B12-deficiency. Levodopa-treatment was more common in PD patients with PN than in those without PN.

Disclosure: Nothing to disclose

EPO3158

Real life experience with Opicapone

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Background and aims: There's a clear scientific evidence of opicapone indication, clinical efficacy and advantages. However, no much literature regarding its use in the real life management is published.

We present our experience with this drug in the daily clinical practice.

Methods: This is a descriptive prospective, real-life study in which data are collected from 30 patients with idiopathic Parkinson's disease (IPD) in moderate stage, H&Y II-III, <400mg daily dose of Ldopa, after the addition of opicapone.

Clinical evaluation by obtaining quality of life and fluctuation scales (PDQ39, Quick19, Global Clinical Impression) at baseline, and after 3 and 6 months, is accomplished.

Results: 3 of the 30 patients had to be discontinued due to side effects.

The overall clinical impression was much improved or improved in 23 patients.

Previous fluctuations were observed in 19 patients. 14 cases were reported as improved, there were no substantial changes in 3 cases, and only 3 patients worsened.

In the PDQ39 analysis, we see an improvement in function and motor capabilities in 17 of the 30 patients. Some previous emotional problems improved in 12 patients. Communication difficulties, and sensitive symptoms improved in 50% of the patients, and there were no changes in sleep disorders and memory complaints

Results were consistent at 3 and 6 month evaluation, so the improvement was maintained.

Conclusion: Opicapone is a well tolerated drug, and we observe a maintained satisfactory response in different items in our patients.

Our experience supports previous studies, from a real-life clinical point of view.

Disclosure: Nothing to disclose

EPO3159

Clinical and fMRI effects of Action Observation and Motor Imagery Training on dual-task performances in Parkinson's disease patients with postural instability and gait disorders

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Background and aims: Dual-task is challenging for Parkinson's disease patients with postural instability and gait disorders (PD-PIGD) and impacts on postural stability and gait safety. This study aimed at assessing brain functional reorganization and gait changes performing dual-task after 6 weeks of action observation training (AOT) and motor imagery (MI) associated with gait/balance exercises in PD-PIGD patients.

Methods: 25 PD-PIGD patients were randomized into 2 groups: the DUAL-TASK+AOT-MI-group performed a 6-week (W6) gait/balance training consisting of AOT-MI combined with practicing the observed-imagined exercises; DUAL-TASK-group performed the same exercises combined with watching landscape videos. Exercises were increasingly difficult up to include dual-task. At baseline and W6, patients underwent: i) functional MRI (fMRI) including a foot-movement task and a dual-task (foot anti-phase movements counting backwards) and ii) gait/balance evaluations with and without dual-task.

Results: At W6 compared to baseline, both groups showed an improvement in gait, whereas only the DUAL-TASK+AOT-MI-group improved gait and balance in dual-task conditions, particularly during the turning phase of gait relative to the DUAL-TASK-group. At W6 the DUAL-TASK+AOT-MI-group compared to the DUAL-TASK-group showed an increased recruitment of motor areas during the foot-movement task and a reduced recruitment of frontal, occipital and temporal areas during both the fMRI foot-movement task and the dual-task.

Conclusion: Our results suggest that increasingly difficult gait/balance exercises improve gait speed in PD-PIGD patients; however, only when exercises were preceded by a motor-learning facilitation strategy (AOT-MI), patients showed gait/balance improvements and increased brain efficiency during dual-task circumstances, which are among the most challenging for PD-PIGD patients.

Disclosure: Nothing to disclose

EPO3160

Brain functional plasticity of the limbic circuit in Parkinson's disease patients with freezing of gait

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Background and aims: To assess brain functional MRI (fMRI) activity during an “empathy” task in Parkinson's disease patients with Freezing of Gait (PD-FoG) relative to healthy controls (HC).

Methods: 24 PD-FoG patients were recruited and performed clinical and neuropsychological evaluations and fMRI. 18 age- and sex-matched HC were also included to perform neuropsychological and fMRI evaluations. PD-FoG patients and HC performed two fMRI tasks: i) the “empathy task” consisted of watching a patient who experienced FoG during a walking task usually evoking FoG; ii) the “control task” consisted of watching a healthy subject performing similar walking tasks without experiencing FoG. HC were emotively educated to the FoG phenomenon before undergoing the fMRI scan.

Results: PD-FoG patients had cognitive deficits relative to HC particularly in attention/working memory and executive functions. During the empathy task, PD-FoG patients showed reduced activity of the sensorimotor part of the mirror neuron system (MNS) relative to HC. During the empathy task relative to the control task, PD-FoG revealed increased recruitment of the right anterior prefrontal cortex and decreased activity of the left inferior parietal cortex. HC showed increased recruitment of bilateral superior/middle frontal gyri during the empathy task and of the MNS performing the “control task”.

Conclusion: Our results suggested that when PD-FoG patients observe a subject experiencing FoG, there is increased brain activity in the limbic part of the MNS. This finding might suggest an involvement of the limbic circuit and, thus, of the emotional processes in the mechanisms underlying FoG in PD.

Disclosure: Nothing to disclose

EPO3161

Activities of daily living impairment before surgery predicts STN-DBS outcome in Parkinson's disease

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Background and aims: Despite Subthalamic Nucleus (STN) Deep Brain Stimulation (DBS) proven safety and efficacy in Parkinson's Disease (PD), postoperative impact on patients' activities of daily living (ADL) is difficult to predict. Aim of this study was to investigate predictors of poor response after STN-DBS in PD at 1-year follow-up.

Methods: We retrospectively analyzed data acquired during pre-DBS assessment (T0) and 1-year follow-up (T1) at Turin University DBS center. To provide an ADL measure, unsatisfactory outcome was defined as less than 20% improvement at UPDRS-II OFFMED/ONSTIM at follow-up. Based on this cut-off, 2 resulting patients' groups, “poor” and “good” responders, were compared for demographical, clinical and cognitive variables.

Results: The cohort was constituted by 203 consecutive patients. Among them, we identified 35 “poor” and 91 “good-DBS-responders” similar for age at disease onset and surgical procedure, and disease duration. The 2 groups had comparable improvement of motor symptoms after DBS (as per UPDRSIII OFF-MED/ON-STIM) and reduction of dopaminergic drugs at T1. Remarkably, Poor-DBS responders had significantly less severe UPDRSII OFF-MED at T0 when compared with Good-DBS responders. Poor-DBS responders also had a not significant improvement of UPDRS-Axial and Motor Fluctuations scores at 12 months.

Conclusion: Our study demonstrates that PD Poor-DBS responders at 1-year follow-up have significantly less impaired ADL at the time of DBS selection. This is in line with recent evidence showing that better quality of life before DBS predicts less improvement after surgery. Post-operatively, not significant improvement of axial symptoms and of time spent in OFF condition are major determinants of unsatisfactory DBS outcome.

Disclosure: Nothing to disclose

EPO3162

Intrinsic functional connectivity correlates of RBD in cognitively unimpaired drug-naïve Parkinson's disease patients

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Background and aims: REM Behavioural Disorder (RBD) is characterized by lack of skeletal muscle atonia during REM sleep and it develops in around 50% of Parkinson's disease (PD) patients. PD patients with RBD present an increased risk of worse motor progression and dementia over the disease course. Using resting-state functional MRI, we investigated intrinsic connectivity correlates of RBD in a cohort of cognitively unimpaired drug-naïve PD patients and correlated neuroimaging findings to clinical and cognitive measures.

Methods: 3T MRI images of 56 drug-naïve PD patients (25 PD-RBD and 31 PD-no-RBD) were acquired. RBD presence and severity was assessed by means of a clinical interview and the RBD Screening questionnaire. Single-subject and group-level independent component analysis was used to investigate intra and inter-network functional connectivity differences within the major neurocognitive resting state networks between patients sub-groups. Finally, linear regression analysis was used to investigate correlations between imaging and clinical data.

Results: Compared to PD-no-RBD patients, PD-RBD showed an increased connectivity within the Salience Network and the Executive Control Network as well as a decreased connectivity within the Fronto-Parietal Network. Within the Default-Mode Network, PD-RBD exhibit both an increased and a decreased connectivity compared to PD-no-RBD. This imaging pattern was found to be correlated with both RBD severity and cognitive outcomes in PD patients.

Conclusion: Our findings demonstrated that an abnormal intrinsic brain connectivity may represent a potential neural correlates of RBD symptoms and severity in PD patients. This aberrant connectivity may potentially be proposed to develop an early biomarker of dementia in PD.

Disclosure: Nothing to disclose

EPO3163

Study design and rationale for an international study of DBS for movement disorders

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Background and aims: DBS improves motor outcomes and quality of life in patients with movement disorders, including Parkinson's disease, disabling tremor, and dystonia. Several factors may affect DBS outcomes within and across geographies, including the surgical procedure, novel features, and patient management practices. There is increasing interest in tracking long-term outcomes to provide ongoing market surveillance, to establish best practices, and to identify opportunities for therapy unmet needs.

Methods: ADROIT (NCT04071847) is an international, prospective, multicenter, post-market, observational study of patients implanted with Abbott DBS systems designed to investigate real-world long-term outcomes over 5 years after device activation. Up to 1,000 subjects will be enrolled at up to 50 sites worldwide. The primary safety endpoint is the incidence of device- or procedure-related serious adverse events. The primary effectiveness endpoint is the change in disease-specific motor score (MDS-UPDRS Part III for Parkinson's disease, FTM-TRS for disabling tremor, BFMDRS for dystonia, TWSTRS for cervical dystonia). Additional endpoints will quantify medication usage, quality of life, global impression, mood, cognition, caregiver burden, MRI usage, and healthcare utilization. Surgical and programming data will also be collected.

Results: The 1st study site was activated in October 2019, and enrollment began in December 2019. Data on the 1st cohort of enrolled subjects will be presented.

Conclusion: ADROIT will quantify safety and effectiveness of DBS using systematic collection of clinician, patient, and caregiver reported outcomes. This study also provides a data collection platform to perform subgroup analyses, exploratory hypothesis testing, and substudy development.

Disclosure: The study is funded by Abbott

EPO3164

Cortical infarction and Abnormal involuntary movement

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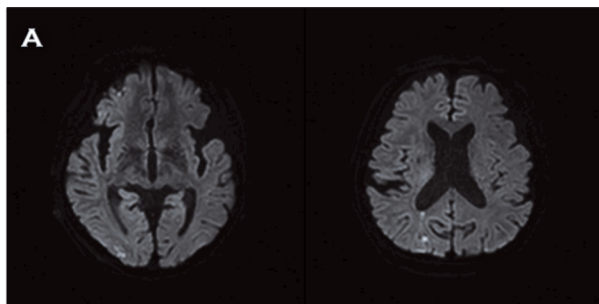
Background and aims: Hemichorea refers to chorea on one side of the body, that is rarely associated with cortical lesions. There are only a few cases of hemichorea associated with cortical infarction, except for the basal ganglia, thalamus and subthalamic nucleus (STN).

Methods: We describe a case of hemichorea which is suspected to be related to frontal-parietal-occipital lobe infarction.

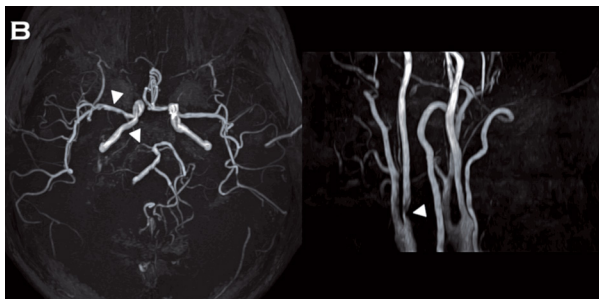
Results: A 79-year-old man was admitted with chorea on the left side, involving upper and lower extremities. There were no other symptoms such as motor weakness or sensory change.

Brain magnetic resonance imaging (MRI) showed multiple small recent infarctions on right frontal-parietal-occipital lobe. Brain magnetic resonance (MR) angiography showed total occlusion in the right posterior cerebral artery (PCA), multiple stenoses in right middle cerebral artery (MCA) and severe focal stenosis in right proximal internal carotid artery (ICA). In addition, perfusion MR revealed hypoperfusion of right MCA and PCA territories.

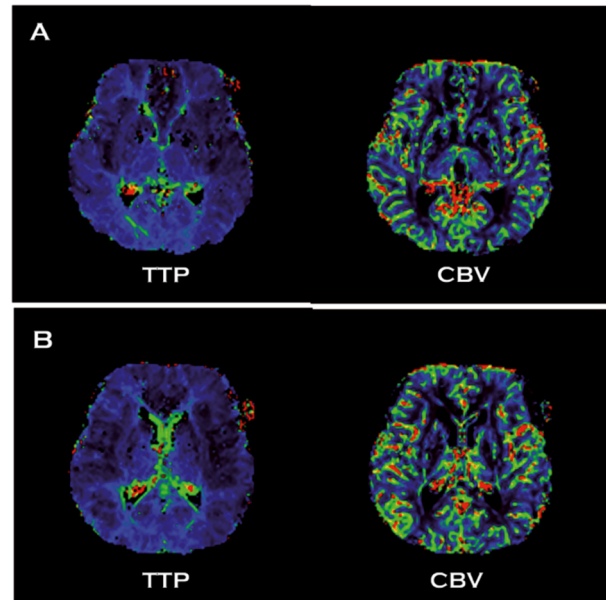
He started risperidone 1mg per day and antiplatelet agents for hemichorea and cerebral infarction, respectively. The movements relieved from the day after he started taking the medicine. From 2 weeks after discharge, risperidone was stopped and no chorea remained.



Brain MRI



MR angiography



Brain perfusion MR

Conclusion: The mechanism of hemichorea in the cortical infarction is unclear. However, in this case, the hypoperfusion of the territory including the basal ganglia, thalamus and STN identified by perfusion MRI, may have affected the symptoms.

Although treatment guideline of the hemichorea related to cerebral infarction are not established, antidopaminergic or neuroleptic drugs are mainly used. We applied risperidone which is an atypical neuroleptic, and it works well.

Disclosure: Nothing to disclose

EPO3165

Low emotional arousal in patients with functional movement disorders: a pupillometry study

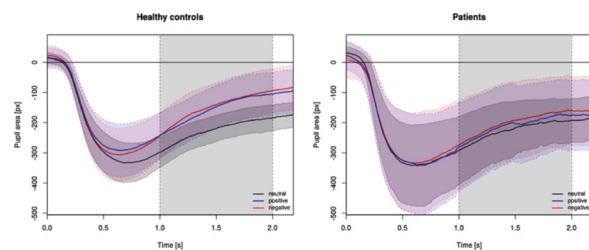
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Background and aims: It has been suggested that emotional hyperarousal is involved in the pathophysiology of functional movement disorders (FMD). However, direct evidence for this phenomenon is lacking. Pupillometry is a validated method for evaluation of emotional arousal by detecting changes in pupil dilation in response to emotionally charged stimuli.

Methods: We assessed emotional arousal in 17 female FMD patients (mean age 43.2 [SD 14.2] years) and 19 matched healthy controls using pupillometry. An infrared eye-tracking camera was used to record changes in pupil dilation during viewing series of positive, negative and neutral pictures from the International Affective Picture System. The time window for analysis was 1-2s after picture onset. Subjective ratings of emotional valence and arousal from all pictures were recorded.

Results: Pupil dilation to positive and negative pictures was significantly larger compared to neutral pictures in controls ($p < 0.001$), but not in FMD patients ($p = 0.262$), who showed significantly lower pupil dilation in response to positive and negative pictures compared to controls ($p < 0.01$). No difference was found in pupil response to neutral pictures ($p = 0.997$). No between-group difference in affective ratings was found.



Conclusion: FMD patients presented with a blunted autonomic reactivity to emotional stimuli and lower emotional arousal than controls. These changes were not

reflected in subjective evaluation of emotional arousal. This finding questions the role of emotional hyperarousal in the pathophysiology of FMD, while it could be interpreted within predictive coding accounts of FMD involving abnormal attention allocation and interoceptive processing.

Disclosure: This study was supported by grant AZV ČR 16-29651.

EPO3166

Cerebrospinal fluid levels of Interleukins 8 and 10 are not increased in functional movement disorders

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Background and aims: Patients with functional movement disorder (FMD) typically present with significant pain and fatigue. Abnormal cerebrospinal fluid (CSF) and/or serum concentrations of cytokines interleukin 8 (IL-8) and 10 (IL-10) have been consistently reported in fibromyalgia, and chronic fatigue syndrome. This pilot study aimed to compare the interleukin-8 (IL-8) and interleukin-10 (IL-10) CSF levels in FMD patients to non-inflammatory neurological and non-neurological disease patients and to assess their relationship to self-reported pain and fatigue in FMD.

Methods: Using ELISA, we measured the IL-8 and IL-10 levels in CSF from 20 patients with clinically established FMD (13 females, mean age 40 [SD 12] years), and 20 controls (13 females, mean age 43 [SD 16] years). The control group included 15 patients with non-inflammatory neurological symptoms and 5 patients with urinary tract disorder undergoing spinal anaesthesia. FMD patients completed standardized questionnaires for self-rated pain (PainDetect) and fatigue (Fatigue severity scale) measures.

Results: No differences in the CSF levels of IL-8 and IL-10 were found between FMD patients and control subjects ($p=0.53$ and $p=0.60$, respectively). The levels of IL-8 were positively correlated with self-rated fatigue in FMD patients (Spearman's $\rho=0.52$, $p=0.027$).

Conclusion: We did not find evidence for glia activation resulting in intrathecal elevation of cytokines in FMD compared to heterogeneous non-inflammatory disorders. However, the relationship between IL-8 levels and self-reported fatigue suggests possible role of this cytokine in the pathophysiology of fatigue in FMD and should be addressed by future studies.

Disclosure: This study was supported by grant AZV ČR 16-29651.

EPO3167

Evaluation of duloxetine effectiveness in pain relief for Parkinson's disease patients

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Background and aims: The issue of creating accurate guidelines for treatment of pain in Parkinson's disease is extremely relevant. And the main problem is differing results of studies when using dopamine replacement therapy in combination with traditional analgesics. The aim of research is to determine effectiveness of duloxetine in relief in PD.

Methods: A double-blind, placebo-controlled study was conducted for 2 months. Patients with Parkinson's disease were selected according to the following criteria: with chronic pain in stage I-III of Hoehn & Yahr scale. From this group of samples in a random order, patients were divided into placebo groups and duloxetine groups. In the second group, patients received 30mg of duloxetine once a day. Results were evaluated using of 11-point Visual Analogue Scale and Short-Form McGill Pain Questionnaire, as well as a miniature pain stimulus were used to determine the subjective threshold of pain sensitivity. Threshold of pain sensitivity for each of the subjects was established after the application of the "multiple random stairs" method.

Results: At the beginning of study, there was no statistically significant difference in demographic and clinical data between duloxetine group and placebo group. Quantitative improvements were observed in evaluations of the scales in favor of duloxetine group ($p=0.04$). In the induced pain stimulus was noticeable increase in pain thresholds in the duloxetine group compared with the placebo group ($p=0.05$).

Conclusion: The efficacy of duloxetine in pain relief was determined in PD, further studies are needed to understand the effectiveness of duloxetine with prolonged use.

Disclosure: Nothing to disclose

Movement disorders 9

EPO3168

The challenges of managing two neurological diseases at a time

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Background and aims: McArdle's disease is an autosomal recessive muscle disorder involving myophosphorylase gene mutations while Parkinson's disease is a movement disorder associated with bradykinesia, resting tremor and rigidity. They are clinically distinct and require different management approaches.

Results: We present the case of a 47-year-old male, with a medical history of presumed viral rhabdomyolysis in 2002, developed progressive and worsening asthenia, with scapular, and later pelvic, weakness, along with muscle pain, leading to significant functional impairment. Blood workup showed persistent CK elevations. He was hospitalized in 2013 and presented with right winged scapula, right proximal upper limb wasting and tetraparesis, with greater upper limb involvement. Additionally, he displayed left upper limb akinesia, rigidity and resting tremor. Muscle biopsy and genetic workup were consistent with McArdle disease. A DaTScan[®] was suggestive of parkinsonism. He started antiparkinson therapy, with transient clinical improvement, and was followed-up in both Neurology and Internal Medicine appointments. Genetic causes of parkinsonism were excluded. Due to complaints from both pathologies and a poor therapeutic compliance, he registered progressive functional impairment. Multiple therapeutic changes were attempted unsuccessfully.

Conclusion: This case illustrates the difficulties that arise from the coexistence of 2 neurologic diseases and the exponential worsening in functional impairment resulting from this interaction. This unusual clinical association leads to a challenging management approach. It must involve a multidisciplinary team, aiming to find the best therapeutic plan, with consideration for both pathologies, reducing thereby the resulting functional impairment.

Disclosure: Nothing to disclose

EPO3169

Patients with Multiple System Atrophy show higher variability of gait compared to Parkinson patients: impact of walking velocity

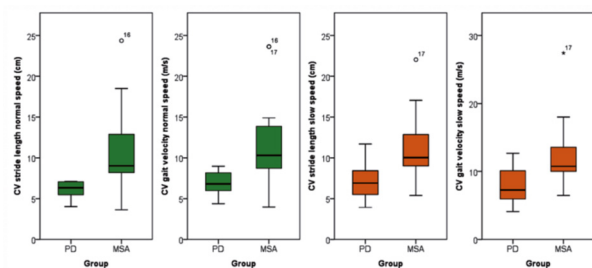
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Background and aims: Gait impairment is a common symptom in movement disorders like Parkinson's disease (PD) and Multiple system atrophy (MSA) leading to an increased risk of falling. Previous studies suggest that gait variability increases with motor impairment in advanced PD, but these aspects have never been analyzed in MSA patients. We aimed to investigate the variability of gait in PD compared to MSA patients with respect to different walking velocities.

Methods: Spatiotemporal gait parameters were recorded in 12 PD and 12 MSA patients using sensor-based gait analysis. Variability (Coefficient of Variance) of stride, swing and stance time, stride length and gait velocity were compared between PD and MSA patients and between self-selected comfortable, fast and slow walking velocity.

Results: Demographic data did not differ between groups except of age and disease duration ($p < 0.05$). UPDRS III for MSA and PD did not show significant difference ($p = 0.071$). MSA patients revealed a higher variability of stride length and gait velocity for comfortable ($p < 0.001$, $p = 0.002$) and slow walking velocity ($p = 0.005$, $p = 0.008$). Swing and stance time variability significantly differed in slow walking velocity ($p = 0.007$, $p = 0.002$). No significant differences were observed in fast walking condition.



Comparison of PD and MSA patients according to variation of stride length and gait velocity in normal (green) and slow speed (orange).

	MSA (n = 12)	PD (n = 12)	p-value
Gender (m:f)	6:6	6:6	n.s
Age, mean (SD)	57.0 (\pm 5.1)	71.3 (\pm 7.1)	< 0.05
Disease duration, mean (SD)	4.3 (\pm 2.1)	10.1 (\pm 8.0)	< 0.05
UPDRS I, median (IQR)	13.0 (9.5; 17)	8.0 (4.3; 12.5)	n.s
UPDRS II, median (IQR)	19 (14; 28.5)	5.5 (2.3; 9.8)	< 0.05
UPDRS III, median (IQR)	34.5 (20; 49.3)	23.5 (16.3; 28)	n.s
UPDRS IV, median (IQR)	0	0	n.s
UPDRS I-IV, median (IQR)	67.00 (52; 81.5)	36.5 (20.5; 54.8)	< 0.05

Patient characteristics.

Conclusion: Our observations revealed higher gait variability in MSA patients for comfortable and slow walking. Increased gait variability particularly reflects severe impairment of gait and postural stability presented by MSA patients, in contrast to PD patients.

Disclosure: Nothing to disclose

EPO3170

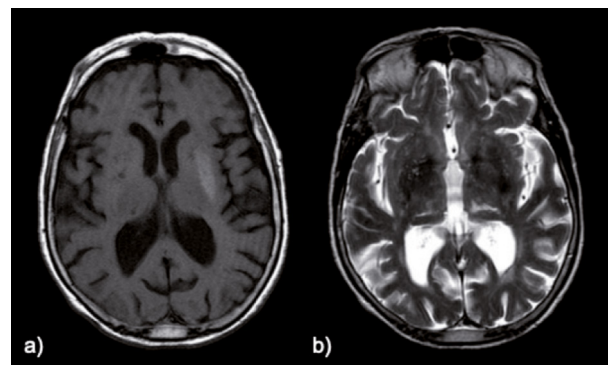
Acute hyperkinetic movement disorders requiring inpatient approach – a 10-year review of a tertiary care hospital

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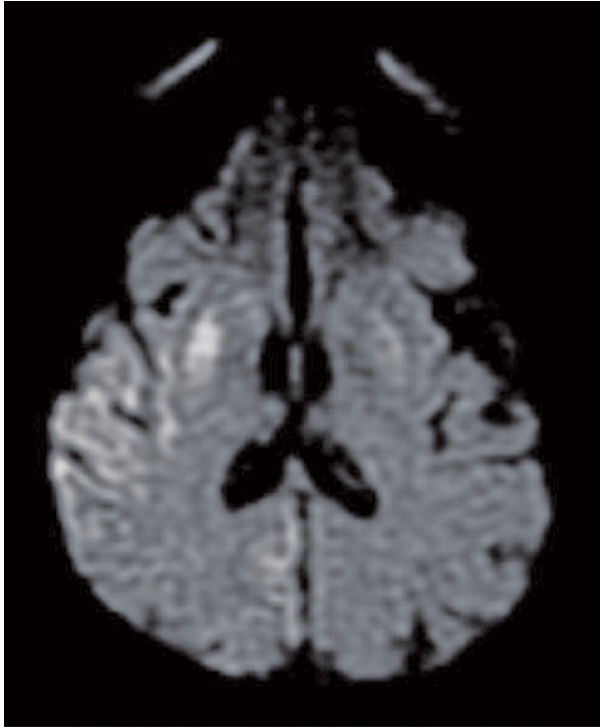
Background and aims: Although the majority of movement disorders are outpatient clinic diseases, an acute presentation or a complication of a chronic disorder may require an inpatient approach. Acute hyperkinetic movement disorders (HMD) are rare but may cause significant functional disability and distress.

Methods: We performed a retrospective analysis of patients with acute or subacute HMD admitted to a Neurology department of a Portuguese tertiary care hospital over 10 years (January 2008 to December 2018).

Results: 14 out of 5238 patients admitted were included. The mean age was 62.6 \pm 20.5 years (30-87). The most common type of HMD was chorea (n=10), followed by myoclonus (n=3). Concerning to etiology, drug-induced HMD (n=4), Parkinson's disease (PD) related dyskinesia (n=4) and Huntington's disease (HD) (n=3) were the most frequent causes. Other etiologies included Creutzfeldt-Jakob disease (CJD) (n=1), nonketotic hyperglycemia (NKH) (n=1) and antiphospholipid syndrome (n=1). 5 patients had an underlying movement disorder (PD or HD). Brain MRI was performed in 7 patients and revealed characteristic findings in 2 cases: T1 hyperintensity and T2 hypointensity in the putamen (NKH), and hyperintensity in diffusion-weighted imaging and T2-FLAIR in the putamen, caudate nucleus and cortex (CJD). All patients, with exception of the CJD patient, improved during hospitalization. The average length of hospital stay was 12.8 \pm 11.4 days (2-44).



Brain Magnetic Resonance Imaging of the nonketotic hyperglycemia case: (a) Axial T1-weighted image hyperintensity and (b) Axial T2-weighted image hypointensity in the putamen on the left.



Brain Magnetic Resonance Imaging of the Creutzfeldt-Jakob disease case: Axial diffusion-weighted imaging hyperintensity in the putamen and caudate nucleus bilaterally, mainly on the right, and on the right temporo-parietal and medial occipital cortex.

Conclusion: We found that HMD is a rare cause of hospitalization. Drug-induced HMD and PD related dyskinesia were the most frequently encountered HMD. Considering the disability associated with this disorders, inpatient treatment can be necessary for therapeutic optimization and functional recovery.

Disclosure: Nothing to disclose

EPO3171

REM Sleep Behavior Disorder and other sleep abnormalities in p. A53T SNCA mutation carriers using PSG

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Background and aims: Available data regarding sleep disturbances, and in particular RBD, in p.A53T carriers are scarce and are based on subjective measures such as questionnaires but not on Polysomnography (PSG). Our aim is to assess whether RBD and other sleep abnormalities occur in both symptomatic and asymptomatic carriers of the p.A53T alpha-synuclein gene (SNCA) mutation, using both subjective and objective measures of sleep.

Methods: We have assessed 15 p.A53T carriers (10 manifesting PD and 5 asymptomatic carriers) with simultaneous Video/PSG recording, Epworth Sleepiness Scale to assess the daytime sleepiness, RBD Screening Questionnaire (RBDSQ) to assess clinical features of RBD, Montreal Cognitive Assessment (MOCA) and the University of Pennsylvania Smell Identification Test (UPSIT) to assess olfaction.

Results: 9/10 PD carriers had evidence of sleep disorder in PSG: In 4/10 PSG showed RBD (2 were treated with antidepressants and only 2 scored >5 in RBDSQ), in 4/10 PSG showed RWA (only 1 scored >5 in RBDSQ) and in 2/10 showed PLM. Only 1/5 asymptomatic carriers manifested RWA in PSG. 7/8 PD carriers with RBD/RWA had abnormal olfactory testing.

Conclusion: RBD or RWA occur in the majority of PD p.A53T carriers, at a higher percentage compared to idiopathic PD and in contrast with other genetic forms of PD. No evidence of a sleep disorder in most of asymptomatic carriers may indicate that such carriers have not yet reached the prodromal phase of the disease. Hyposmia in almost all subjects with RBD/RWA, may be indicative of the pattern of disease progression.

Disclosure: Nothing to disclose

EPO3172

Adherence to pharmacotherapy and subtypes of non-demented patients with Parkinson's disease

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Background and aims: Non-adherence to pharmacotherapy in Parkinson's disease (PD) is associated with worsen clinical state and poor quality of life (QoL). Identification of risk patients for non-adherence is key role in clinical practice.

Methods: We included 124 cognitively intact patients (72 men, mean PD duration 7.42y, LEDD 1191.05mg). PDQ-8, GDS, NMSS, WOQ-9, MDS-UPDRS III and IV were used. Level of adherence was detected by 8-Item Morisky Medication Adherence Scale. K-Means grouping (cluster analysis) was used to create empirical subtypes.

Results: Using cluster analysis we identified 4 PD subtypes. Subtype 1 was characterized by worsen motor state, frequent nonmotor symptoms (NMS) and poor QoL, but without complications. Subtype 2 was characterized by higher LEDD and complications (other parameters were with lower scores). Subtype 3 was characterized by low score in observed parameters (relatively good clinical condition). Subtype 4 was characterized with higher scores in all observed parameters. Patients from each subtype were assigned to groups according to levels of adherence ($V=0.262$, $p=0.009$). We identified that patients from subtypes 1 and 4 were with lower adherence to pharmacotherapy and patients from subtype 3 were with higher levels of adherence.

Conclusion: Patients with worsen motor state, presence of NMS and complications are more prone to worse adherence which is associated with poorer QoL. Therefore, in these patients is necessary to choose appropriate interventions for improving the rate of adherence.

Reference: Morisky DE et al. Predictive Validity of a Medication Adherence Measure in a Patient Setting. J Clin Hyper 2008.

Disclosure: This work was supported by the Grant of the Ministry of Health of the Slovak Republic 2018/32-LFUK-6, VEGA 1/0704/17, and by the research grant from Novartis Slovakia s.r.o.

EPO3173

Electrochemical skin conduction alterations characterize idiopathic Parkinson's disease

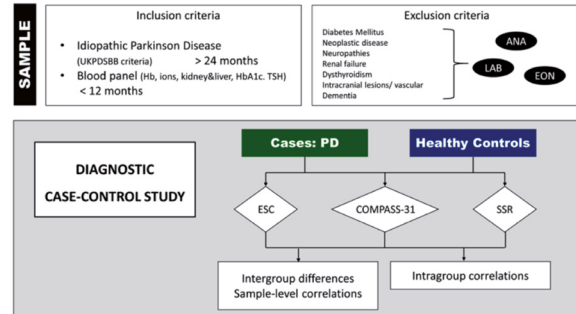
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Background and aims: Autonomic dysfunction is an important feature of idiopathic Parkinson's disease (PD) and determinant of the quality of life. Early on, forewarns a more progressive course.

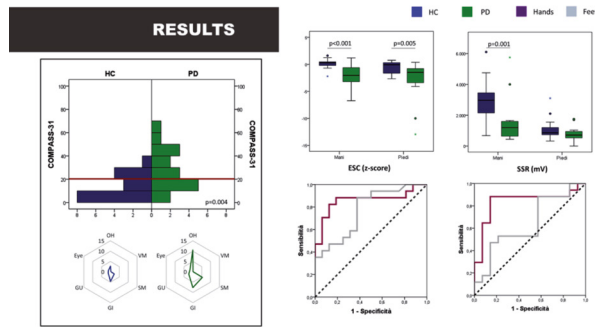
Electrochemical skin conductance (ESC) is a novel technique that rapidly assesses sympathetic function as sudomotor activity and can be used in a routine outpatient visit. We characterized the sympathetic involvement in PD using ESC and compared its accuracy to Sympathetic Skin Response (SSR) and COMPASS-31, a questionnaire on autonomic dysfunction.

Methods: 17 mild-to-moderate PD and 16 healthy control subjects were enrolled. Peripheral or central nervous system disorders were excluded based on history, biochemical panel and examination. Both groups were evaluated with ESC, SSR and COMPASS-31.

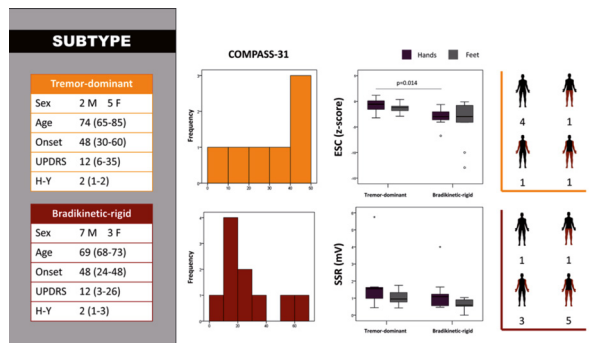


Flowchart of the study

Results: PD patients had more vegetative symptoms on the questionnaire (27.69 vs 12.19 $p=0.004$) and sympathetic dysfunction as observed both on ESC (z-score hands -2.07 vs 0.14 $p<0.001$, feet -1.49 vs -0.07, $p=0.005$) and SSR (amplitude hands 1.494mV vs 3.003mV, $p=0.001$, feet 0.783mV vs 1.121mV, $p=0.2$) with a trend toward higher impairment in the upper extremities (ESC $p=0.060$, SSR $p=0.061$). A moderate-to-elevate agreement between the 2 neurophysiological studies was observed (hands $\rho=-0.711$, feet $R=0.437$). SSR ($p=0.083$) but not ESC showed a lateralization concordant with the dominant motor side. Tremor-dominant PD showed a substantial sparing of sudomotor dysfunction compared to bradikinetin-rigid PD (ESC hands -0.56 vs -3.01).



Main results



Results according to subtype

Conclusion: ESC alterations are a common finding in PD that correlates with a bradikinetic-rigid phenotype, showing a characteristic upper limb prevalence.

Disclosure: Matteo Tagliapietra receives a training grant from Pfizer

EPO3174

Constipation and urinary dysfunction segregate with cognitive impairment in de novo Parkinson’s disease: evidence for a cholinergic subtype from the MoNS-PD cohort

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Background and aims: There is evidence of neurotransmitter dysfunction based nonmotor symptoms (NMS) dominant clinical endophenotypes in Parkinson’s disease (PD) and the cholinergic-type is driven by cognitive impairment (CI). Constipation and urinary dysfunction (UD) also have cholinergic basis. We investigated the co-occurrence of these NMS in cognitively impaired denovo MoNS-PD cohort from Moscow Russia in international collaboration with the UK.

Methods: Data for 132 denovo untreated PD (mean age 70.1±8.4, disease duration 1.8±1.3 yrs, median Hoehn-Yahr stage 2, mean unified PD rating scale (UPDRS II+III, 26.3±12.9) and NMS scale score (59.6±38.7) were analysed along with assessments for CI (MOCA, a battery for mild CI (MCI), constipation (NMSQuestionnaire (NMSQuest) question №5, NMSS question 21) and UD ((NMSQuest question 8+9, NMSS (domain 7)).

Results: Screening with MOCA (cutoff 26) showed CI in 95 (72%) and enriched assessments with MMSE, semantic fluency, cognitive domains of NMSS, NMSQuest and CISI-PD (clinical impression of severity index) revealed CI in 31.3% (MCI 27.6% and dementia 3.7%). Constipation (46.3% in CI versus 25.8% in non-CI PD (p<0.05)) and UD (65.9% versus 42.2% in non CI-PD (p<0.05)) were significantly more prevalent in CI PD.

Conclusion: Our data supports occurrence of CI in denovo PD with higher rates than previously published and notes for the 1st time the clinical presentation of a cholinergic CI dominant endophenotype with associated constipation and urinary dysfunction.

Disclosure: The work is supported by an educational personal fellowship grant to Dr Nataliya Titova from Parkinson’s Disease Nonmotor Group (PDNMG).

EPO3175

Changes in Activities of Daily Living and Motor Function in Patients Switching from Entacapone or Placebo to Opicapone who Ended BIPARK-I Extension on Opicapone 50mg

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients in two large multinational trials (BIPARK-I and II) [1,2].

Methods: Following completion of the double-blind phase of BIPARK-I, placebo (PLC)- and entacapone (ENT)-treated patients switched to OPC in a 1-year open-label extension (OLE) study. This exploratory post-hoc analysis evaluated the impact on Unified Parkinson's Disease Rating Scale (UPDRS) parts II (activities of daily living) and III (motor function) in levodopa-treated PD patients who switched from PLC or ENT to OPC and ended the 1-year OLE on OPC 50mg. Results were analysed using a linear mixed-effect model for repeated measurements with region as factor and baseline as covariate.

Results: In the OLE study, 199 patients switched from PLC (n=99) or ENT (n=100) to OPC (Table 1). Overall, 44/98 (44.9%), 40/100 (40.0%) and 38/98 (38.8%) patients treated with PLC, ENT and OPC 50mg in the double-blind trial who entered the OLE study ended it on OPC 50mg, respectively (Full Analysis Set). PLC switchers experienced improvements in UPDRS-II (-2.7; p=0.0004) and UPDRS-III (-5.1; p<0.0001) scores, whereas, in ENT switchers, the changes were -0.6 (UPDRS-II; p=0.4179) and -1.4 (UPDRS-III; p=0.2404) (Table 2).

Table 1. Baseline characteristics (Safety Set)

Characteristic	DB PLC/OL OPC N=99	DB ENT/OL OPC N=100	DB OPC 50-mg/OL OPC N=98
At double-blind baseline			
Male gender, n (%)	61 (61.6)	64 (64.0)	61 (62.2)
Age, mean years	64.4	63.2	63.3
Disease duration, mean years	8.3	7.6	7.4
Daily OFF-time, mean hours	6.2	6.4	6.2
At OLE baseline			
Daily OFF-time, mean hours	5.1	4.9	4.3
Hoehn & Yahr stage (ON), mean	2.4	2.2	2.3
Presence of dyskinesia ^a – yes, n (%)	39 (39.4)	43 (43.0)	41 (41.8)
Daily levodopa dose, mean mg	661.2	606.0	675.2

^aFrom Unified Parkinson's Disease Rating Scale IV item 32

DB, double-blind; ENT, entacapone; OL, open-label, OLE, open-label extension; OPC, opicapone; PLC, placebo

Table 1

Table 2. Change from OLE baseline to OLE endpoint in UPDRS parts II and III scores in patients who ended the OLE on OPC 50-mg (MMRM; Full Analysis Set)

Characteristic	DB PLC/OL OPC N=44	DB ENT/OL OPC N=40	DB OPC 50-mg/OL OPC N=38
UPDRS-II			
n	42	37	37
LS mean change from baseline	-2.7	-0.6	0.1
SE	0.7388	0.7908	0.7943
95% CI	-4.2, -1.2	-2.2, 0.9	-1.5, 1.7
p-value	0.0004	0.4179	0.8808
UPDRS-III			
n	43	38	38
LS mean change from baseline	-5.1	-1.4	-1.5
SE	1.0836	1.1550	1.1664
95% CI	-7.3, -3.0	-3.6, 0.9	-3.8, 0.8
p-value	<0.0001	0.2404	0.1999

CI, confidence interval; DB, double-blind; ENT, entacapone; LS, least squares; MMRM, mixed-effect model for repeated measurements; OL, open-label, OLE, open-label extension; OPC, opicapone; PLC, placebo; SE, standard error of the least squares mean

Table 2

Conclusion: Patients switching from ENT or PLC to OPC who ended 1-year OLE on OPC 50mg either experienced significantly less disability (PLC) or no worsening (ENT) in UPDRS parts II and III.

1. Ferreira et al., *Lancet Neurol.* 2016;15(2):154-165.
2. Lees et al., *JAMA Neurol.* 2017;74(2):197-206.

Disclosure: Study supported by Bial - Portela & C^a, S.A.

EPO3176

Off-time independently affects to QOL in advanced Parkinson's Disease (APD) patients, but not in non-APD patients; An explanatory analysis of the JAQPAD study.

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Background and aims: The “5- (times oral levodopa tablet intake/day) or 2- (hours of OFF time/day) or 1 (hour/day of troublesome dyskinesia)” criteria identify advanced Parkinson's disease (APD) patients with lower QOL level (EAN 2019). However, which PD symptom is impacting more negatively APD and non-APD patients' QOL is still unknown. The objective of this explanatory analysis is to identify the factors that play key roles in QOL of non-APD and APD patients.

Methods: We used JAQPAD study database which was a cross-sectional survey of large population (n=3,457) assessing the impact of PD on QOL in Japan. APD was defined by 5-2-1 criteria. The multiple regression analyses were separately conducted with non-APD and APD patients using QOL questionnaires PDQ-8 as the main outcome measure with age, gender, H&Y stage, PD duration, employment, off-time duration, troublesome dyskinesia duration, number and frequency of PD medication per day, nursing care level, WOQ-9, SE-ADL, and NMSQ.

Results: Patient's age, PD duration and NMSQ score significantly contributed to both non-APD and APD patients' QOL. Off-time contributed to only APD patients, while work status did just to non-APD patients.

Conclusion: This study shows that factors which worsen patients' QOL may differ between non-APD and APD. With respect to patient's QOL, NMS significantly affected in all stages of PD, while off-time may have a negative impact only in the advanced stage. The results of this study could offer new insights for providing appropriate therapy and improving satisfaction for PD patients.

Disclosure: This work was funded by AbbVie GK. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication. Y. Tsuboi has served as an advisor for AbbVie GK and receives research support from the Japan Agency for Medical Research and Development and Kyowa Kirin. M. Ishido, J. Watanabe and T. Hashimoto are employees of AbbVie GK and may receive stock or stock options. Y. Yoshinaga is a former AbbVie GK employee. K. Kurihara and T. Mishima report no COI. S. Fujioka received research support from Kyowa Kirin and JSPS KAKENHI [15K19501].

EPO3177

Constipation in de novo Parkinson's Disease predicts dementia: a PPMI study.

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Background and aims: Constipation is a common and bothersome multi-factorial non-motor symptom (NMS) of Parkinson's disease (PD) and may occur even in the prodromal phase. Similar to a range of other NMS, such as cognitive impairment and olfactory dysfunction, cholinergic and other non-dopaminergic pathways could be implicated in its development; however, the relationship between constipation and cognitive dysfunction in PD has been poorly investigated so far.

Methods: Data for 396 de novo PD patients was obtained from the Parkinson's Progression Markers Initiative (PPMI) database. SCOPA-AUT (item 5 and 6) was used to assess constipation at baseline. At follow-up (up to 6 years) patients were categorised as having normal cognition or dementia, according to the PPMI protocol. Multivariate Cox survival analyses were carried out including constipation scores at univariate and, as covariates previously validated clinical and non-clinical predictors of cognitive impairment, including age, RBD, CSF Aβ42, UPSIT and 123I-FP-CIT caudate uptake.

Results: During a mean follow-up of 4.9 years, 37 subjects developed dementia. Conversion to dementia was highly associated with constipation (hazard ratio [HR] 1.379; confidence interval [CI] 1.104-1.723; p=0.005). Other predictors of change in cognitive status were: UPSIT (HR 0.921; 95% CI 0.876-0.968; p=0.001), CSF Aβ42 (HR 0.999; 95% CI 0.998-1.000; p=0.021) and mean 123I-FP-CIT caudate uptake (HR 0.264; 95% CI 0.124-0.564; p=0.001).

Table 1. Analysis of the association between baseline constipation (and other clinical features and biomarkers) and conversion to dementia from normal cognitive status in de novo Parkinson's disease patients.

Univariable analysis			Multivariable Analysis		
Variables	HR (95% CI)	p value	Variables	HR (95% CI)	p value
Constipation score	1.510 (1.251-1.822)	<0.001	Constipation score	1.379 (1.104-1.723)	0.005
Age	1.064 (1.024-1.106)	0.001	Age	1.034 (0.986-1.084)	0.169
RBDSQ	1.186 (1.064-1.322)	0.002	RBDSQ	1.058 (0.947-1.181)	0.319
CSF Aβ42	0.999 (0.998-1.000)	0.002	CSF Aβ42	0.999 (0.998-1.000)	0.021
UPSIT	0.899 (0.861-0.939)	<0.001	UPSIT	0.921 (0.876-0.968)	0.001
Mean ¹²³ I-FP-CIT caudate uptake	0.189 (0.100-0.357)	<0.001	Mean ¹²³ I-FP-CIT caudate uptake	0.264 (0.124-0.564)	0.001

Abbreviations: RBDSQ: REM Sleep Behavior Disorder Questionnaire Score; UPSIT: University of Pennsylvania Smell Identification Test; CSF: Cerebrospinal fluid; Aβ42: Amyloid β 1-42

Table

Conclusion: Our findings provide evidence that constipation may be an independent predictor of conversion to dementia in PD, suggesting that constipation and cognitive impairment could share a common pathophysiological substratum.

Disclosure: Nothing to disclose

EPO3178

Acute craniocervical dystonia and hemichorea secondary to a right fronto-insular ischaemic lesion

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Background and aims: Hyperkinetic movement disorders are rare in acute stroke. The cases of acute dystonia described in the literature were mostly associated with posterior circulation strokes involving the basal ganglia

Methods: Case report of craniocervical dystonia and left hemichorea secondary to right fronto-insular ischaemia.

Results: A 72-year-old male, with a history of arterial hypertension and atrial fibrillation, came to the emergency department with left hemiparesis of sudden onset. On the neurological examination he was somnolent but easily arousable, had left sensitive and motor neglect, right-sided ocular deviation, left homonymous hemianopia, left central facial palsy and dysarthria (NIHSS:9). Brain CT-scan showed loss of cortical differentiation in the right middle cerebral artery (MCA) territory (M1, M2, M4 and insula). In the Angio-CT the right M1 segment was occluded. The patient underwent thrombectomy with total recanalization. 16 hours after the procedure, the previous deficits remitted, but he developed orofacial dystonia with blepharospasm, cervical dystonia, and ballistic movements of the left hemibody that in a few hours became choreic.(video) Brain MRI showed restricted diffusion of the right fronto-insular cortex. Treatment with sulpiride 50mg was initiated. After seven days there was an almost complete symptomatic remission

Conclusion: Although movement disorders in the setting of acute stroke are usually associated with basal ganglia ischaemia, there are reports of chorea in insular injury and craniocervical dystonia in lesions of the cerebellum and parietal cortex, but not in fronto-insular lesions. These manifestations may be caused by the disruption of the normal functioning of the cortico-basal circuits.

Disclosure: Nothing to disclose

EPO3179

Asymmetry index as a simple clinical predictor of efficacy and complications of Levodopa therapy of Parkinson's disease

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Background and aims: Levodopa is most effective in Parkinson's disease (PD) treatment, however this prescription is connected with development of complications: motor fluctuations and dyskinesias.

Search for clinical predictors of early complications development is essential for optimization of PD patients' treatment.

Aim: To identify clinical predictors of efficacy and early complications of Levodopa therapy.

Methods: 124 patients at the 3rd stage of PD. All patients were assessed for anamnestic data: age at onset, time of treatment prescription, succession of prescription of various anti-parkinsonic medication groups, rate of dosage increase, dosage by the 3rd stage, and characteristics of non-motor symptoms onset. At the time of inclusion all patients were assessed for: parkinsonism symptoms (MDS-UPDRS), with separation of axial and limb symptoms and assessment of asymmetry index by the 3rd stage.

Results: Asymmetry index was calculated based on the ratio of manifestations severity on left and right sides, the patients were divided into 2 groups: those that retained the manifestations asymmetry, and those that had manifestations severity leveled. The groups were comparable by age of onset and duration of the disease. Patients with manifestations asymmetry featured more severe parkinsonism based on MDS-UPDRS scores. However, despite the severity of clinical symptoms patients with asymmetry reacted better to Levodopa medications and required lower doses (table 1). At the same time, despite lower doses retention of asymmetry was linked to higher risk of therapy complications: motor fluctuations and dyskinesias (fig. 1).

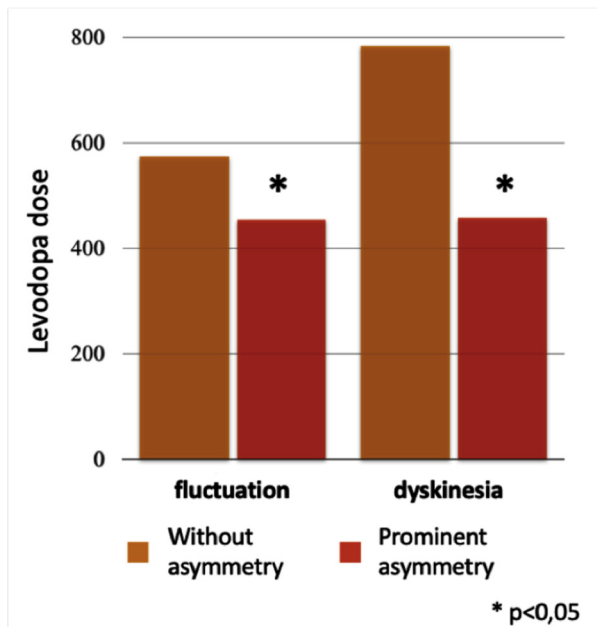


Fig.1 Levodopa dosage when complication occurred

	Low asymmetry (M±σ)	High asymmetry (M±σ)
Age, basic visit	62,4±8,6	60,9±8,7
Age of onset symptoms	53,9±9,9	51,4±10,4
Time of third stages, years	6,0±3,2	6,5±3,6
Levodopa dosage when 3 stage begins, mg	478,6±196,2	492,2±168,4
Levodopa dosage when fluctuation begins, mg	574,2±184,0*	454,6±179,7
Time of fluctuation begins, years	5,4±3,2	5,6±3,9
Levodopa dosage when dyskinesia begins, mg	783,0±416,1*	458,0±317,3
MDS-UPDRS 3 part, score	42,7±18,8	52,4±20,5*
MDS-UPDRS, summary score	88,6±26,3	99,7±29,3*
		* p<0,05

Tabl.1 Comparison of low and high asymmetry groups

Conclusion: Assessment of asymmetry index in PD patients will allow to predict efficacy and risks of complications of Levodopa therapy.

Disclosure: Nothing to disclose

EPO3180

Comparative transcriptomics of sporadic Parkinson’s disease and Tuberculosis gene expression data: a data – driven case for a second hit, outside in copper – phagosome disorder

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Background and aims: The purpose of our study is to detect and compare common, significantly enriched pathways in peripheral blood mononuclears (PBMC) and CNS tissue donated by sporadic Parkinson’s disease (sPD) patients, and compare their transcriptomic profiles with those donated by tuberculosis (TB) patients.

Methods: We performed comparative transcriptomic analyses between gene expression studies published in the GEO Datasets repository, retrieved as queries of sPD and TB each vs healthy controls. Differential gene expression, multiple comparison’s testing and pathway enrichment analyses were performed via the GeneTrail2 software.

Results: Datasets retrieved involved (sPD): 2 PBMC studies, 1 Substantia Nigra (SN) and 1 Dorsal Motor Nucleus of the Vagus (DMNV) study, as well as (TB) 1 PBMC and 1 study with monocyte (Mc) gene expression profiles. Among significantly enriched pathways were the influenza A (IAV) associated “Viral mRNA Translation” and “L13a-mediated translational silencing of Ceruloplasmin expression”, common between DMNV, active Tb Monocytes (aTb Mc), post-treatment TB and both sPD PBMC datasets. Notably, these common pathways were detected across 2 different tuberculosis datasets and 3 different sPD datasets, with a CNS (vagus) dataset among the latter.

Conclusion: Our results support the hypothesis that remnant, postinfectious epigenetic changes on PBMCs inflicted by Mycobacterium Tuberculosis (Mtb) may alter their phenotype, facilitating non-abortive intracellular residency for a subsequent pathogen (i.e. IAV). This pathogen may then be transmissible to the CNS via sites such as the vagal projections, and prime sPD pathogenesis by disrupting metal ion homeostasis in a lifecycle – dependent manner.

Disclosure: Nothing to disclose

EPO3181

PRRT2 mutations are associated with a wide intrafamilial and interfamilial phenotypic variability

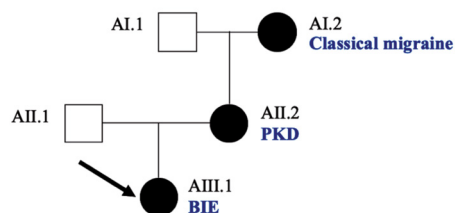
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Background and aims: Mutations in the Proline-Rich Transmembrane Protein 2 (PRRT2) gene are associated with a wide phenotypic spectrum including benign infantile epilepsy (BIE), Paroxysmal Kinesigenic Dyskinesia (PKD), hemiplegic migraine and episodic ataxia. We describe the different clinical syndromes associated with PRRT2 mutations in two families.

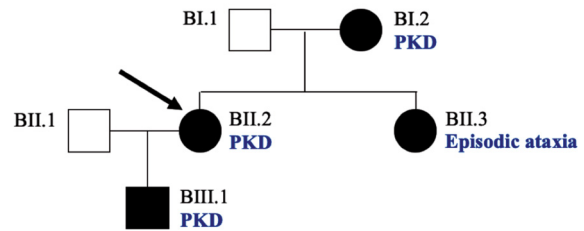
Methods: A neurologist collected clinical history and performed neurological examination. EEG and brain MRI of the probands were performed.

Results: Family A [figure 1]: The PRRT2 R217Pfs*8 heterozygous mutation segregated with neurological disease in the family. AIII.1 presented infantile-onset epilepsy characterized by jaw and limb clonus. The neurological examination between crises and brain MRI were normal. AIII.1 started a therapy with CBZ which induced remission of seizures. Subject AII.2 was affected by PKD presenting dystonic crises triggered by movements and responsive to CBZ. The grandmother AI.2 was diagnosed with classical migraine. Family B [figure 2]: The PRRT2 p.A211Sfs*14 heterozygous mutation segregated with neurological disease in the family. BII.2 experienced episodes of dysphagia and choreoathetosis triggered by fever and physical activity. The EEG showed fronto-temporal slow and sharp-wave alterations on the left hemisphere. The mother BI.2 and the son BIII.1 were affected with the same disorder. The sister BII.3 was affected by episodic ataxia.



Family A ~ R217Pfs*8 (NM_001256443 c.649_650insC)
PKD: Paroxysmal Kinesigenic Dyskinesia; BIE: Benign Infantile Epilepsy.

Family A ~ R217Pfs*8 (NM_001256443 c.649_650insC) PKD: Paroxysmal Kinesigenic Dyskinesia; BIE: Benign Infantile Epilepsy.



Family B ~ p.A211Sfs*14 (NM_001256442 c.629dupC)
PKD: Paroxysmal Kinesigenic Dyskinesia.

Family B ~ p.A211Sfs*14 (NM_001256442 c.629dupC) PKD: Paroxysmal Kinesigenic Dyskinesia.

Conclusion: Considering the intrafamilial variability reported here, all the phenotypic differences among patients having PRRT2 mutations cannot be explained by the different causative mutations only. Many other factors, such as genetic modifiers and early environmental triggers, can be responsible for the wide clinical spectrum associated with PRRT2 mutations.

Disclosure: Nothing to disclose

EPO3182

The main reasons of dissatisfaction with Deep brain stimulation in Parkinson's disease although with great motor improvement

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Background and aims: In the last 33 years, Deep Brain Stimulation (DBS) has been proven by numerous studies to be a successful method of treating Parkinson's disease. Although patients and family members are properly informed before surgery, after surgery we can meet unrealistic expectations. We wanted to test the most often reasons for being unsatisfying with DBS results although we could witness great motor improvements.

Methods: We did interviews about their main problems before DBS and satisfaction with DBS in 200 operating patients before DBS, 3 months, 6 months and 1 year after DBS. In the same time, we compared all their personal data, Functional Independence Measure (FIM) instrument, Unified Parkinson Disease Rating Scale (UPDRS), and quality of life scale (QoL) (PDQ-39) as main outcome instruments.

Results: From 200 interviewed patients, 2 patients (1%) after 3 months, 7 (3.5%) after 6 and 5 (2.5%) after 1 year weren't satisfied with DBS. All had great improvement in motor symptoms (UPDRS III 55%, UPDRS II 35%, FIM 50%, QoL 35%). The reasons of dissatisfaction were changes in family (divorce, breaking the relationship, changing roles), work (needlessness for managing role after years of absenteeism, changing the roles), hard dealing with new good symptoms control and independencies, losing a picture of chronically ill person, and hidden expectations

Conclusion: The main reasons for "patients' unsatisfied results" are personal, professional, family and social maladjustments, and hidden preoperative expectations.

We need for better insight in preoperative expectation and to find good psychoeducation programme to improve overall outcome and quality of life.

Disclosure: Nothing to disclose

EPO3183

Analysis of speech parameters in Parkinson's disease

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Background and aims: The development of computational tools, which analyse the symptoms of Parkinson's disease (PD) and might help to adjust the appropriate treatment, is very desirable.

The objective of this study was to determine whether the acoustic analysis of voice recordings may be useful tool to track the motor symptoms in PD patients during the levodopa treatment with reference to the Unified Parkinson's Disease Rating Scale (UPDRS).

Methods: 27 Polish-language PD patients (mean age: 64.0±10.2 years; mean disease duration: 8.4±3.9 years; mean UPDRS off/on: 33.3±12.8/15.7±10.4) were included to the study. Recordings of "a", "e", "i", "u" and "o" vowels were used for voice analysis. The severity of PD symptoms was evaluated by the UPDRS-III. Voice recordings were carried out simultaneously with the UPDRS-III assessment in off state and in on state after taking of a regular levodopa dose. The acoustic data were expressed using three vectors: noise content, periodicity and non-linearity, which were calculated based on voice parameters. The non-linear and the linear correlations between the vectors of voice parameters analysis and the UPDRS-III score were assessed by, accordingly, the Spearman's rank correlation coefficient (ρ) and the Pearson correlation coefficient (r).

Results: For each vowel we found significant correlations between each vector of voice analysis and the corresponding UHDRS-III score. See table 1.

Table 1. The results of Spearman's rank correlation coefficient (ρ) and the Pearson correlation coefficient (r) tests for specified vectors of voice parameters analysis and UPDRS-III score.

Vowels	Noise content		Periodicity		Non-linearity		All parameters	
	ρ	r	ρ	r	ρ	r	ρ	r
"a"	0.29*	0.22*	0.42*	0.41*	0.50*	0.42*	0.70*	0.63*
"e"	0.39*	0.38*	0.43*	0.52*	0.58*	0.52*	0.68*	0.66*
"i"	0.49*	0.41*	0.54*	0.40*	0.50*	0.46*	0.74*	0.62*
"u"	0.32*	0.32*	0.43*	0.48*	0.63*	0.58*	0.74*	0.62*
"o"	0.45*	0.42*	0.46*	0.42*	0.58*	0.52*	0.69*	0.57*

*p<0.05

Conclusion: The acoustic analysis of voice is convenient and reliable method to follow motor fluctuations in PD patients and it may be helpful to adjust the treatment.

Disclosure: Nothing to disclose

EPO3184

Predictive measures for fall events in patients with cerebellar disorders

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Background and aims: Cerebellar patients are at high risk of recurrent and severe falls. The aim of the study was to identify relevant factors that are associated with fall events retrieved by clinical fall assessment, in-laboratory gait quantification, and off-laboratory mobility measures.

Methods: 93 patients with cerebellar disorders (mean age 57±18 years, 35 females) were included in the study. Each patient underwent a standardized fall risk assessment, an in-laboratory gait measurement on a pressure-sensitive gait mat and an off-laboratory monitoring of physical activity using a wearable inertial sensor. Fall events were prospectively assessed through a 6-month follow-up using fall calendars and telephone interviews. A logistic regression model was used to assess the fall status regarding relevant predictive variables.

Results: Patients showed a characteristic cerebellar gait disorder with broadened base of support and increased gait variability. 51 out of 80 patients reported fall events in the follow-up assessment with 23% occasional, 41% frequent, and 23% severe fallers, which made medical attention necessary. In the regression model, most significant variables were the fall status before initial assessment (OR 4.49, $p=0.02$), the self-assessed fear of falling (OR 1.14, $p=0.048$), and gait variability (OR 4.67, $p<0.01$).

Conclusion: Our results emphasize the association between fall events and increased gait variability in cerebellar patients. Furthermore, previous fall events and self-assessed fear of falling are relevant and easy to obtain markers predictive for falls. In future studies, these findings may be used to develop a fall risk management and prevention programs to reduce falls in cerebellar patients.

Disclosure: Nothing to disclose

EPO3185

Hyperekplexia in patient with GNAO1-related syndromes.

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Background and aims: The phenotypic spectrum of GNAO1-related neurodevelopmental disease includes early onset epileptic encephalopathy and a range of movement disorders with or without epilepsy. In most cases movement disorders fluctuate and are poorly responsive to medical therapy. Hyperekplexia (pronounced startle responses to tactile or acoustic stimuli and hypertonia) is not characteristic symptom of GNAO1-related syndromes. Our objective is to report a case of 7-year-old girl with severe hyperekplexia and GNAO1-related syndrome.

Methods: 7-year-old girl was born to non-consanguineous patients after uncomplicated premature birth. She was referred to our hospital because of epilepsy with rare seizures and psychomotor developmental delay. 1st seizure in our patient appeared in 2nd week of age. startle response started from 3 years of age. Frequency of startle response fluctuated. In some periods the symptoms appeared many times a day, even after a slight acoustic stimulus like the sound of the car outside the window. In neurological examination she showed generalized hypotonia and involuntary movements of the face and limbs more prominent in the upper extremities (chorea). Occasional dystonic features (cervical dystonia) were seen. During hospitalization we observed multiple pronounced startle responses. 1stly we suspect reflex epilepsy. We made electroencephalography, registering the startle response, but we did not find any elektophysiological and clinical correlation.

Results: Whole-exome sequencing revealed de novo mutation in GNAO1 gene (the gain-of-function, c.607G>A). In our patient early onset focal epilepsy, developmental delay, hypotonia and movement disorders coexists with further development of hyperekplexia.

Conclusion: Hyperekplexia can be one of the symptom in GNAO1-related neurodevelopmental disease.

Disclosure: Nothing to disclose

MS and related disorders 6

EPO3186

Relationships between selected parameters of spectral optical coherence tomography and patients' disability in the natural history of multiple sclerosis.

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Background and aims: Spectral optical coherence tomography (SOCT) is a useful marker of neurodegeneration in multiple sclerosis (MS). Most studies conducted to date assess SOCT in patients receiving disease-modifying therapies. The aim of the study was to evaluate relationships between peripapillary retinal nerve fiber layer (pRNFL) thickness, total macular volume (TMV) and disability of treatment-naive patients with clinically isolated syndrome (CIS) and various MS types.

Methods: We enrolled 15 CIS patients and 111 MS patients (Table 1). The history of optic neuritis (ON) was confirmed in the case of: 3 eyes from the CIS patients, 35 eyes from the relapsing-remitting MS patients, 12 eyes from the 2ndary progressive MS patients, 1 eye from the primary progressive patients and 14 eyes from the benign MS patients. All participants underwent SOCT (Copernicus HR-SOCT) with pRNFL thickness and TMV evaluation. Disability of subjects was assessed using the Expanded Disability Status Scale (EDSS).

Investigated subgroups	No. of patients	The median disease duration (years)	The median EDSS score (points)
CIS	15	1	0
Relapsing-remitting MS (RRMS)	65	3	2.0
Secondary progressive MS (SPMS)	14	9.5	4.3
Primary progressive MS (PPMS)	11	4	5.0
Benign MS (BNMS)	21	16	2.0

Table 1. The clinical characteristics of the investigated patients.

Results: In the eyes without ON, a low statistically significant correlation (SSC) between mean pRNFL thickness and mean EDSS score as well as a moderate SSC between mean TMV and mean EDSS score were found

($R=-0.33$, $p<0.0001$ and $R=-0.42$, $p<0.0001$, respectively). A high SSC was found between mean TMV and mean EDSS score in the eyes after ON ($R=-0.51$, $p<0.0001$). There was no SSC between mean pRNFL thickness and mean EDSS score in the eyes after ON ($R=-0.16$; $p=0.207$).

Conclusion: In MS natural history, the mean TMV more closely correlates with patients' disability than the mean pRNFL thickness, especially in eyes after ON.

Disclosure: Nothing to disclose

EPO3187

Rural-urban inequalities in socioeconomic status of Polish multiple sclerosis patients.

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Background and aims: The diagnosis of multiple sclerosis (MS) affects socioeconomic aspects of patients' daily lives during their greatest social and professional activity. Routine assessment of socioeconomic status may be helpful in determining MS type and severity of the disease. There is little data on rural-urban inequalities in socioeconomic status of MS patients. The aim of the study was to determine selected socioeconomic consequences of MS in Poland in relation to the disease type and patients' place of residence.

Methods: A retrospective, observational study to assess a cohort of 375 Polish MS patients (260 women and 115 men). Socio-economic data was collected based on the patients' responses to questions from a questionnaire. Clinical data was obtained from available medical records. The course of MS was classified as relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS).

Results: Those with relapsing-remitting MS had a significantly longer time of occupational activity, higher economic status, higher level of education, better relationships with life partner and were less likely to benefit from disability pension as well as to be a member of MS Society than patients with progressive types of the disease (Table 1). Those living in rural areas had a significantly shorter time of occupational activity, more often experienced a drop in income, received disability pension and were less educated than urban residents (Table 2).

Type of socio-economic parameter	Countryside	Place of residence Small city	Big city	p-value
Educational level N(%)				
Primary	7 (5.9%)	1 (1.0%)	6 (3.8%)	<0.0001
Vocational	42 (35.3%)	20 (20.6%)	23 (14.5%)	
Secondary	42 (35.3%)	44 (45.4%)	56 (35.2%)	
Higher	28 (23.5%)	32 (33.0%)	74 (46.5%)	
Relationship with life partner after MS diagnosis N(%)				
Improvement	17 (17%)	16 (18.2%)	21 (15.7%)	0.6052
Deterioration	19 (19%)	13 (14.8%)	25 (18.7%)	
No change	64 (64%)	59 (67%)	88 (65.6%)	
Economic status N(%)				
High	41 (34.5%)	40 (41.2%)	68 (42.8%)	0.2553
Average	73 (61.3%)	48 (49.5%)	82 (51.6%)	
Low	5 (4.2%)	9 (9.3%)	9 (5.7%)	
Occupational activity N(%)				
Unemployed	60 (50.4%)	43 (44.3%)	61 (38.4%)	0.0592
Employed before MS diagnosis	41 (34.5%)	45 (46.4%)	80 (50.3%)	
Employed after MS diagnosis	6 (5%)	6 (6.2%)	11 (6.9%)	
Never working	12 (10.1%)	3 (3.1%)	7 (4.4%)	
Drop in income due to MS N(%)				
	57 (47.9%)	38 (39.2%)	59 (37.1%)	0.0067
Disability pension N(%)				
	59 (49.6%)	42 (43.3%)	54 (34.0%)	0.0294
Knowledge about existence of MS Society in the place of residence N(%)				
	36 (30.3%)	40 (41.2%)	93 (58.5%)	<0.0001
Membership in the MS Society in the region of residence N(%)				
	16 (13.5%)	23 (23.7%)	27 (17.0%)	0.1383

Table 2. Socio-economic aspects of study cohort according to patients' place of residence.

Type of parameter	Total	RRMS	SPMS	PPMS	p-value
The median duration of the disease (range), years					
	9.0 (0.5-44)	6.0 (0.5-42)	15.0 (1-44)	8.5 (1- 38)	<0.0001
Mean EDSS score (median)					
	3.7 ±1.7 (3.5)	2.6 ±1.0 (2.5)	5.3 ±1.1 (5.0)	5.3 ±1.3 (5.5)	<0.0001
Educational level N(%)					
Primary	14 (3.7%)	8 (57.1%)	4 (28.6%)	2 (14.3%)	<0.0001
Vocational	85 (22.7%)	31 (36.5%)	36 (42.4%)	18 (21.2%)	
Secondary	142 (37.9%)	77 (54.2%)	39 (27.5%)	26 (18.3%)	
Higher	134 (35.7%)	98 (73.1%)	25 (18.7%)	11 (8.2%)	
Relationship with life partner after MS diagnosis					
Improvement	56 (17.4%)	37 (20.4%)	12 (13.0%)	7 (14.3%)	0.0555
Deterioration	59 (18.3%)	24 (13.3%)	25 (27.2%)	10 (20.4%)	
No change	207 (64.3%)	120 (66.3%)	55 (59.8%)	32 (65.3%)	
Economic status					
High	149 (39.7%)	106 (49.5%)	30 (28.8%)	13 (22.8%)	0.0002
Average	203 (54.2%)	99 (46.3%)	66 (63.5%)	38 (66.7%)	
Low	23 (6.1%)	9 (4.2%)	8 (7.7%)	6 (10.5%)	
Occupational activity N(%)					
Unemployed	164 (43.7%)	49 (22.9%)	75 (72.1%)	40 (70.2%)	0.0001
Employed before MS diagnosis	166 (44.3%)	126 (58.9%)	24 (23.1%)	16 (28.1%)	
Employed after MS diagnosis	23 (6.1%)	22 (10.3%)	1 (1.0%)	0 (0%)	
Never working	22 (5.9%)	17 (7.9%)	4 (3.8%)	1 (1.7%)	
Drop in income due to MS					
	154 (41.1%)	53 (24.8%)	70 (67.3%)	31 (54.4%)	0.0001
Disability pension N(%)					
	155 (41.3%)	47 (22.0%)	78 (75.0%)	30 (52.6%)	0.0001
Knowledge about existence of MS Society in the place of residence N(%)					
	169 (45.1%)	85 (39.7%)	59 (56.7%)	25 (43.9%)	0.0336
The membership in the MS Society N (%)					
	66 (17.6%)	23 (11%)	28 (27%)	15 (26%)	0.0003

Table 1. Clinical and socio-economic characteristics of patients according to MS variant.

Conclusion: The disease variant and, to a lesser extent, the place of residence affect the socio-economic consequences of MS.

Disclosure: Nothing to disclose

EPO3188

Effects of pulse methylprednisolon therapy on fatigue during multiple sclerosis relapse

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Background and aims: Fatigue is a common disabling symptom of multiple sclerosis (MS) patients and may be present at all stages of MS. We aimed this study to determine the effects of pulse methylprednisolon (MP) therapy on fatigue during MS relapse.

Methods: All patients received 1000mg intravenous MP for 5 days, followed by tapering dose of oral prednisolone for 3 days. Fatigue severity scale (FSS) scores were measured before, 7 and 21 days after treatment.

Results: 60 patients (42 females) in relapse were included. Mean age was 38.43 ± 11.26 years. Mean baseline FSS score was 4.66 ± 1.57 . 58.3% patients had fatigue ($FSS \geq 4$). Mean baseline Expanded Disability Status Scale (EDSS) score was 4.15 ± 1.62 . Mean age in fatigue patients was 39.43 ± 12.03 and 36.82 ± 9.92 in no fatigue ($FSS < 4$), with no significant difference ($t = -0.870$, $p = 0.387$). Disease duration in fatigue group was 7.22 ± 5.56 years and 7.17 ± 5.53 in no fatigue group, no significant difference ($t = -0.037$, $p = 0.969$). Mean FSS score improved on 7 (3.79 ± 1.56) ($p < 0.001$) and 21 (3.675 ± 1.65) ($p < 0.001$) day after therapy.

Conclusion: Our results proved that pulse MP therapy has an effect on fatigue during MS relapse, with significant improvement occurring early after therapy initiation. This could be caused partially due to the disability improvement but also as a result of underlying inflammatory condition treatment. There was no correlation between fatigue and gender, age and disease duration in our study.

Disclosure: Nothing to disclose

EPO3189

Effectiveness and health care utilization of patients with MS treated with subcutaneous interferon beta-1a (sc IFN beta-1a) according to age: A cohort study using a US claims database

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Background and aims: This study compared by age the proportion of multiple sclerosis (MS) patients free of relapse, and health care utilization, over 2 years (y) after subcutaneous interferon beta-1a (sc IFNβ-1a) initiation.

Methods: This cohort study using MarketScan[®] Databases included patients with MS that initiated sc IFNβ-1a between Jul2010-Dec2015, with at least 6-months history before initiation. Follow-up was until end of study period, insurance, occurrence of event, treatment discontinuation. Hazard ratio (HR) and 95% confidence interval (CI) were used to compare time to first relapse.

Results: Among 5,340 patients included, 14.5% were aged 18-30y, 27.5% 31-40y, 30.5% 41-50y, and 27.5% were 51+y. Relapse-free probability at 2-y ranged from 91.44% in 18-30y to 92.82% in 51+y. Compared to 18-30y, the HR for relapse at 2-y, 95%CI were in 31-40y: 1.00 (0.70, 1.43), 41-50y: 0.79 (0.55, 1.12), 51+y: 0.86 (0.60, 1.24). In all age groups, hospitalization due to MS were ≤ 0.01 and neurology visits 0.2 episodes per patient per month, over 2-y. Mean number of magnetic resonance imaging (MRI) performed per patient per month over 2-y ranged from 0.25 (0.16-0.34) in 18-30y to 0.14 (0.12-0.16) in 51+y and outpatient visits due to MS from 0.68 (0.57-0.78) to 0.75 (0.67-0.82).

Conclusion: The trend observed suggest that relapses rate might decrease with increasing age. Outpatient care related to MS increased with age while MRI performed decreased. These results might suggest that older patients initiating sc IFNβ-1a have more stable MS disease, reflected in lower relapses, and less need to request for MRI than younger patients.

Disclosure: The study was sponsored by Merck KGaA, Darmstadt, Germany.

EPO3190

Late Onset of Neuromyelitis Optica Spectrum Disorders: A retrospective study in Tunisia

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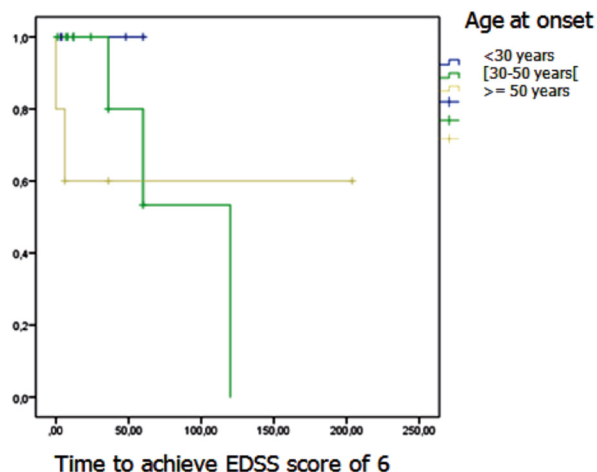
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Background and aims: Although the age of neuromyelitis optica spectrum disorder (NMOSD) onset is usually between 30 and 40 years, there have been rare recent studies regarding late-onset neuromyelitis optica spectrum disorder (LO-NMOSD).

We aimed to investigate the clinical characteristics of and the prognosis for LO-NMOSD in a Tunisian cohort.

Methods: 30 patients, followed for NMOSD in the Neurology Department of the National Institute of Neurology of Tunis Mongi Ben Hmida, were reviewed retrospectively. Clinical, laboratory, and magnetic resonance imaging (MRI) parameters were investigated.

Results: A total of 30 patients were included in this study and were divided into 2 subgroups based on their age of onset: LO-NMOSD (≥ 50 years of age at onset) versus early-onset neuromyelitis optica spectrum disorder (EO-NMOSD) (< 50 years of age at onset). We found that 4 patients (13%) had an age of onset of more than 50 years. Compared with EO-NMOSD, all the patients with LO-NMOSD had a spinal cord involvement at onset (100% vs 35%), were positive for the anti-aquaporin 4 antibodies (AQP4) (100% vs 73%) and were negative for the antinuclear antibodies (100% vs 23%). The brain MRI revealed less lesions in the subgroup with late-onset ($p=0.05$). Furthermore, the patients with LO-NMOSD had more susceptibility to a short term disability with a shorter time to achieve an EDSS score of 6.



Conclusion: Age of onset could be an important predictor of lesion location and clinical course of patients with NMOSD.

Disclosure: Nothing to disclose

EPO3191

Clinical predictors of polypharmacy in a single-center cohort of minimally disabled MS patients

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Background and aims: Background: Multiple Sclerosis (MS) is associated with significant morbidity and disability accrual. Treatment with multiple therapies is frequent and has been consistently linked to higher degrees of disability.

Objective: To evaluate the frequency and clinical/demographic predictors of polypharmacy in a single-center cohort of minimally disabled MS patients.

Methods: Retrospective, observational study identifying consecutive MS patients under disease modifying therapy (DMT) with minimal disability, defined as Kurtzke Expanded Disability Status Scale (EDSS) value ≤ 3 . Clinical and demographic variables were collected from patient files. Logistic regression was performed to test for potential predictors of polypharmacy. We defined polypharmacy as the use of ≥ 5 medications, including DMT.

Results: 294 patients were reviewed and 174 patients fulfilled inclusion criteria: 126 were female (72.4%) with a mean age of 43.5 (± 11.53) years, median duration of disease of 11 (IQR 10) years and median EDSS value of 2 (IQR 1). Polypharmacy was documented in 24.1% ($n=42$) of patients. A median number of drugs of 6 (IQR 2). Increasing age (OR 1.111; CI 95% 1.068-1.157; $p<0,01$), higher disease duration (OR 1.072; CI95% 1.021-1.125; $p<0,01$), higher EDSS value (OR 1.965; CI95% 1.203-3.211; $p<0,01$), presence of comorbidities (OR 21.310; CI95% 8.180-55.514; $p<0,01$) and urinary sphincter impairment (OR 4.200; CI95% 1,427-8,025; $p<0,01$) were significantly associated with higher risk of polypharmacy.

Conclusion: In our cohort of minimally disabled MS patients, polypharmacy was observed in 24.1% of cases. Age, higher degrees of disability, longer duration of disease, comorbidities and urinary symptoms were significantly associated with a higher risk of polypharmacy.

Disclosure: Nothing to disclose

EPO3192

Thalamic fraction volume predicts cognitive performance in a Portuguese cohort of Relapsing-Remitting MS patients

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Background and aims: Previous research has linked MS cognitive impairment to subcortical gray matter damage. We aimed to investigate whether thalamic volume is related to cognitive performance in a Portuguese cohort of RR MS patients.

Methods: Cross-sectional study, consecutive enrollment of RR MS patients, who underwent cranial MRI at our center between July/2018 and July/2019. Clinical examination was performed within 6 months from the MRI scan, testing for processing speed (Symbol Digit Modalities Test [SDMT]) and verbal memory (California Verbal Learning test II [CVLT-II]). Cognitive t-scores correcting for the effects of age, sex, and educational level, were calculated. Volumetric processing was performed with volBrain[®], following standardized MR acquisition protocol including coronal 3D T1-weighted spoiled gradient recall (SPGR). Thalamic fraction volume (TFV) was computed as thalamic volume/normalized whole-brain volume (nWBV) ratio. Linear regression models were created to investigate possible predictors of cognitive performance.

Results: 44 patients studied, 35 of which female (79.5%), median age of 41 years (IQR 15), median disease duration of 7 years (IQR 11) and median EDSS 2.0 (IQR 1.5).

Statistical analysis revealed significant correlations between TFL and CVLT ($r=0.479$; $p=0.001$) and SDMT ($r=0.318$; $p=0.035$) scores. A regression model accounting for the effects of age, disease duration and nWBV, showed that TFV ($p=0.004$) predicted CVLT t-score ($R^2=0.239$; $p=0.031$). A model exploring the relationship between SDMT t-score, age, EDSS and TFV highlighted TFV ($p=0.039$) as an independent predictor of SDMT ($R^2=0.173$; $p=0.05$).

Conclusion: TFV independently predicted cognitive test performance in this cohort, suggesting a specific relationship between cognitive function and thalamic atrophy

Disclosure: Nothing to disclose

EPO3193

Dimethyl Fumarate in Multiple Sclerosis – The experience of a portuguese center

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Background and aims: Dimethyl fumarate (DMF) is an oral drug approved in relapsing remitting multiple sclerosis (RRMS). It has proven efficacy in clinical trials but real-world data is missing. Our aim is to report effectiveness of DMF in a real-world population with RRMS.

Methods: Retrospective study including patients with RRMS treated with DMF. Demographic and clinical data were collected.

Results: A total of 149 patients were included, 72.5% female ($n=108$), with mean age of 36.16 years (SD 9.7) and mean disease duration of 3.77 years (SD 5.29). DMF was the first treatment in 45.6% ($n=68$). The remaining patients were previously treated with 1.53 treatments (SD 0.84), and started DMF mainly for convenience (71.6%, $n=58$) and due to side effects (14.8%, $n=12$). After a mean treatment time of 14.57 months (SD 11.88), ARR significantly decreased (0.66 vs. 0.15, $p<0.01$), without significant EDSS changes (1.5 vs. 1.5, $p=0.61$). In the subgroup of patients with previous treatments, a significant decrease in ARR (0.38 vs. 0.09, $p<0.01$) was observed, also without changes in EDSS. Side effects were reported in 18.1% of patients ($n=27$), with flushing ($n=12$) and gastrointestinal ($n=11$) being the most common. Suspension of DMF was required in 8.7% of patients ($n=13$), due to therapeutic ineffectiveness ($n=5$), side effects ($n=4$) and pregnancy ($n=4$).

Conclusion: In our population, DMF proved to be effective, with reduction in ARR, without progression of disability and reduced frequency of side effects.

Disclosure: Nothing to disclose

EPO3194

Neuromyelitis optica spectrum disorders patient register in Russian Federation

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Background and aims: Neuromyelitis optica spectrum disorder (NMOSD) is a unifying term for demyelinating diseases that mainly involve optic nerve and spinal cord. In 2015 the International Panel for NMO Diagnosis was convened to revise the diagnostic criteria and to define the nomenclature. According to the revised by Wingerchuk et al. diagnostic criteria, NMOSD diagnosis can be established even with unknown AQP4-IgG status. There is no global epidemiological studies, so the definite prevalence of NMOSD is still unknown. Whereas there is no data about NMOSD in Russia, the aim was to create the NMOSD register to describe the demographic and clinical characteristics of Russian patients with NMOSD

Methods: Multi-center retrospective analysis of NMOSD cases from the Russia was conducted. The register for each patient include the following sections: informed consent, demographic data, environmental factors, family history, accompanying illnesses, date of first clinical manifestations, date of diagnosis, AQP-IgG serological status, core clinical characteristics, neuroimaging characteristics, annual relapse rate, severity of disability and pathogenetic therapy.

Results: At the moment 72 patients with NMOSD included in register. Data will be updated and systematized to the April of 2020

Conclusion: The register is a unique data source. Register will help to evaluate the incidence and prevalence of NMOSD in Russia and compare to other countries.

Disclosure: Nothing to disclose

EPO3195

The frequency of myocardial ischemia in female patients with primary progressive multiple sclerosis

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Background and aims: The aim of the present study was to use myocardial perfusion imaging (MPI) in female patients with primary progressive multiple sclerosis (PPMS), in order to evaluate their myocardial status.

Methods: MPIs with ^{99m}Tc tetrofosmin stress – rest single photon emission computer tomography (^{99m}Tc – SPECT), were evaluated in 20 female MS patients with atypical cardiac symptoms and compared with 36 age-matched individuals without known cardiac disease exhibiting similar symptoms (control group). Smoking, hypertension, diabetes mellitus, dyslipidemia, obesity and cardiac heredity were also compared between the 2 groups. MPI was assessed using 17 segment polar map and with a scale of 0 to 4 scoring.

Results: Among the 20 MS patients, 8 (40%) had abnormal MPI in contrast to 7/36 (19.4%) in the control group, demonstrating a trend towards statistical significance ($p=0.09$). In addition, a small trend of statistical significance with SSS and diabetes mellitus was noted in patients with MS ($R=0.303$, $p=0.193$), while in control group the abnormal MPI correlated with obesity and cardiac heredity ($R=0.376$, $p=0.024$ and $R=0.351$, $p=0.036$ respectively).

Conclusion: PPMS female patients may be at increased risk for cardiovascular events, independently of the presence of other cardiological risk factors. Furthermore, MS patients with diabetes mellitus may be at an additional risk and should be screened with MPI in early stages of their disease for appropriate diagnosis and management. Due to the small number of our patients, these results should be considered preliminary and verified with larger number of patients.

Disclosure: Nothing to disclose

EPO3196

Efficacy outcomes in cladribine tablets-treated patients in CLARITY were similar between patients who did vs. did not enter CLARITY extension

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Background and aims: Patients with relapsing-remitting multiple sclerosis treated with cladribine tablets (CT) 10mg (3.5mg/kg cumulative dose over 2 years, CT3.5) in CLARITY were rerandomised 2:1 to receive further CT or placebo in the CLARITY Extension (EXT) study. To address potential confounding and confirm that the patients entering EXT were a representative sample of the patients starting the core study, baseline characteristics and efficacy were compared in patients who entered EXT vs those who did not (non-EXT).

Methods: Baseline characteristics, clinical efficacy, and magnetic resonance imaging (MRI) outcomes over 96 weeks in CLARITY were compared between CT3.5-treated EXT (N=284, randomised set) and non-EXT patients (N=132).

Results: Disease characteristics at CLARITY baseline of both groups were similar; the use of disease-modifying drugs prior to study enrolment was notably higher in the non-EXT than in the EXT patients (Table 1). Clinical and MRI outcomes during CLARITY were similar in both groups, with overlapping confidence intervals and standard deviations (Table 2).

Table 1. Disease characteristics at CLARITY baseline in CT3.5-treated patients

	EXT (N=284)	non-EXT (N=132)
Disease duration, mean (SD)	4.36 (5.11)	5.09 (5.66)
EDSS score, mean (SD)	2.79 (1.24)	2.93 (1.27)
Number of T1 Gd+ lesions, mean (SD)	1.1 (3.1)	0.9 (1.9)
Volume of new/enlarging T2 lesions, mean (SD)	15.73 (17.32)	13.67 (14.53)
Use of disease-modifying drugs before study enrolment, %	21.5	34.1

EDSS, Expanded Disability Status Scale; Gd+, gadolinium enhanced; SD, standard deviation

Table 2. Patient outcomes during 96 weeks of CLARITY among CT3.5-treated patients

	EXT (N=284)	non-EXT (N=132)
Annualised qualifying relapse rate (95% CI)	0.11 (0.08-0.14)	0.17 (0.13-0.24)
6-month confirmed EDSS progression	8.8%	7.6%
Number of new T1 Gd+ lesions, mean (SD)	0.09 (0.32)	0.10 (0.27)
Number of new/enlarging T2 lesions, mean (SD)	0.32 (0.61)	0.45 (0.79)

CI, confidence interval; EDSS, Expanded Disability Status Scale; Gd+, gadolinium enhanced; SD, standard deviation

Conclusion: Baseline characteristics and efficacy outcome data were similar in CT3.5-treated EXT vs non-EXT patients, suggesting that patients who were superior responders to CT3.5 during CLARITY were not preferentially enrolled into CLARITY EXT. These results may assist in the interpretation of durability of efficacy outcomes from CLARITY and CLARITY EXT.

Disclosure: This work was funded by EMD Serono, Inc., a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany.

EPO3197

Dimethyl Fumarate Responsive Combined Central and Peripheral Demyelination

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Background and aims: Combined central and peripheral demyelination (CCPD) is an autoimmune demyelinating disease, affecting both central and peripheral nervous system. The pathogenesis is largely unknown, and treatment options are limited and usually ineffective.

Methods: Here, we present a patient with CCPD, responsive to dimethyl fumarate.

Results: Case report: A 39-year-old man presented with ascending paresthesia, proximal weakness and hyperreflexia in lower extremities, ataxia with positive Romberg sign and urinary incontinence. Multiple T2/FLAIR hyperintense periventricular and deep white matter lesions with contrast enhancement in cranial MRI, 1 in cervical and 3 lesions in thoracic MRI were found. Nerve conduction studies showed conduction block on median, tibial and right ulnar nerves. CSF examination showed 15 lymphocyte, high protein level (87mg/dl), normal IgG index. Oligoclonal band, anti-AQP4, anti-MOG, anti-neurofascin-155 and 186 were found to be negative. Intravenous methylprednisolone for 7 days was given and improved motor deficits. Because areflexia, glove and stocking hypoesthesia were found on follow-up examination on 4th month, with 2 new lesions on brainstem and cerebellum, interferon beta-1b was started. Due to additional neurological findings and new cervical and thoracic lesions with contrast enhancement on 8th month, interferon beta-1b was changed with dimethyl fumarate. He had no new attack or MRI lesion, 24 months after dimethyl fumarate. Control nerve conduction studies were found to be normal, except for mild prolongation of right tibial F-response latency.

Conclusion: Dimethyl fumarate may be considered as a treatment option in patients with antibody-negative CCPD.

Disclosure: Nothing to disclose

EPO3198

The role of serotonin in modulation of Th17-immune response in multiple sclerosis.

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Background and aims: Serotonin may participate in multiple sclerosis (MS) pathogenesis by modulating immune cell activity. The aim of this study was to clarify the effects of serotonin and fluoxetine on Th17-cells which play crucial pathogenic role in MS.

Methods: 30 patients with relapsing–remitting form of MS during clinical remission and 20 healthy controls were examined. All patients were subjected to a standard neurological examination with assessment of the EDSS score. Levels of serotonin in plasma were determined by HPLC. The percentage of Th17-cells was determined by flow cytometry (CD4⁺ CD26⁺ CD161⁺). CD4⁺-T-cells were stimulated with anti-CD3/anti-CD28-antibodies in the absence/presence of serotonin/fluoxetine at concentrations of 10⁻⁴M, 10⁻⁵M and 10⁻⁶M whereafter levels of IL-17, IFN-gamma, GM-CSF and IL-21 in supernatants were assessed by ELISA. Statistical analysis was performed using Prizm 6 software.

Results: The concentration of serotonin in plasma was not different between the groups. The percentages of Th17-cells as well as the production of cytokines were comparable. Serotonin at a concentration of 10⁻⁴M suppressed cytokine production in all groups (p<0.01) without affecting on cell viability and proliferative response. At concentrations of 10⁻⁵M and 10⁻⁶M, serotonin had no effect on cytokine production. Fluoxetine at a concentration of 10⁻⁶M suppressed IL-17, IFN-gamma and GM-CSF production by CD4⁺-T-cells in all groups (p<0.01) without affecting on cell viability and proliferative response. At concentrations of 10⁻⁴M and 10⁻⁵M fluoxetine suppressed cytokine production (p<0.001), but reduced cell viability and proliferative responses (p<0.01).

Conclusion: These data suggest anti-inflammatory effect of serotonin on Th17-cells in MS.

Disclosure: The reported study was funded by RFBR according to the research project № 18-315-00436.

EPO3199

A Systematic Literature Review of Brain Volume Loss and Disability or Cognition Outcomes in Patients With Relapsing-Remitting Multiple Sclerosis

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Background and aims: Brain volume loss (BVL) develops during the course of multiple sclerosis, in both white and grey matter (GM), reflecting irreversible tissue damage. BVL, particularly GM, may be indicative of disease progression in relapsing-remitting multiple sclerosis. This systematic literature review (SLR) investigated the homogeneity of publications reporting the relationship between BVL and disability or cognition outcomes.

Methods: An SLR was conducted in Pubmed[®], Web of Science[®], and SCOPUS[®] from 01/01/1990 – 01/06/2019 for publications reporting statistical relationships between brain volume measures (total, GM, thalamic, or select others) and disability or cognition measures.

Results: A total of 2,087 records were screened; 137 met all criteria. Sample sizes ranged from 8–3,635 patients with a median of 58 (mean (standard deviation [SD]): 220.5 (544.9)). Cross-sectional studies were most common (36%, n=51), followed by prospective cohort (24%, n=33), clinical trial post-hoc (15%, n=21), and retrospective cohort (12%, n=17). Nearly half were single-centre studies (47%, n=65), 39% (n= 53) were multi-centre, and 13% (n=18) not specified. Most studies were conducted in Europe (58%, n=80). Normalized GM was the most commonly reported measure (38%, n=52) then total brain volume/percentage brain volume change (24%, n=33), and thalamic volume (14%, n=19). Expanded Disability Status Scale score was reported in 80% (n=110), with cognition endpoints less frequently reported (n=47, 34.3%). There were methodologic differences in the assessment of the statistical relationships.

Conclusion: There was significant methodologic heterogeneity in the studies reporting a relationship between BVL measures and disability or cognition outcomes, including a wide range of BVL measures and disability and cognition instruments.

Disclosure: DB, PJ, DA, PC: Genesis Research – employees DS & TT: Bristol-Myers Squibb – employees.

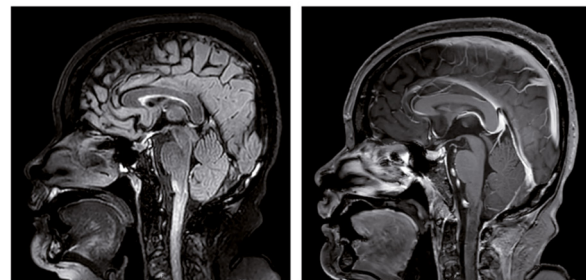
EPO3200

Cannabis: a successful treatment for painful tonic spasms in neuromyelitis optica spectrum disorder

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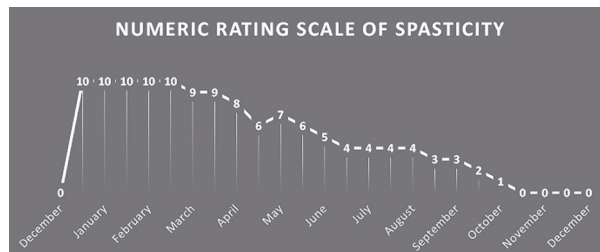
Background and aims: Painful tonic spasms (PTSs) occur in ¼th of neuromyelitis optica spectrum disorder (NMOSD) patients. Carbamazepine is the most effective medication despite the risk of severe adverse cutaneous reactions. We describe the 1st case of PTSs in NMOSD successfully treated with adjunctive cannabis extract.

Methods: A 39-year-old female with longitudinally extensive transverse myelitis was diagnosed with aquaporin-4 IgG-positive NMOSD 10 months ago. 2 weeks prior to visiting, she experienced excruciating PTSs of all extremities, neck, and face every 3-5 minutes (accumulating to 100-200 times/day), lasting 50 seconds each. A spinal MRI revealed unchanged hyperintense signals on T2-weighted images without enhancement, rendering a relapse less likely. Having had carbamazepine-induced Steven-Johnson syndrome, she was treated with baclofen 50mg/day, clonazepam 5mg/day, pregabalin 450mg/day, and tizanidine 4mg/day. However, PTSs were not improved.

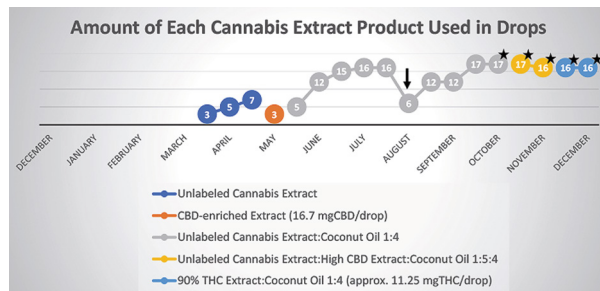


Sagittal MRI study of the brain and spinal cord demonstrated long segment of hyperintense signals from cervicomedullary junction to C3 level on T2-FLAIR (left) without definite enhancement on gadolinium-enhanced T1-weighted imaging (right).

Results: The patient took unauthorised cannabis extract sublingually for adjunctive treatment. The dose was titrated to the optimum of THC 60mg/dose 3 times daily, together with the previous anti-spastic medications. The symptom gradually subsided to 2 mild attacks a day. Within 6 months, self-reported numeric rating scale of spasticity improved from 10 to 0. Notably, the cannabis extract was discontinued twice during hospitalisation leading to PTSs recurrence within 2 days, thus the treatment was resumed.



Numeric rating scale of spasticity (0-10) reported retrospectively by the patient. The score was 0 for no spasticity and 10 for the worst possible spasticity.



Amount of each cannabis extract product used in drops. The arrow indicated when cannabis was discontinued during hospitalisation. Starting from late October, the patient received three times daily dosing, indicated by a star.

Conclusion: PTs were successfully treated with cannabis in an NMOsD patient. CB1 receptor agonists, including THC, had been proven to ameliorate spasticity in experimental autoimmune encephalomyelitis model. Besides the approval for spasticity in multiple sclerosis, cannabis is a potential treatment option for PTs in carbamazepine-allergic NMOsD patients.

Disclosure: Nothing to disclose

EPO3201

Evaluation of Falls and Fall Risk Factors in Multiple Sclerosis Patients

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Background and aims: Falls in people with multiple sclerosis (MS) play an important role on fulfilling the daily activities. In literature it has been reported that more than 50% of people with MS fall in any 6 months period, especially in the 1s using walking aid. The present study was done to explore risk factors associated with falls in this population.

Methods: 50 RRMS patients and 30 healthy controls were included. Falls in the past year were recorded and prospectively monitored for 6 months. Extended Disability Status Scale (EDSS), Timed 25 - Foot Walking Test and MS Walking Scale-12 (MSWS) were used to determine physiological factors. Participants performed Static and dynamic balance test on the Korebalance computerized posturography system. Beck Depression Scale, Montreal Cognitive Assessment for cognitive factors and Falls Efficacy Scale- International (FES-I) for the fear of falling were used to evaluate neuropsychological factors.

Results: A total of 48 falls from 24 patients (48%) and 32 falls in 6 months period from 17 patients (34%) were recorded. Fall rates were similar between MS patients and healthy controls. FES-I scores were significantly higher and static balance scores were significantly lower in MS patients. In MS group, falls were related with higher MSWS and FES-I scores.

Conclusion: Fear of falling is an important factor related with falls in MS patients even in the 1s without aid. Patient rated measure of walking ability test MSWS is an effective tool to estimate fall risk and can be used in clinical practice.

Disclosure: Nothing to disclose

EPO3202

Neuropathic Pain and The Quality of Life in Multiple Sclerosis

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Background and aims: Pain is an unpleasant emotional sensation originating from a particular area of the body related to or not due to tissue destruction about a person's past experiences. There 2 types of pain: nociceptive and neuropathic pain. Neuropathic pain (NP) is 1 of the common complaints affecting the quality of life, and the prevalence of NP is almost 30% among patients with multiple sclerosis (MS). In this study, we aimed to evaluate the frequency and severity of NP in MS patients and the effect of NP over the quality of life.

Methods: We enrolled the patients with MS who were fulfilling the 2017 McDonald diagnostic criteria. We collected demographic and clinical data. The frequency and severity of NP were assessed with Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and Douleur Neuropathique 4 questions (DN4) and we used SF-36 to evaluate the efficacy of NP over the quality of life.

Results: We enrolled 100 patients, 68 of them were female. The mean age was 37.12±14.08 years, the mean disease duration was 7.08 ±5.87 years, and the mean EDSS was 2.1±1.2. The evaluation of the LANSS and DN4 questionnaires showed that 40.2% of MS patients had NP, and SF-36 showed that quality of life impaired in 35.7% of the patients due to the NP.

Conclusion: NP is common among patients with MS. NP may affect the quality of life. MS patients should be evaluated for NP.

Disclosure: Nothing to disclose

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EPO3203

MOG IgG Related Disorders: Different Clinical Presentations

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Background and aims: Myelin Oligodendrocyte Glycoprotein (MOG) is the type1 integral membrane protein located on the extracellular surface of oligodendrocytes and the outermost side of the myelin sheath. Only available in CNS. There are many different clinical presentations associated with anti-MOG antibodies. We found it worthy to present patients with anti-MOG antibody positivity with different symptoms.

Methods: Anti-MOG antibody positivity was detected in 12 patients (9F/3M). The ages of the patients were between 19-54.

Results: 20-year-old and 25-year-old female patients presented with unilateral optic neuritis and also had oligoclonal band type 2 positive and MS lesions. The 1st patient was started with fingolimod and the other patient with glatiramer acetate. Patients with bilateral optic neuritis had no demyelinating lesion. Azathiopurine was started in 2 patients. 1 patient who had unilateral optic neuritis had an attack of optic neuritis in the other eye for 2 months and the other patient 4 months later and started on azathiopurine. The patient presented with hemihypoesthesia and had atypical brain lesions and is still being followed without medication. Rituximab was initiated in 2 patients with NMOSD, 2 patients with transverse myelitis and patient with bilateral optic neuritis. No new attack was observed in the patients who received preventive treatment and were followed up without medication.

Conclusion: As seen in our patients with anti-MOG antibody positivity, these patients may present with different clinical presentations. therefore, anti-MOG antibody positivity alone does not appear to be a definitive diagnostic parameter. It supports the presence of autoimmunity. Treatment decision should be made according to the patient.

Disclosure: Nothing to disclose

EPO3204

The Usability of Body Fluid Biomarkers in Multiple Sclerosis Clinical Practice Guideline Recommendations: First Results from a Systematic Review.

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Background and aims: The last decades have been marked by the development of Disease-Modifying Therapy (DMT) and the search for Body Fluid Biomarkers (BFBs) for patients with Multiple Sclerosis (MS). More than 80 BFBs were studied, of which more than 30 were validated. Clinical Practice Guidelines (CPGs) help integrate current best evidence in making decisions about the care of individual MS patients. We aimed to know how BFBs are used in CPG recommendations to guide decisions in the management of patients with MS, including prevention, diagnosis, and therapy.

Methods: We performed a systematic and extensive literature search without language restrictions of guidelines used in MS since 1993, when the first DMT was marketed, up to March 15, 2019. The following databases were searched: MedLine, EMBASE, LILACS, PEDro, NGCH, GIN, and Google Scholar.

Results: We identified 404 records, 76 CPGs were included for the review. The only 24 CPGs had at least one recommendation suggesting the use of Body Fluid Testing (BFT). Cerebrospinal fluid oligoclonal IgG bands analyses were used in 7 CPGs for MS diagnosis and prognosis, JC virus antibody and DNA - in 5 CPGs for differential diagnosis and therapeutic decision-making, neutralizing antibodies to Interferon-beta or Natalizumab - in 7 CPGs for DMT efficacy monitoring, myelin basic protein - in 1 CPG. Other CPGs recommended using routine BFT to monitor overall MS patients' health.

Conclusion: There remain unmet needs for BFBs in CPG recommendations for the diagnosis and treatment of patients with MS despite the number of experimental, validated and clinically useful MS BFBs.

Disclosure: Nothing to disclose

EPO3205

Menopause in multiple sclerosis patients

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Background: There is increasing evidence that sex hormonal variations and age have an influence in the course of the disease. MS patients are getting older and MS and menopausal symptoms could be overlapped, therefore is a great need to understand the impact of menopause in MS patients.

Aim: To study menopausal and MS symptoms in MS women and their influence in the disease evolution.

Methods: Retrospective study. MS women with perimenopause and menopause (no more than 5 years) were recruited from our center. We collected demographic information, menarche, DMTs, quality of life, MS and menopause symptoms.

Results: 30 patients were included, 15 in perimenopause (mean age 48) and 15 in menopause (mean age 49). 40% of all patients have a decrease of quality of life and increase of depressive symptoms, 50% reported worsening of the disease comparing with the non menopause period.

Most frequent symptoms in menopause MS patients were: Hot flashes (85%), vaginal dryness (70%), weight increase (60%) and adverse mood (60%). 85% of patients have no changes in fatigue, pain, spasticity and urinary symptoms. Differences in number of children and smoking status have no correlation with an increase of menopausal symptoms

Conclusion: As stated above there is no increase in typical MS symptoms in these patients, however menopausal symptoms are present in most of them, leading to report a worsening in the disease and their well-being. Therefore, it is important to recognize the menopausal symptoms and to treat them to improve the quality of life and well being of our patients

Disclosure: Nothing to disclose

EPO3206

The Evaluation of Anxiety in Multiple Sclerosis by a Useful Method: State-Trait Anxiety Inventory

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Background and aims: The present study aims to examine psychometric properties of the Spielberger State-Trait Anxiety Inventory (STAI-1 and STAI-2, respectively) in a Multiple Sclerosis (MS) population and to assess the anxiety level which might be related to cognitive decline and depression.

Methods: A prospective study evaluated 44 patients with relapsing remitting MS and 47 age-, sex-, and education-matched healthy adults. All MS patients and HCs completed the STAI-Y-1 and the STAI-Y-2. To evaluate global cognitive status, MS patients underwent the Brief International Cognitive Assessment for MS (BICAMS). The BICAMS includes the following 3 tasks: the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT2), and the revised Brief Visuospatial Memory Test (BVMTR). All patients also completed the Fatigue Severity Scale (FSS) to assess subjective fatigue; the Beck Depression Inventory-II (BDI-II) to assess depressive symptoms. Moreover, daily living was evaluated by a MS quality of life (MSQoL).

Results: When compared to the control group, the high level of state anxiety in MS patients occurred in 37.1%, and the high level of trait anxiety in our MS sample was found in 48.3%. we found that total score of both scales correlated weakly or moderately with scores of the cognitive battery, depression, and the fatigue scale.

Conclusion: Our data showed that the STAI-1 and the STAI-2 are useful methods to measure the severity of anxiety in MS patients in clinical practice.

Disclosure: Nothing to disclose

EPO3207

Safety of Ixazomib Targeting Plasma Cells in Multiple Sclerosis

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Background and aims: Ixazomib, a proteasome inhibitor, is licensed for the treatment of multiple myeloma, a malignant plasma cell disorder. In MS, the production of antibodies by plasma cells and B cells play a critical role in its pathogenesis and disease progression.

The purpose of this study is to investigate the safety of ixazomib and if it can reduce or clear oligoclonal bands (OCBs) from the cerebrospinal fluid in MS.

The Phase Ia/Ib trial using Ixazomib will be carried out in relapsing remitting multiple sclerosis, primary progressive multiple sclerosis and secondary progressive multiple sclerosis. The primary outcome will be safety, followed by effect on cerebrospinal fluid OCBs.

Methods: It is a double-blind, randomised and placebo controlled trial with 76 participant (50 on active drug; 26 on placebo) for up to 24 months. 1 cohort of patients (n=38) will have relapsing MS and the other cohort (n=38) will have progressive MS.

Measures of adverse events will be compared between active and placebo. The efficacy will be measured with the proportion of OCB IgG compared between active and placebo. The outcome will be monitored with sequential MRI and EDSS comparing the treatment group to placebo.

Results: The trial is due to commence in early 2020.

Conclusion: The trial will be targeting a novel disease pathway in MS; that of long lived plasma cells. There is not any convincing evidence yet that currently DMT eliminate intrathecal OCB. If successful it would be the first drug of its kind to be used in MS.

Disclosure: Nothing to disclose

EPO3208

Reliability of the manual muscle test of the Neurostatus EDSS

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Background and aims: This study evaluated the reliability of three manual muscle tests of the Neurostatus EDSS. The influence of fatigue and spasticity on reliability was explored.

Methods: This was a single-center, prospective cross-sectional and longitudinal study. The inter- and intra-rater reliability was evaluated using a 1-way random effects ANOVA model. The influence of fatigue and spasticity was evaluated exploratively by using plots and in subgroups using a linear mixed effects model (LME) for each test separately. We used the Modified Tardieu Scale (MTS) for the evaluation of spasticity and a numeric rating scale for the evaluation of fatigue.

Results: The interrater reliability is mainly moderate. The Intra-class Correlation Coefficient (ICC) of the overall interrater reliability is 0.52 [0.30, 0.72]. The ICC for subgroups with high and low spasticity is higher for low spasticity than for high spasticity. However, the statistical evidence is not strong enough to conclude that there is a difference between these subgroups.

The pooled overall value for the intra-rater reliability is ICC=0.74 [0.59, 0.83]. Plots of the overall ratings of the muscle test against the sum scores of the MTS as well as the LME analysis do not indicate an influence of spasticity on the intra-tester reliability.

We did not find an influence of fatigue on the test results.

Conclusion: The study demonstrated that the evaluated three muscle tests of the neurostatus EDSS can only be a reliable outcome tool when it is applied by 1 tester. Fatigue didn't influence the reliability. Spasticity might influence intertester reliability and needs further evaluation.

Disclosure: This study received a grant from the Swiss MS-Society and was financially supported by the specialized groupe physiotherapy and MS of physioswiss and the Institute for Physiotherapy Research

EPO3209

One-Year Interim Analysis of Health-Related Quality of Life in RRMS Patients Treated With Alemtuzumab in a Real-world Clinical Setting (LemQoL Study)

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Background and aims: The real-world LemQoL study utilises patient-reported outcomes (PROs) to evaluate health-related aspects of life quality (HRQL) in alemtuzumab-treated RRMS patients in Europe and Israel. Here we report Year 1 (Y1) LemQoL interim results.

Methods: LemQoL is an ongoing 36-month, prospective, open-label, observational, multicentre study. PROs assessed include (lower scores indicate improvement) MS Impact Scale-29 (MSIS-29; scale 0–100), MSIS-29 bladder/bowel dysfunction (scale 0–5), Modified Fatigue Impact Scale-5 (MFIS-5; scale 0–20), Patient-Determined Disease Steps (PDDS; scale 0–8), and Hospital Anxiety/Depression Scale (HADS; scale 0–21). Symbol Digit Modalities Test (SDMT; scale 0–1, higher score indicates improvement) and Health-Related Productivity Questionnaire-MS V2 were also evaluated.

Results: As of August 2019, enrolment was complete (N=319) and Y1 data were evaluable in 275 patients. Mean MSIS-29 physical and psychological impact scores improved at Y1 from baseline (mean change [95% CI], -6.5 [-9.1, -3.9] and -6.7 [-9.8, -3.6], respectively, coprimary endpoints). Mean scores for other PROs improved at Y1 (mean change [95% CI] from baseline, MFIS-5: -1.5 [-2.0, -1.0]; HADS Anxiety: -0.8 [-1.3, -0.3]; PDDS: -0.3 [-0.5, -0.1]). Scores were stable for MSIS-29 bladder/bowel dysfunction (-0.1 [-0.2, 0.04]), SDMT (0 [-0.01, 0.01]), and HADS Depression (-0.3 [-0.7, 0.1]). Mean weekly lost employment productivity hours decreased at Y1 (-3.1 [-5.6, -0.6]). Incidence of adverse events was 85.9%, with serious adverse events reported in 13.5% of patients.

Conclusion: These interim real-world data demonstrate that productivity and major HRQL outcomes improved or were stable in alemtuzumab-treated RRMS patients. Alemtuzumab safety through Y1 was generally consistent with the pivotal studies.

Disclosure: STUDY SUPPORT: Sanofi

EPO3210

Comparative transcriptomics of multiple sclerosis vs. Viral infections: common roles for nuclear transport, neuroactive peptide signalling and the spliceosome

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Background and aims: There are accumulating evidence in the literature that viral infections provide an environmental trigger for the onset of multiple sclerosis (MS) in genetically susceptible individuals. The purpose of this study is to discover common pathways between multiple sclerosis and viral infections, on a genomic and functional level.

Methods: The Gene Expression Omnibus (GEO) database was inquired using a query containing the keywords “Virus”, “Multiple Sclerosis”, “Infection”. Included studies involved ex vivo samples of peripheral blood mononuclear cells (PBMCs) following a case – control design. Finally, in order to create a transfection model, a study from active demyelinating plaques was used for comparative genomics.

Results: The initial search retrieved 35 studies. Applying the predetermined inclusion criteria, 2 MS vs Healthy Controls (HC) studies and 3 studies of viral infection vs. HC (Dengue, SARS Coronavirus and Rotavirus infections). Multiple common, differentially expressed genes (DEGs) and associated significantly enriched pathways emerged between the MS vs viral infection subgroups. The “Epstein Barr infection” pathway was salient among MS-related viral infection pathways (False Discovery Rate (FDR) <0.05). Furthermore, comparative transcriptomics revealed 4 common gene signatures of 80 to 150 genes, associated with nuclear transport, neuroactive peptide binding and the spliceosome (FDR<0.0001).

	Multiple sclerosis vs. HC (II)	SARS Coronavirus vs HC	Acute Rotavirus infection vs. HC	Multiple Sclerosis vs. HC
KEGG Pathways				
Spliceosome	3.36e-8	1.69e-10	0.0435	0.0287
Neuroactive ligand-receptor interaction	7.55e-6	1.06e-7	0.0095	6.25e-6
Biological Process				
RNA export from nucleus(6)	0.0017	2.28e-4	0.0167	0.0171
nuclear export(8)	2.22e-5	0.0140	9.30e-4	0.0122

Conclusion: Ours is the first study to directly compare viral infection mechanisms with the molecular pathophysiology of MS in a transcriptomic level. Our results indicate a “response to infection” phenotype in MS PBMCs, associated with alternative splicing and disruptions of transcriptional homeostasis.

Disclosure: Nothing to disclose

EPO3211

Biomarkers of neurodegeneration predict early disability in Multiple Sclerosis patients.

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Background and aims: Neurodegeneration in Multiple Sclerosis (MS) occurs from early disease stages. Several molecules have been investigated as suitable biomarkers of axonal damage in MS, but none is routinely used in clinical practice. Moreover, Tau Protein and beta-amyloid protein (Abeta) are markers currently used in other neurodegenerative diseases. The aim of our study is to evaluate if cerebrospinal fluid (CSF) Tau protein and Abeta protein, at the diagnosis could predict early MS disability.

Methods: CSF Abeta and Tau levels were determined with commercial enzyme-linked immunosorbent assay in newly diagnosed MS patients. We collected demographic, clinical data. We calculated disability outcomes at last follow-up (minimum 1year): MS severity score (MSSS) and MSSS age-related (ARMSS) to correct increase of disability related to age.

Results: We enrolled 55 patients, 34 with a relapsing-remitting disease course. Mean follow-up was 2years (SD±1.5y). Mean value of Tau and Abeta were respectively 128.5±69pg/ml and 557.7±258.6pg/ml. Patients with higher CSF Tau levels at diagnosis developed higher disability evaluated with ARMSS (R=0.4, p=0.002) and MSSS (R=0.4, p=0.06). A weak correlation was found with lower CSF Abeta and higher MSSS (R=-0.2, p=0.2). Lower Abeta was found in patients with spinal lesions dissemination (p=0.07).

Conclusion: Our study established a prognostic role of neurodegenerative CSF markers, in particular Tau protein, in predicting early disability in MS patients independently from age. Longer follow-up and larger population are needed to confirm our preliminary data.

Disclosure: Nothing to disclose

EPO3212

Search of biomarkers of cognitive impairment in Multiple Sclerosis at diagnosis: preliminary findings

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Background and aims: Cognitive impairment (CI) is a frequent and disabling symptom in Multiple Sclerosis (MS). Axonal damage may contribute in CI development from early stages. Nevertheless no biomarkers are at the moment available to track CI in MS patients. To evaluate the correlation of cerebrospinal fluid (CSF) axonal biomarkers, in particular: light-chain neurofilaments (NFL), Tau and Beta amyloid protein (Abeta) in MS patients with CI at the diagnosis.

Methods: We enrolled 30 newly-diagnosed MS patients and evaluated cognition using Brief International Cognitive Assessment for MS (BICAMS) battery. NFL, Abeta and Tau levels were determined with commercial enzyme-linked immunosorbent assay.

Results: Of our patients (mean age of 38.2±10.8 years), twelve (40%) had CI defined as a T-score below 35 (equivalent to z-score below -1,5) in at least one test of BICAMS. Patients with CI had greater neurodegeneration marked with: higher mean levels of NFL (1,238.7±706.9 vs 1,154.3±943.8pg/ml, p=0.3), higher mean levels of Tau (176.5±70.3 vs 133.9±76.9pg/ml, p=0.1), lower mean levels of Abeta (567.7±431.7 vs 586.6±211.6pg/ml, p=0.1). Patients with impairment in verbal memory showed higher Tau levels (R -0.3, p=0.07).

Conclusion: CI has important burden on quality of life of MS patients and should be looked for even at diagnosis. BICAMS easily detects CI in MS patients. Few data regarding NFL, Abeta and CI in MS, are reported in literature, but our preliminary results are consistent with a correlation. Axonal damage biomarkers seems to reflect cognition from early stages and Tau, at the moment, seems the more informative.

Disclosure: Nothing to disclose

EPO3213

Lymphocyte Levels Across Age Groups in Teriflunomide-treated Patients: Pooled Analysis from the Clinical Trials and the Real-World TERI-PRO Study

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Background and aims: Teriflunomide is a once-daily oral immunomodulator approved for treating relapsing MS and relapsing-remitting MS, depending on the local label. Efficacy and safety of teriflunomide were established in phase 3 trials of patients with relapsing forms of MS (TEMPO [NCT00134563], TOWER [NCT00751881], TENERE [NCT00883337]) and clinically isolated syndrome (TOPIC [NCT00622700]). Treatment satisfaction increased after switch to teriflunomide in the real-world TERI-PRO study (NCT01895335). Here, we assess lymphocyte levels in teriflunomide-treated patients stratified by age.

Methods: Patients were stratified by age at study entry (pooled TEMPO/TOWER/TENERE/TOPIC and TERI-PRO: ≤ 25 , >25 to ≤ 35 , >35 to ≤ 45 , >45 years; TERI-PRO included an additional age group of >55 years). Lymphocyte levels (baseline and Year 1) and safety outcomes were assessed. Lower limit of normal (LLN) was defined as $<1.0 \times 10^9$ cells/L.

Results: In phase 3 and TERI-PRO patients, $\geq 92\%$ and $\geq 90\%$, respectively, maintained lymphocyte levels above LLN at Year 1 after teriflunomide, regardless of age group. Across age groups, mean lymphocyte levels were $\geq 1.63 \times 10^9$ cells/L and $\geq 1.66 \times 10^9$ cells/L at year 1 in phase 3 and TERI-PRO teriflunomide-treated patients, respectively. In phase 3 teriflunomide-treated patients, safety was similar across age groups; however, TERI-PRO patients aged >35 years had higher incidences of infections than those ≤ 35 years ($\geq 29\%$ vs $\leq 24\%$).

Conclusion: Teriflunomide did not lower lymphocyte counts below LLN in most phase 3 and TERI-PRO patients over 1 year, regardless of patient age at study entry. The safety profile with teriflunomide was similar across age groups in phase 3 patients, but age-related increases in infections were observed in TERI-PRO patients.

Disclosure: STUDY SUPPORT: Sanofi

EPO3214

The role of optical coherence tomography in differential diagnosis of multiple sclerosis and CNS involvement in autoimmune connective tissue diseases

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Background and aims: The purpose of this study was to assess whether application of optical coherence tomography (OCT) measurements can provide a useful biomarker for distinguishing multiple sclerosis (MS) from central nervous system (CNS) involvement in autoimmune connective tissue diseases (CTDs).

Methods: Spectral domain OCT examination was performed in 59 patients with MS, 30 patients with CNS involvement in CTD, and 32 healthy controls. Thickness of RNFL, ganglion cell complex (GCC), ganglion cell layer-inner plexiform layer (GCIPL), and volume of the macula were analyzed in non-optic neuritis eyes and compared between groups.

Results: Patients with MS had significantly smaller thickness of macular RNFL ($p=0.0146$) and superior optic disc RNFL ($p=0.0202$), as well as GCC and GCIPL ($p<0.001$ and $p=0.0002$, respectively) among the examined groups. MS group was also characterized by a significantly smaller macular volume ($p=0.0149$). The post-hoc analysis with multiple comparisons of mean ranks test revealed significant differences in all abovementioned parameters only between MS and healthy controls group (2-sided p-values with a Bonferroni adjustment: 0.0163 and 0.0176, 0.0006, 0.0001, 0.0129 respectively). The comparison of OCT results between patients with MS and CTDs group revealed no statistically significant difference.

Conclusion: A prominent retinal thinning, demonstrated with OCT, may constitute a useful biomarker of MS in general population. However, among individuals with a confirmed CNS involvement, the use of OCT is not a sufficient tool to discriminate between MS and CNS involvement in autoimmune CTD.

Disclosure: Nothing to disclose

EPO3215

A 164 second smartphone based film successfully conveys the importance of early intervention in MS

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Background and aims: Early treatment in MS aims to stop later disability and often needs to be considered in the absence of symptoms. This preventative approach is a complex concept to convey to a naïve population. We produced a film appealing to a modern audience: 164 second duration, conceptual, without dialogue and accessible across formats. We assessed its success at delivering the message to people with MS (pwMS) and a wider population.

Methods: 3 populations were included: pwMS from the UK MS Register, pwMS from outpatient clinics and a general population (Ethical approval ref: 19/LO/0282). Based upon industry standard, pre-specified outcomes were 50% viewer retention (viewing for ≥ 30 seconds) and 50% understanding of the concepts. The film was embedded into a website, participants were asked to review the film and the four concepts were explained. Participants answered questions about the concepts.

Results: In the total population 887/1102 (80%) watched ≥ 30 seconds with an average duration of 149/164 seconds (91%), significantly above the pre-specified outcome percent ($p < 0.0001$). In the MS Register population 757/959 (78.9%) pwMS had total understanding (4/4 concepts) versus 29/42 (69%) in pwMS from outpatients and 136/149 (91%) in the general population. Understanding in all cohorts were significantly above the expected outcomes ($p < 0.0001$) with significantly greater understanding in the general population compared to pwMS ($p < 0.0001$).

Conclusion: As part of a preventative medicine strategy, a short, targeted film can successfully convey the importance of early intervention to both pwMS and a general audience.

Disclosure: R Nicholas is funded by the Imperial Biomedical Research Centre (BRC) and R Nicholas and D Wilkie are funded by Multiple Sclerosis Trials Collaboration (MSTC).

EPO3216

Exacerbations of Multiple Sclerosis during pregnancy

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Background and aims: According to Confavreux (1998), the frequency of exacerbations of multiple sclerosis (MS) during pregnancy is significantly reducing. The reason for this is accompanied by immunosuppression immune and hormonal change in the body of a woman during pregnancy.

Methods: 173 pregnant women suffering from MS were examined. Before pregnancy 119 women received disease-modifying therapy (DMT): glatiramer acetate – 70 people, interferons - 42 women, fingolimod - 3 patients, cladribine – 2 people, natalizumab – 2 patients.

Results: Exacerbations of MS confirmed clinically and by MRI data were registered for 24 pregnant women. Exacerbation occurred in the I trimester of pregnancy for 12 patients, for 6 – in the II trimester, for 6 women in the III trimester of pregnancy. Among them 13 people (3 – glatiramer acetate, 8 - interferon β 1-b, 1 - fingolimod, 2 - natalizumab) received therapy with DMT before pregnancy, 9 women did not receive therapy. For women receiving drugs of the II line of therapy (aggressive course), exacerbations were registered in 60% of cases. The patient receiving fingolimod therapy before pregnancy had 3 exacerbations: one in each trimester. All patients received corticosteroid therapy from 5000 to 7000mg per course. 23 patients after exacerbation and corticosteroid therapy had healthy children. According to ultrasound procedure pathologies were not revealed.

Conclusion: Management of pregnancy and childbirth for MS patients does not differ from those of the general population. More often exacerbations occur for women who have not previously received DMT and with the initially aggressive course of the disease.

Disclosure: Nothing to disclose

EPO3217

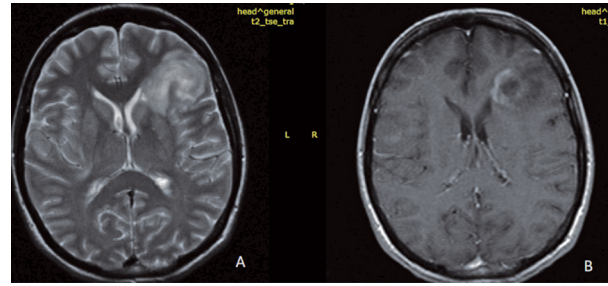
Levamisole-Induced Leukoencephalopathy in Russian Population: 24 cases

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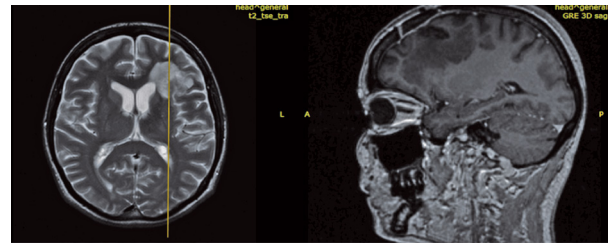
Background and aims: Levamisole is a synthetic imidazothiazole derivative that has been used as an antihelminthic agent since 1970s. Due to its immunomodulatory effect that includes T-cell activation and proliferation as well as macrophage and neutrophil function increase it is also used in several inflammatory and malignant conditions treatment. Demyelinating leukoencephalopathy is a severe complication of levamisole use.

Methods: A single-center retrospective analysis of 24 levamisole-induced leukoencephalopathy cases medical history, clinical presentation, brain MRI, and CSF analysis was performed.

Results: All patients had a history of levamisole use as an anthelmintic 1–4 weeks prior to the symptoms onset. The dose range was of 50–150mg. The female:male ratio was 16:8, the mean age of symptoms onset was 47.2±11.4 years. The presenting symptoms are shown in the Figure 1. CSF analysis was available in 6 patients, with normal CSF pattern polyclonal IgG in 3 patients, oligoclonal bands in CSF with normal serum pattern in 2 patients, and common oligoclonal bands both in serum and CSF in 1 patient. Lymphocytic pleocytosis up to 107/3 cells was found in 5 patients and mild increase of protein level up to 0.6g/l was found in 3 patients. All brain MRI were abnormal with hyperintense T2 and FLAIR lesions, some lesions hypointense on T1, and all lesions enhancing contrast (Figure 2). Follow-up MRI showed decrease of lesions volume and ring-like or total regression of contrast enhancement (Figure 3).



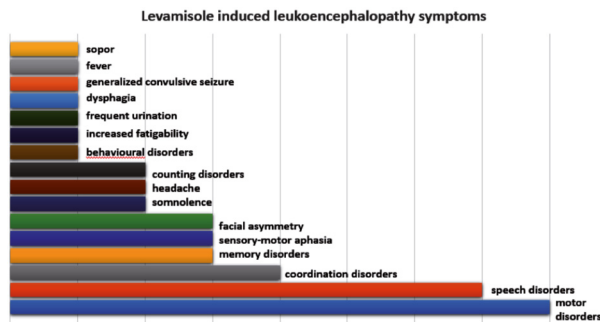
Brain MRI with hyperintense T2 and FLAIR lesions and all lesions enhancing contrast in T1



Follow-up MRI

Conclusion: Due to potential severe complications associated with immunomodulatory effect, levamisole use as an antihelminthic is not recommended.

Disclosure: Nothing to disclose



Levamisole induced leukoencephalopathy symptoms

EPO3218

Is OCT a real marker of neurodegeneration in MS?

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Background and aims: The search for reliable and inexpensive method of evaluation of neurodegeneration in MS is still ongoing.

The purpose of the study was to evaluate the changes of the retinal nerve fiber layer (RNFL) thickness within 4 years of observation by optical coherence tomography (OCT) and to compare it with cortical thickness of the brain.

Methods: Prospective study was conducted from January 2016 to January 2020. The OCT and MRI were performed once per year. 30 treatment naive patients (10 males and 20 females) with average age 45.13 ± 7.23 years, average duration of the disease 12.67 ± 4.99 years with a relapsing-remitting course of the disease according to McDonald 2010 criteria were involved in this study. Statistical analysis was performed using Microsoft Excel. Following characteristics were included: the severity of disease by the EDSS, average thickness of RNFL, thickness of the gray matter by linear measurement in T2-weighted images in upper frontal, pre-central, postcentral, occipital gyri in the both hemispheres.

Results: According to the obtained data, atrophic processes on the RNFL were observed withing 4 years of observation ($r=0.65$, $p=0.02$). No significant difference was observed between disability (EDSS step) and RNF thickness as well cortical thickness

Degenerative process of the brain cortex was observed in right postcentral ($p=0.03$), left postcentral ($p=0.02$) and left occipital gyri ($p=0.03$).

Conclusion: Degenerative processes in MS pathiens occur in retina and brain cortex. However these 2 processes proceed independently. The 4-year period is not sufficient to determine the relationship between neurodegeneration on OCT and brain MRI.

Disclosure: Nothing to disclose

EPO3219

Effectiveness of dimethyl fumarate as first line therapy in MS patients

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Background and aims: Interferon- β , glatiramer acetate and dimethyl fumarate are 1st line of disease-modifying therapies in patients suffering from relapsing-remitting multiple sclerosis (RRMS). Currently, there are no precise guidelines for modifying treatment in this group of patients. The aim of this study was to evaluate and compare activity of multiple sclerosis 1 year before and 1 year after switching treatment from interferon- β or glatiramer acetate to dimethyl fumarate.

Methods: 62 adult patients were included in this study, age 19-61 years. All of them had been initially treated with disease-modifying drugs (DMDs) by injection: interferon or glatiramer acetate. Analyses were done with SAS v.9.4 and Statistica, v.13.1.336.0.

Results: The most common reason for drug change in interferon- β group were adverse effects or clinical ineffectiveness (55% of patients) and in glatiramer acetate - new lesions on MRI scans (60% of patients). We observed significantly lower incidence of adverse effects after switching therapy to DMF. Moreover, there was no statistically significant correlation between radiological relapses and EDSS score over entire time of our observation. Presented study shows a statistically significant decrease in radiological relapses as a consequence of changing treatment from glatiramer acetate to dimethyl fumarate ($P=0.01$). Concurrently, switching from interferon to dimethyl fumarate reduced the number of clinical relapses ($P=0.01$).

Conclusion: The results of our study show that altering the treatment from both interferon- β and glatiramer acetate in patients with disease progression was beneficial for them. Further research is necessary to develop precise therapeutic guidelines regarding switching between first line DMDs.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 3

EPO3220

Different effects of cardiolipin and myristoyl-L-carnitine on the humane carnitine palmitoyltransferase II variants S113L, P50H and Y479F

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Background and aims: Muscle carnitine palmitoyltransferase II (CPT II) deficiency is associated with various mutations in *cpt2* gene. The recombinant CPT II variant S113L shows a reduced thermostability compared to the wild type (WT) and can be stabilized by myristoyl-L-carnitine (MC). In the present work, the variants P50H and Y479F have been characterized. Additionally, the effect of cardiolipin (CLP) on the 3 variants and the WT was analysed.

Methods: The enzyme activity of recombinant CPT II (WT, S113L, Y479F, P50H) was determined spectroscopically under different conditions. Nano differential scanning fluorimetry (nanoDSF) was used to investigate the protein stability.

Results: All CPT II variants showed normal activity. WT and Y479F showed stable activity at 1mg/ml at 30°C for 60min. However, activity of S113L and P50H strongly decreased to 60% and 0%, respectively. Increasing temperatures up to 42°C correlated with shorter half-lives of all variants compared to WT. Addition of CLP resulted in stabilisation of CPT II activity at various temperatures. This effect was less for the variants compared to WT. Addition of MC stabilized activities of WT and variants even more. This effect was least pronounced for P50H. The reduced thermostability of the variants, particularly that of P50H ($\Delta T_m=10^\circ\text{C}$), was confirmed with nanoDSF.

Conclusion: All variants clearly differed in their thermostability. However, clinical symptoms were similar in all genotypes. The functional consequences of the stabilisation by CLP and MC in vivo remain open.

Disclosure: Nothing to disclose

EPO3221

Non-dystrophic myotonias: clinical features and mutation spectrum of a large cohort of German patients

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Background and aims: Non-dystrophic myotonias (NDM) are clinically and genetically heterogeneous diseases caused by mutations in *CLCN1* and *SCN4A*. The study aim was to describe the clinical and genetic spectrum of NDM in the German population.

Methods: We retrospectively identified all patients with genetically confirmed NDM, diagnosed in our center in the past 25 years. The following data were analyzed: demographics, muscular symptoms, cardiac involvement, CK, EMG, genetic results, medications.

Results: 69 patients (age 44.8±14.8 years; 53.6% males) were included in the study. 47 patients had *CLCN1*-myotonia, 22 *SCN4A*-myotonia. The most frequent presenting symptom was myotonia in *CLCN1* (81%) and weakness in *SCN4A* (42%). With disease progression myalgia were present in 43% *CLCN1* and 44% *SCN4A*. Cardiac involvement was present in 15% of patients (8 *CLCN1* and 2 *SCN4A*). CK was normal in 69% of *CLCN1* and 62% of *SCN4A*, hyperCKemia was higher in *SCN4A* than *CLCN1* (1268±837U/L vs. 374±110U/L). EMG detected myotonic runs in 89% of *CLCN1* and 74% of *SCN4A* patients without cooling test. 42% of *CLCN1*-myotonia had the common c.2680C>T (p.Arg894X) mutation. 7 new mutations were identified. 39/69 patients were taking anti-myotonic drugs; half of the patients had previously tested an average of 3 anti-myotonic drugs without satisfactory results.

Conclusion: The clinical features of our cohort were comparable to literature data, however the prevalence of cardiac involvement requires further investigation. The mutation spectrum was similar to the Scandinavian patients, furthermore 7 new mutations were found. Besides this genetic heterogeneity, the limited response to anti-myotonic drugs also constitutes a challenge for clinicians.

Disclosure: Nothing to disclose

EPO3222

3 individuals with mutation in exon 1f of PLEC and myasthenic phenotype

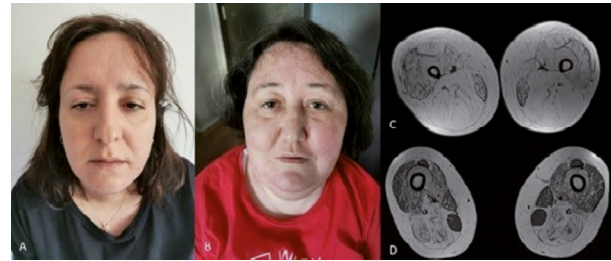
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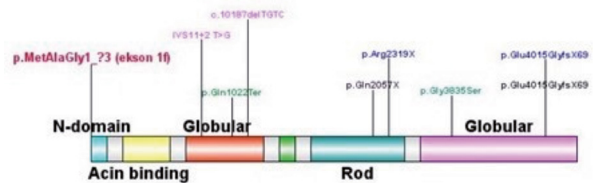
Background and aims: Plectin (PLEC) is one of the largest proteins and consists of the N-terminal domain encoded by multiple short exons undergoing alternative splicing and a constant C-domain. PLEC 1f plays an important role in stabilizing the neuromuscular junction (NMJ). We identified a recessive known c.1_9del PLEC gene mutation, which was previously associated with limb girdle muscular dystrophy 17 (LGMD17R) in 3 females displaying LGMD and myasthenic phenotype.

Methods: Exome sequencing was performed at the Broad Institute's Genomics Platform, using Illumina exome capture on a cohort of >1800 patients with limb girdle muscle weakness as part of the MYO-SEQ Project. DNA samples were submitted to the Newcastle MRC Centre Biobank for Neuromuscular Diseases (ethical approval number 08/H0906/28).

Results: We identified a recessive known c.1_9del PLEC gene mutation containing an initiation codon in exon 1f in 3 females from consanguineous families. The patients were not related, but from the same geographical region by the Black Sea in Turkey. All individuals presented with slowly progressive limb girdle muscular dystrophy without any dermatologic component, calf pseudohypertrophy and dystrophic changes observed in muscle biopsy. Additionally, neurological examination revealed ptosis, facial weakness easily fatigability and muscle cramps in all 3 cases. In 1 patient a repetitive nerve stimulation showed a borderline decrement and a slight improvement under the treatment with salbutamol was observed in all three individuals.



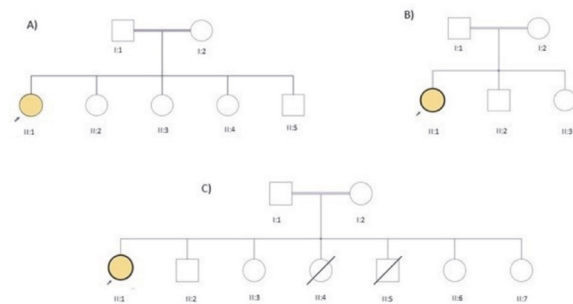
A) and B) Ptosis and facial weakness C) and D) Transformation of the adductor magnus, adductor longus, biceps, semitendinosus and semimembranosus muscles. Sparing of sartorius and gracilis muscles.



Location of PLEC mutations associated with myasthenic phenotypes. Identified by us mutation c.1_9del in red.

Conclusion: We further characterize LGMD R17 plectin-related phenotype in terms of myasthenic symptoms and muscle MRI. Our findings support the hypothesis of a crucial role of plectin 1f isoform in NMJ.

Disclosure: MYO-SEQ was funded by Sanofi Genzyme, Ultragenyx, the LGMD2I Research Fund, Samantha J Brazzo Foundation, the LGMD2D Foundation, the Kurt+Peter Foundation, Muscular Dystrophy UK, and the Coalition to Cure Calpain 3.



Pedigrees of 3 c.1_9del PLEC individuals.

EPO3223

5-year prospective study of quality of life in patients with myotonic dystrophy type 2

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Background: Although myotonic dystrophy type 2 (DM2) is clinically milder than DM1, quality of life (QoL) is similarly impaired in these 2 disorders. There are no prospective studies that assessed QoL in DM2.

Aim: To determine QoL in patients with DM2 during a 5-year follow-up period.

Methods: Study comprised 49 DM2 patients at baseline. After 5 years, 7 of them died, 8 were lost to follow-up, 2 developed another disease, 1 moved to another country, and 1 refused to be tested. Thus, SF-36 and INQoL questionnaires were administered in 30 patients at baseline (47% males, 49±10 years old, disease duration 13±11 years) and at follow-up (54±10 years old).

Results: After 5-year follow-up, none of the subscales on SF-36 and INQoL questionnaire differed compared to baseline testing ($p>0.05$). Percentage of deceased was higher among males compared to females (42% vs. 7%, $p<0.01$). Muscle strength was better in survivors ($p<0.01$). Following SF-36 subscales were worse at baseline in patients who later died: physical functioning, general health, social functioning, mental health, physical and mental composite scores and SF-36 total score ($p<0.01$). INQoL activities subscore was worse in non-survivors ($p<0.01$). Independent predictors of lethal outcome were male gender and INQoL activities score ($\beta=0.41$ and $\beta=-0.39$, respectively; R square adjusted=0.35).

Conclusion: SF-36 and INQoL questionnaire did not show good responsiveness in DM2 patients during a 5-year follow-up period. INQoL activities score may be considered as a predictor of the lethal outcome in DM2.

Disclosure: Nothing to disclose

EPO3224

Myasthenia gravis associated with other autoimmune diseases - what we found out from our clinical practice?

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Background and aims: Autoimmune diseases (AD) are chronic conditions caused by the loss of immunological tolerance to self-antigens. Recent epidemiological studies have shown a possible shift of one AD to another or the fact that more than 1 AD may coexist. Myasthenia Gravis (MG) is an autoimmune neuromuscular disease, caused by antibody mediated activity that lead to a reduction of acetylcholine at the neuromuscular junction. Extensive literature search did not reveal many case reports of an association between MG and other autoimmune diseases, so our goal is to highlight it and its possible clinical implications.

Methods: This is a retrospective and observational study with a lot of 51 patients divided in 2 groups (by blood tests and imaging explorations): MG vs associated AD.

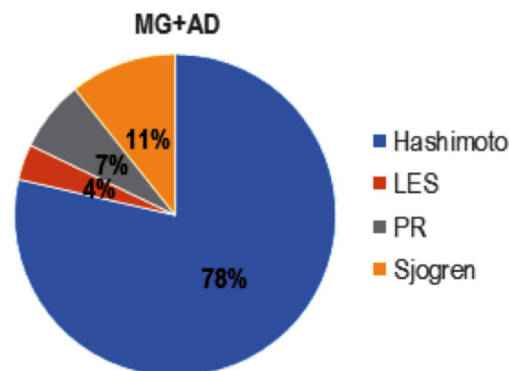


Fig. 1: Autoimmune disease association

Results: In our group of 51 patients with MG, other AD were associated in 49% of cases. The most prevalent one was Hashimoto's thyroiditis followed by Sjogren, rheumatoid polyarthritis and systemic lupus erythematosus. There was a female predominance. In both groups the majority of patients had generalized type of MG (96%) with ocular onset (68% vs 50%). On the other hand in the AD group there were more patients with spinal onset than in the other group (23% vs 16%) with an average myasthenia gravis deficit score (QMG) of 8.5 (vs 9.87), most of them with QMG below 10 points (59%). There were more tymectomies in the AD group (48% vs 38%).

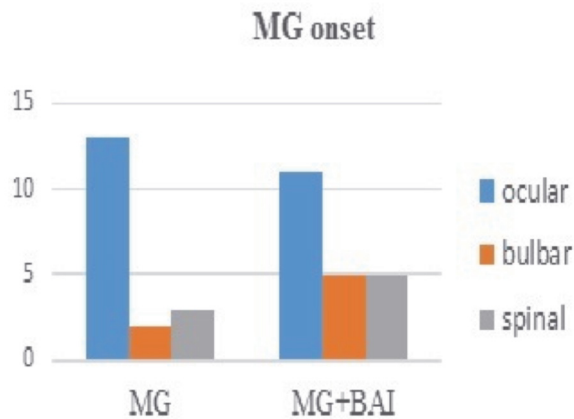


Fig.2: Myasthenia gravis onset

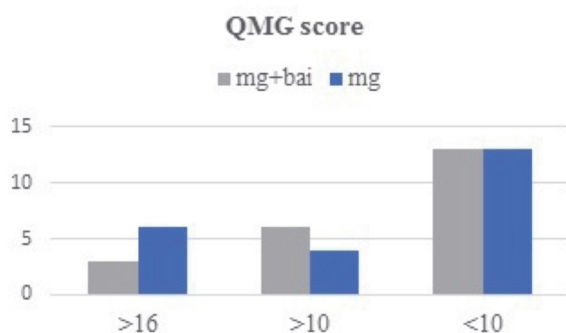


Fig.3: QMG score

Conclusion: Screening for AD should be done in everyday practice at patients with an MG, because of the greater risk of developing another AD disease and its clinical implications.

Disclosure: Nothing to disclose

EPO3225

King Denborough syndrome-myopathy with dysmorphic features suggesting risk of malignant hyperthermia.

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Background and aims: King Denborough syndrome (KDS) is a rare, genetic disease characterized by a susceptibility of malignant hyperthermia (MH), myopathy and variable dysmorphic features including short stature, lumbar lordosis, thoracic kyphosis, pectus carinatum, cryptorchidism. Disease is predominately associated with various mutations in RYR1- that encodes a ryanodine receptor. Product of this gene plays a relevant role in excitation- contraction coupling and its disorders are associated with several neuromuscular diseases (MH, central core disease, minicore myopathy).

Methods: We present 2 patients with characteristic phenotype accompanied by myopathy.

Patient 1 is 4.5y old boy with delayed motor development, characteristic dysmorphic features, elevated CK (max. 422 U/l, normal range 39-308U/l). His muscle MRI showed features of asymmetrical atrophy and fat degeneration in the proximal muscles of lower limbs.

Patient 2: 3.5y old boy with motor (started to walk at the age of 30 months) and speech delay. The neurological examination revealed predominant lumbar lordosis and hyperextension of knees, hypoplastic mandible and significant muscles hypotonia. CK was normal.

Results: Patient no 1 NGS revealed heterozygous change in RYR1 gene (c.11933G>A; p.Arg3978His). Genetic test analysis in patient no 2 indicated 2 heterozygotic variants of unknown pathogenicity c.4178A>G and c.13644+105C>T in RYR1 gene.

Conclusion: Considering the severity of MH, children with myopathy and characteristic dysmorphic features should be suspected of KDS. The RYR1 test should be performed at the beginning of diagnostic process and before any surgery with general anesthesia, especially those performed in case of KDS for cryptorchidism and skeletal deformities.

Disclosure: Sanofi Grant

EPO3226

Different alterations in DMD gene in 62 Russian children with Duchenne muscular dystrophy as a result of a two-stage molecular genetic analysis

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Background and aims: Duchenne muscular dystrophy (DMD) is a rare muscle disorder inherited by X-linked recessive type and affecting approximately 1 in 3,500 male births worldwide.

Methods: The study included 73 boys, aged from 3 months to 11 years with elevated creatinine phosphokinase (CPK), according to laboratory tests. After medical genetic counseling molecular genetic analysis was performed for all patients. The MLPA method was used to detect large deletions and duplications in the DMD gene, the analysis of point mutations was carried out by next generation sequencing (NGS), if the MLPA method did not reveal pathogenic variants.

Results: Totally, in all 62 patients we revealed different alterations in DMD gene. Among them 36 (58%) patients had gross deletions and 4 (6%) had gross duplications in the DMD gene. Interestingly, more than half of the patients had deletions in the region of exons 45-51 of the DMD gene. The remaining 22 (36%) patients had point mutations which were revealed by NGS. It was 12 nonsense, 5 splicing mutation, 3 small deletions and 2 small duplication. Among point mutations 8 (36%) were novel.

Conclusion: Our study showed the high efficiency of the 2-stage molecular genetic diagnosis algorithm, while revealing a large percentage of novel point mutations in Russian patients with Duchenne muscular dystrophy.

Disclosure: Nothing to disclose

EPO3227

27 years of molecular diagnosis of dystrophinopathies by multiplex PCR in Morocco

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Background and aims: Dystrophinopathies, X-linked recessive disorders, are the most common genetic neuromuscular disorders during childhood. They gather 2 phenotypes of different severity; Duchenne Muscular Dystrophy (DMD, MIM#310200) and Becher Muscular Dystrophy (BMD, MIM#300376). These diseases are caused by a large spectrum of heterogeneous mutations in the dystrophin gene on the Xp21.2 chromosome. Deletions involving the Dystrophin (DMD) gene are the most common underlying cause of these disorders, representing 68% of mutations. The goal of this study is to determine the frequency of different deletions of the DMD gene in Moroccan patients.

Methods: We analyzed the data of 365 male Moroccan patients suspected for dystrophinopathies, seen in our department between November 1992 and January 2019. These patients were screened for deletion of the Dystrophin (DMD) gene using a multiplex polymerase chain reaction (PCR).

Results: Among the 365 patients screened, 159 (43.5%) had a deletion of the DMD gene. Deletions spanning 1 exon made up 29% of deletions. Followed by 3-exon deletions (19%) and the rest of deletion types <10% each. 91% of deletions were in 1 of the known mutation hotspots. 73% of the deletions were found in the 5' hotspot (Exon 44 to Exon 52), 18% were located on the 3' hotspot (Exon 3 to Exon 19) and only 6% of deletions spanned both hotspots.

Conclusion: We report here our experience in the molecular diagnosis of dystrophinopathies by the multiplex PCR technique. It is a good first-line strategy in our public health due to its low- cost with a good cost-to-benefit ratio.

Disclosure: Nothing to disclose

EPO3228

International standards of care for Duchenne muscular dystrophy implementation in Ukraine

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Background and aims: It is known that Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder that affects 1:3,500-1:5,000 live male births in the world. According to statistic dates, 226 patients with DMD were registered in 2018 in Ukraine. When the population consisted 42 million 249 thousand. Taking into consideration that not all patients have already been examined by genetic testing, we have decided to improve diagnostics and treatment DMD in our country according to International standards of care.

Methods: Nowadays we have been continuing to create medical centres for DMD patients in Ukraine. The multidisciplinary team which is working in the centre gives DMD patients a comprehensive care. It includes functional assessment for ambulatory and non-ambulatory patients, respiratory function measurement, corticosteroid therapy; prevention scoliosis and contractures, management of contractures with stretches and with orthotics. We applied clinical, neurophysiologic, laboratory methods and genetic techniques: multiplex ligation-dependent probe amplification (MLPA) and next generation sequencing (NGS).

Results: We have examined new 33 DMD patients. Delayed motor milestones, calf pseudohypertrophy, toe walking, Gower's sign have been found during a neurological examination. 23 deletions, 4 duplications have been identified. Moreover, 6 nonsense mutations have been found. Every patient started to receive physiotherapy and corticosteroid therapy after his motion functional assessment. Consequently, the disease-modifying therapy (ataluren) has been prescribed for the patients with confirmed DMD nonsense mutation.

Conclusion: The application of the International standards of care for DMD patients in Ukraine is important step to fill in the gap in diagnostics and support of the DMD patients.

Disclosure: Nothing to disclose

EPO3229

Serum immunoglobulin free-light chains in myasthenia gravis: a biomarker of B-cell activity?

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Background: Autoreactive B-cells produce excess of free-light chains (FLC) during immunoglobulin synthesis excreted by kidneys with an half-life of 2-6 hours. Increased FLC serum levels could be considered a marker of B-cells activity. Myasthenia gravis (MG) is an autoimmune disease affecting the neuromuscular junction mainly mediated by antibodies (Abs) against the acetylcholine receptor (AChR). The clinical presentation is variable and not related to Ab level.

Aims: To evaluate serum kappa and lambda FLC in AchR-MG at disease onset according to a possible role as biomarkers of disease activity.

Methods: We assessed serum FLC levels (by nephelometry) from 20 AChR-MG patients in comparison with 20 multiple sclerosis (MS) and 10 healthy controls (HC). The following demographic and clinical features were collected at MG diagnosis: age and gender, symptom-onset (according to MG Foundation of America classification), neurophysiological results, AchR-Ab level (evaluated with enzyme-linked immunosorbent assay) and disease severity (according to Osserman).

Results: We found a statistically significant increase in kappa and lambda FLC in AChR-MG patients in comparison to MS and HC. None of the demographic and clinical features we collected related to FLC levels.

Conclusion: Kappa and lambda FLC resulted a sensitive marker of AchR-MG. Further investigations are need to evaluated their role as biomarkers of disease activity.

Disclosure: Nothing to disclose

EPO3230

Magnetic Resonance Imaging (MRI) in Periodic Paralysis

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Background and aims: Periodic paralysis (PP) consists of 3 conditions (hypokalaemic periodic paralysis, hyperkalaemic periodic paralysis and Andersen Tawil Syndrome). To date, very few small studies describe neuromuscular MRI changes in these groups. Characterising MRI changes may provide a biomarker for future trials and insight into pathogenesis

Aims: 1. Define the presence, frequency and pattern of lower limb neuromuscular MRI abnormalities in patients with genetically proven PP.

2. Describe differences in MRI abnormalities in the subsets.
3. Describe longitudinal changes.

Methods: Ethics approval was attained from the Joint National Hospital for Neurology and Neurosurgery (NHNN) Research Ethics Committee. Patients with genetically proven PP underwent scans after review at the Muscle Channelopathy service at the NHNN. 38 muscles per scan were scored using the Modified Mercuri semi-qualitative scale by a blinded Neuromuscular Radiologist. 10% of scans were reviewed by a 2nd blinded Neuromuscular Radiologist with a subsequent consensus meeting. Clinical data was retrospectively collated from electronic medical records.

Results: There were a total of 77 scans. 20 patients had longitudinal imaging. Analysis is ongoing. Analysis to date, suggests that distinct changes exist consisting predominantly of fatty infiltration. Changes are more marked in the thighs over calves, and are most severe in patients with hypokalaemic PP. Atrophy is seen in patients with sodium channel mutations. Qualitative patterns suggest posterior compartment predominance and pelvic muscle involvement.

Conclusion: This will be the largest review of neuromuscular MRI in patients with PP. There are definite STIR signal and fatty infiltration changes in patients with periodic paralysis with differences between subsets.

Disclosure: Nothing to disclose

EPO3231

Frequency of myoedema in patients with muscular disorders

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Background and aims: Myoedema is the short local ridge that is observed immediately after muscle percussion. It was 1st described in 1871 by Tait L. in patients with tuberculosis but it is not correlated to any specific neurological condition. As far as its clinical significance is concerned, myoedema is an electrically silent physiological phenomenon which is not indicating a neuromuscular disorder.

Methods: 891 individuals were included retrospectively in the study. The aim was to record the frequency of this phenomenon among patients with different muscular disorders and to evaluate its correlation with some specific entities.

Results: Myoedema was found in 60 patients out of 891 (6.7%) in bicep brachii muscle. Nine of them (15%) were excluded since they did not complete the diagnostic examinations. As far as the group that myoedema was revealed is concerned, the most frequent diagnosis were asymptomatic hyperckemia 13/60 (21.6%), LGMD (LGMDD1, LGMDD3, LGMDR2) 10/60 (16.6%), myotonic Dystrophy type 1 and 2, 4 (6.6%), FSHD1, 2 (3.3%), Autoimmune inflammatory myopathy 2 (3.2%), other myopathies 3/60 (5%), other primary muscle disorders 2/60 (3.2%) whereas 6/60 (10%) patients had evidence of myopathy in biopsy but not specific diagnosis could be made. In 8.3% (5/60) myoedema was not due to primary muscle disorder.

Conclusion: Myoedema is a nonspecific clinical sign that can be observed in various diseases. It is not pathognomonic of a disease and the exact pathophysiological mechanism is not yet known. It is thought to be the result of local mechanical irritation of the muscle fibers and probably Ca²⁺ concentration plays a key role.

Disclosure: Nothing to disclose

EPO3232

The detection of intention for finger moving with machine learning on myotonic dystrophy type 1.

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Background and aims: The premotor potential reflects motor planning. Myotonic dystrophy patients in the advanced stage show the difficulty of communication. We investigated the efficacy of electroencephalogram and machine learning about detecting the intention for finger moving in myotonic dystrophy type 1 patient.

Methods: The task was to push the key with the right index finger with an auditory signal every 10 seconds. The control was the auditory signal only. Each task repeated 100. Electroencephalogram divided into epochs that include one 2nd before the signal. We constructed the classifier with a support vector machine. We evaluated a voting classifier which made from some classifiers. The voting classifiers consisted of 2 ways. The 1st includes 4 channels that showed the best performance as the best channel classifier. The 2nd constructed from fixed channels that Fp1, Fp2, C3, and C4 as the fixed classifier.

Results: 3 patients participated. We selected 4 channels for each patient and constructed the best channel classifier. The sensitivity and specificity with these classifiers were 1.0 and 0.93 on case 1, 1.0 and 0.94 on case 2 and 1.0 and 0.86 on case 3 (table1). The sensitivity and specificity with the fixed classifiers were 1.0 and 1.0 on case1, 1.0 and 1.0 on case2 and 1.0 and 0.90 on case 3 (table2). The fixed classifiers did not show good performance for the other.

		Case 1	Case 2	Case 3
Case 1	Sensitivity	1.0	0.36	0.36
	Specificity	1.0	0.35	0.59
Case 2	Sensitivity	0.29	1.0	0.36
	Specificity	0.62	0.93	1.0
Case 3	Sensitivity	0.61	0.36	1.0
	Specificity	0.31	0.54	0.86

table1. The best channel classifier

		Case 1	Case 2	Case 3
Case 1	Sensitivity	1.0	1.0	1.0
	Specificity	1.0	1.0	0.77
Case 2	Sensitivity	0.68	1.0	1.0
	Specificity	0.41	1.0	1.0
Case 3	Sensitivity	1.0	0.0	1.0
	Specificity	0.89	0.67	0.89

table2. The fixed classifier

Conclusion: This study demonstrated the usefulness of Electroencephalogram for detecting premotor signals in myotonic dystrophy type 1 patient.

Disclosure: Nothing to disclose

EPO3233

Clinical And Genetic Characteristics of Bethlem Myopathy Patients from Turkey

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Background and aims: Collagen VI related myopathies are the rare hereditary disorders characterized by early contractures, slow progressive proximal muscle weakness and skin involvement. The most common groups are Bethlem myopathy (BM) and Ullrich congenital muscular dystrophy (UCMD). BM usually begins in the 1st 2 years and shows generally AD inheritance.

Methods: Herein, we evaluated clinical and genetic findings of 9 patients from 9 unrelated families diagnosed with BM at the Department of Neurology, Istanbul Faculty of Medicine between 1989-2018.

Results: 4 of them were sporadic cases whereas 5 patients were autosomal recessive. The mean onset age was 5.9±2.6 years. The most common initial signs were waddling gait with difficulty climbing stairs and standing up from a squatting position. The distribution of the contractures was in both-the proximal and distal joints, most significantly elbow, knee, wrist and finger joints. Deltoid, biceps, triceps, gluteus maximus, iliopsoas and hip adductors muscles were most severely affected muscles. Rigid spine and scoliosis (3/9), gastrocnemius hypertrophy (3/9), gluteus maximus atrophy (4/9) and keloid scar (2/9) were noted. MRI findings showed fatty atrophy in the gluteus maximus with partial preservation of the gracilis and sartorius muscles (5/6), 'sandwich sign' in vastus lateralis (3/6) and 'central shadow' sign in rectus femoris (1/6) muscles. 9 mutations were found in Col6A1/Col6A2/Col6A3 genes, 5 of them (c.838G>T; c.901-1G>C; c.8377_8379delGTC, C.955-10C>7; c.2092_2097delGCGGGCinsACAGGT) were novel. Splicing site mutations were common in our cohort. The most frequently mutated gene was COL6A3 in BM patients from Turkey.

Conclusion: Our study indicated genotypic and phenotypic heterogeneity of collagen VI related myopathies in Turkey and revealed novel mutations.

Disclosure: Nothing to disclose

Neurogenetics 2

EPO3234

Withdrawn

EPO3235

Clinical cases of MELAS in adult neurological practice: rare disease with own rules

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Background and aims: Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) is rare inherited mitochondrial disease with variety of manifestations. Mostly often cause of MELAS is missense mitochondrial DNA (mtDNA) mutation (m.3243A>G) in MT-TL1 gene encoding mitochondrial transfer RNAs for leucine.

Methods: 2 patients with MELAS (age 18; male and female) were managed into department due to recurrent episodes of stroke-like episodes, recurrent seizures, myopathy and lactic acidemia. In both patient diagnoses were made in childhood and confirmed by molecular-genetic investigation.

Results: Due to improvement in diagnostics and treatment patients with MELAS grow up and after 18 years age went from pediatric neurologists to adult neurology practice. Adequate management of 2 patients observed required multidisciplinary team: neurologist, cardiologist (cardiomyopathy), endocrinologist (hypothyroidism, hypogonadotropic hypogonadism), ENT specialist (sensorineural hearing loss), ophthalmologist (optic atrophy, pigmentary retinopathy), physical and occupational therapists. There is no evidence-based approach for treating such patients and usual principles of stroke management for MELAS stroke-like episodes are absolutely inapplicable, that make difficulty to stroke center neurologists. NO-production stimulation: L-arginine and citrulline; multimodal energy donors (neuromyoprotectors): idebenon, lipoic acid, succinic acid derivatives and L-carnitine administration in high dosage were successfully used in our patients with clear improvement of neurological manifestations.

Conclusion: Nowadays patients with MELAS are rare, but life expectancy of them increases therefore their number in adult neurology practice will increase also. Their management require multidisciplinary approach and administration of specific medicines, despite lack of their effectiveness evidence.

Disclosure: Nothing to disclose

EPO3236

Novel mutation in DJ-1 (PARK7) gene in patients with Parkinson's disease

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Background and aims: Mutations in DJ-1 gene (PARK7) lead to early-onset autosomal recessive Parkinson's disease (PD) characterized by age of onset before 30 years, combination of motor and non-motor symptoms (psychosis, anxiety and cognitive impairment) and rapid progression. The pathogenic role of DJ-1 heterozygous mutations is still under discussion. More than 20 rare mutations in DJ-1 have been described, predominantly missense mutations and deletions, and PARK7 remains an extremely rare form of PD worldwide.

Methods: We present 2 sporadic cases of late-onset PD. In both cases we performed MLPA genetic testing.

Results: We found heterozygous duplication of DJ-1 exon 1, a mutation not previously described.

Patient R., female, 74-year-old, age at the disease onset 54 years, Hoehn-Yahr stage 2, treated with piribedil, exhibited rest and postural hand tremor, predominantly in the right hand, moderate left-sided bradykinesia and rigidity, and mild cognitive impairment. Treatment with L-dopa had significant positive effect on tremor.

Patient S., female, 55-year-old, age at the disease 53 years, Hoehn-Yahr stage 1, drug-naive, exhibited rest tremor in the left hand and the leg, slight left-sided bradykinesia and rigidity, anxiety and depression, without cognitive impairment. Treatment with L-dopa reduced tremor and bradykinesia.

Conclusion: These 2 patients carrying exon 1 duplication in DJ-1 gene are characterized by a mild disease course with slow progression of symptoms, tremor-dominant phenotype and good response to L-dopa treatment. We suggest that partial dysfunction of DJ-1 protein in heterozygous carriers of mutations leads to the development of the more benign form of PD.

Disclosure: Nothing to disclose

EPO3237

Genotype-Phenotype correlation in FTD: a rare GRN mutation identified in Italian Population

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Background and aims: Frontotemporal lobar degeneration (FTLD) defines a group of neurodegenerative brain disorders with predominant degeneration of frontal and/or temporal lobes¹. Since the first demonstration of FTLD-associated progranulin gene (GRN) mutation², over 150 GRN mutations were identified (82 pathogenic). We report the cases of 2 patients carrying the same frameshift mutation in exon 6 of GRN (c.468_474del).

Methods: #Patient1

A right-handed 63-years-old man presented with a 1-year history of progressive attention deficit associated with apathy.

His mother received late onset Alzheimer's Dementia diagnosis (70aa). Mini-Mental State Examination (MMSE) score was 23.53/23.8; Frontal Assessment battery (FAB) and Aachen Aphasia test (AAT) highlighted no pathological alterations. Brain magnetic resonance imaging (MRI) showed left-frontal lobar atrophy. Patient was diagnosed with Behavioral variant of Frontotemporal Dementia (BvFTD)³. Given his family history, we performed the genetic analyses for GRN and microtubule-associated protein tau gene (MAPT) mutations, identifying mutation (c.468_474del) of GRN.

Results: #Patient2

A right-handed 61-years-old woman presented with a 1-year history of a progressive speech impairment. She reported no significant familial history. MMSE score was 20.46/23.8; FAB 13.01/12. AAT showed deficits in naming, writing, and repetition. Brain MRI showed left-frontal and temporal lobes atrophy. The patient was diagnosed with Progressive Non Fluent Aphasia³. Given the early onset, we performed GRN and MAPT genetic examination and identified GRN mutation (c.468_474del).

Conclusion: To date, according to our knowledge, GRN (c.468_474del) mutation was not identified in the Italian population. Our cases highlight the heterogeneous spectrum of clinical presentations associated to this mutation.

Disclosure: Nothing to disclose

EPO3238

Adult-onset Krabbe disease presented with homonymous hemianopsia

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Background and aims: Krabbe disease(KD) is an autosomal recessive lysosomal storage disease (LSD). According to deficiency of galactocerebrosidase, it causes demyelination in both central and peripheral nervous system. Adult-onset KD is very rare. We present a case of adult-onset KD with initially presented with visual disturbance.

Methods: A 58-year-old woman was visited our hospital for visual disturbance. She had no medical history. On examination, left-sided homonymous hemianopsia was found in visual field test. Her eye movements were normal. Other neurologic examinations were normal. Her other complaints were prolonged general weakness and hearing difficulty since childhood.

Results: Brain MRI revealed symmetric white matter high signal intensities in bilateral parieto-occipital lobes of T2, and callosal dysgenesis involving posterior body and splenium. Spine MRI was normal. Visual-evoked-potentials showed prolonged latencies and distorted shapes on bilateral side and nerve-conduction-studies of extremities were normal. Laboratory studies for metabolic disease were performed, and found that the activity of galactocerebrosidase was reduced (0.17umol/h/L). Genetic testing of GALC gene found homozygous c.1901T>C(p.Leu634Ser) variants.

Conclusion: Adult-onset KD often chronic and slowly progressive. Our patient showed no typical symptoms of KD, there were only visual disturbance. Her characteristic MRI findings have allowed us to suspect metabolic storage diseases. In adult-onset KD, MRI shows parietooccipital periventricular white matter and posterior corpus callosal signal changes.

We report an adult-onset KD unusually presented by visual disturbance for the 1st time in Korea. If MRI findings suggestive of metabolic disease with corticospinal tract involvement, clinicians need to further investigate the possibility of genetic variant of adult-onset LSD, including KD.

Disclosure: Nothing to disclose

EPO3239

The single – nucleotide – variant – susceptibility – map in Multiple sclerosis patients in polish population – pilot study.

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Background and aims: Heterogenetic background of autoimmunity pathway components has been suggested in MS pathogenesis. The main aim of our study was to evaluate the association between selected polymorphisms (SNP, single nucleotide polymorphisms) in candidate genes and our MS patients.

Methods: The study group consisted of 94 relapsing-remitting MS patients and the same number of healthy volunteers. DNA was extracted from the peripheral blood leukocytes using a classical salting out method. The all SNPs were genotyped by TaqMan SNP genotyping assay using the real-time PCR method in OpenArray technology.

Results: Among the analyzed polymorphisms, we have observed the enhanced frequency of some genotypes in cases of several variants in MS group in compare to the healthy controls. Distribution of all genotypes of this SNP in MS group and in controls: CC – 46% vs 66%; CT – 42% vs 26%; TT – 6.4% vs 2.1%. Analysis of 3 polymorphisms in the CTLA4 gene showed, in the case of only 1, statistically significant differences in the frequency of occurrence of the risk genotype. In rs3087242 genotype AA was more frequent in MS patients group in compare to controls (68.1% vs 6.4%, $p < 0.001$). None of the CD40, FCRL5, IL13, IGIF, FCRL5 and PADI4 variants, were associated with the risk of MS compared to controls.

Conclusion: The results indicated that PTPN22 and CTLA4 variants were correlated with MS susceptibility in Poland. This is a pilot study – the 1st stage of our research.

Disclosure: Nothing to disclose

EPO3240

Sensorineural hearing loss and late onset ataxia as the initial presentation of a novel ATP1A3 mutation

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Background and aims: A 50-year-old male presented to the neurology clinic with features of cerebellar ataxia. He suffered sensorineural hearing loss of unknown cause since the age of 20. Gait abnormalities had been noted over a period of 3 years and recently the patient had experienced precipitated episodes of disequilibrium. Along with sensorineural hearing loss, the patient also had visual field deficits, brisk lower limb reflexes, bilateral Babinski responses and pes cavus.

Methods: A targeted next generation panel sequencing ataxia gene panel identified a novel heterozygous missense mutation in the ATP1A3 gene (c.823 G>A) with bioinformatic tools predicting a pathogenic change in the cytoplasmic loop in between the 1st and 2nd transmembrane domains of the $\alpha 3$ isoform.

Results: This genotype contributes to the evolving clinical spectrum of ATP1A3-related neurological disorders. Distinct phenotypes have been identified including ‘Rapid-Onset Dystonia Parkinsonism’ (DYT12), ‘Relapsing Encephalopathy with Cerebellar Ataxia’ (RECA), ‘Alternating Hemiplegia of Childhood’ (AHC) and ‘Cerebellar Ataxia, Areflexia, Pes Cavus, Optic atrophy and Sensorineural hearing loss’ (CAPOS) syndrome. Overlapping phenotypes are often seen. These are inherited in an autosomal dominant manner and our patient had a deceased 1st-degree relative who suffered from idiopathic late-onset cerebellar ataxia.

Conclusion: Currently ATP1A3-related disorders are thought of as paediatric conditions whereas the 1st symptom of neurological decompensation in our patient developed in early adulthood. Our patient also had a slow clinical course which is uncharacteristic of the previously described syndromes. This case adds to the clinical spectrum of ATP1A3-related disorders and documents a novel ATP1A3 related phenotype.

Disclosure: Nothing to disclose

EPO3241

SCN1A mutation and focal epilepsy: diagnosis and application in adults

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Background and aims: SCN1A gene mutations cause a spectrum of epileptic seizures, from febrile, focal or generalized seizures, with benign evolution, to generalized epilepsy with febrile seizures plus, or Dravet syndrome, with a worse prognosis. Our aim is to present 2 clinical case reports in a family with mutation in SCN1A gene.

Methods: We reviewed the medical history, physical examination and complementary tests performed.

Results: We present a 4-year-old girl with normal psychomotor development and 1st febrile seizure at 10 months, with generalized clonic semiology. Later on, she developed generalized, right hemiclonic, and tonic-clonic seizures. With 2 years and 8 months, bilateral frontal-centro-temporal epileptiform activity and a focal motor seizure were registered in the EEG. Valproic acid treatment was initiated, with significant improvement in seizures control. Etiological study was completed with a normal brain MRI, and a genetic study where a mutation in the SCN1A gene was found. Her mother, 26 years old, had a prior history of generalized tonic-clonic febrile seizures with 15 months, with normal psychomotor development and partial response to valproic acid treatment. In successive EEG a left parieto-temporal epileptic focus was evidenced, with normal brain MRI. After pregnancy, her treatment was changed to Levetiracetam. After the diagnosis of her daughter, the same mutation was found in her genetic study.

Conclusion: In adults with epilepsy and personal or familiar history of febrile seizures during childhood, the study of the SCN1A gene should be considered, as it may have prognostic and therapeutic implications, both in patients and their offspring.

Disclosure: Nothing to disclose

EPO3242

A mutation in a novel lysosomal gene causes adult-onset generalized dystonia in an Italian patient

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Background and aims: The advent of next-generation sequencing (NGS) provided an impressive step forward in the identification of the genetic causes of inherited dystonias, leading to the description of many novel genes in the last ten years. Our aim is to find the genetic cause of adult-onset generalized dystonia in an adult Italian patient through a NGS approach.

Methods: The subject underwent a neurological examination, a brain MRI and neurophysiological studies. Whole-exome sequencing (WES) was performed on genomic DNA of the patient. Functional studies (immunoblotting, enzymatic activities, and electron microscopy) were conducted on patient-derived fibroblasts to prove mutation pathogenicity.

Results: From the age of 30 years the proband developed involuntary dystonic movements affecting the right limbs. After 5 years from disease onset, dystonia became generalized, involving the trunk, limbs, neck, and vocal cords. Brain MRI displayed atrophy and marked symmetrical hypointensity in T2- and T2*-weighted sequences of basal ganglia. The suspected consanguinity of the parents suggested a homozygous mutation as the cause of the disease. A filtering analysis for rare homozygous variants with protein impact unraveled only one candidate variant in a gene involved in lysosomal and autophagic pathways. Functional studies on patient-derived fibroblasts showed a striking defect of lysosomal and autophagic functions.

Conclusion: This work represents the 1st association of a mutation in a novel lysosomal gene with a form of adult-onset generalized dystonia and provides strong in vitro evidence of mutation pathogenicity. The identification of this novel gene confirms the important role of lysosomes and autophagy in the pathogenesis of neurodegenerative dystonias.

Disclosure: Nothing to disclose

EPO3243

Familial Creutzfeldt-Jakob disease homozygous to the E200K mutation: Clinical characteristics and disease course

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Background and aims: Introduction: Most cases of Creutzfeldt-Jacob disease (CJD) in Israel are familial, due to an unusual cluster of the disease among Jews of Libyan origin carrying the E200K mutation in the gene encoding for the prion protein (PRNP).

Objective: To characterize the demographic, clinical features and disease course of familial Creutzfeldt-Jacob disease (fCJD) patients homozygous to the E200K mutation.

Methods: The Israeli National CJD Database was screened for patients homozygous to the E200K mutation. Patients' demographic data, clinical presentation, neurological findings and tau protein levels were assessed.

Results: 10 homozygous E200K patients were identified (80% men). Average age of onset was 47.5±6.1 years (range 40-56) and the average age of death was 49.3±7.7 years (range 42-63) with average disease duration of 27.7±9.7 months (range 2-97). Initial clinical presentation included behavioral change in 4/10 patients, cognitive decline in 3/10 patients and focal neurological deficit in 2/10 patients. Compared to 228 heterozygous E200K fCJD patients, homozygous patients were significantly younger at disease onset (47.5 years vs 59.7 years, p<0.001), had longer disease duration (27.7 vs 8.5 months, p<0.001) and presented more frequently with behavioral change (4/10 vs. 34/228, p=0.05). Levels of tau protein in the CSF did not differ between groups.

Conclusion: Homozygous E200K fCJD is characterized by younger age of onset and longer disease duration. Behavioral change as a presenting symptom was more common in homozygous patients. homozygous CJD patients do not seem to have a more severe and shorter disease course than heterozygous CJD disease.

Disclosure: Nothing to disclose

EPO3244

Kabuki syndrome: epilepsy features

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Background and aims: West syndrome is polietiological disease. Epilepsy isn't specific for Kabuki syndrome (KS).

Purpose: To investigate features of a West syndrome in a patient with a Kabuki syndrome.

Methods: Anamnesis, EEG, MRI data of patient M were investigated.

Results: Patient M, 20 months, had seizures 1 per day. The perinatal anamnesis was not burdened, the expressed delay of development was noted since birth. From 1.5 months of serial epileptic spasms 2-3 times per day began. The atypical (modified) hypsarhythmia was defined on EEG. Atrophic changes in frontal departments of both hemispheres were revealed by MRI. Diagnosis the atypical West syndrome was established. Therapy with vigabatrin, levetiracetam, valproic acid didn't achieve seizure control. A short-term course of hormonal therapy was conducted with a positive effect at the 7-8 months. However, the course was discontinued due to adverse events. Phenotypical characteristic of a KS (a long palpebral fissure, an ectopia of a lower eyelid, arks eyebrows, a wide nose bridge, skeletal abnormalities, fetal type of fingers, mental retardation) was noted. Epilepsy panel was conducted with a negative result. KMT 2D gene mutation on the 12th chromosome was revealed by sequenation of a genome. At genetic inspection of parents, the similar mutation was found in the father who is clinically healthy.

Conclusion: This clinical case has shown a refractory form of epilepsy rare for genetic Kabuki syndrome - West syndrome with the early beginning of spasms with the good answer to hormonal therapy and insufficient efficiency of vigabatrin and other AEDs

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EPO3245

POLG and PRKN gene mutations in Early-onset Parkinson's disease: A case report.

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Background and aims: POLG gene mutations may cause variable neurological manifestations, being rare in patients with typical Early-onset Parkinson's disease (EOPD). EOPD related to PRKN mutations require homozygous or compound heterozygous mutations, although single heterozygous pathogenic variant has been proposed as a genetic susceptibility factor. We present a case of EOPD with combination of heterozygous POLG variants and heterozygous PRKN mutation.

Methods: Case report.

Results: A 37-year-old man, without relevant personal or family history, presented with right-side predominant hand tremor at the age of 29 years, followed by lower limbs and head tremor, clumsiness and rigidity in both hands. The neurological examination revealed right-side predominant rest tremor, mild bilateral postural tremor in hands and rigidity and bradykinesia in right limbs. Blood tests and magnetic resonance imaging were normal. Brain DaT-SCAN SPECT imaging showed loss of presynaptic dopamine transporters, predominantly in both putamen. The genetic test showed two heterozygous pathogenic variants in POLG gene (c.752C>T (p.Thr251Ile) and c1760C>T (p.Pro587Leu)) and a heterozygous pathogenic variant in PRKN gene (c.155del (p.Asn52MetfsTer29)). He started treatment with rasagiline and rotigotine with good response during follow-up.

Conclusion: Heterozygous variants in POLG gene found in this patient have been previously described as pathogenic and may have a causal relationship with EOPD. PRKN mutation, given its heterozygous status, could act as a susceptibility factor. Several combinations of genetic variants linked to polygenic EOPD have been reported. We highlight this case due to the unusual combination of genes involved, which could have a double impact on the development of EOPD.

Disclosure: Nothing to disclose

EPO3246

The X-linked form of Charcot-Marie-Tooth disease with GJB1 and PMP22 gene mutation.

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Background and aims: The X-linked form of Charcot-Marie-Tooth disease (CMTX) is the 2nd common form of hereditary motor- sensory neuropathies. The clinical features of CMTX include progressive muscle atrophy and weakness, sensory loss and also the central nervous system manifestation can be found. Males are more severely affected than females. We report one Slovak family with X-linked Charcot-Marie-Tooth neuropathy who had typical clinical features, but females were more severely disabled than males.

Methods: Clinical examination, electrophysiologic studies, MRI of the brain and molecular genotyping testing was performed.

Results: Motor-nerve conduction velocities were significantly slowed and evoked muscle action potentials were severely reduced. 2 mutations were identified in 2 different genes. The patient was confirmed heterozygote for the Thr118Met substitution in the PMP22 gene and heterozygote for the Val95Met in the GJB1 gene. However, the pathogenic effect of Thr118Met substitution in the PMP22 gene is disputable according to some studies. In this report we will confirm that the Val95Met substitution in the GJB1 gene is pathogenic in this family.

Conclusion: X-linked form of Charcot-Marie-Tooth disease is caused by mutations in the GJB1 gene. A lot of allelic variants can be identified using of exome sequencing, thus focusing us on possible not yet confirmed rare clinical manifestation of both genes mutations (PMP22 and GJB1) with females more affected.

Disclosure: Nothing to disclose

EPO3247

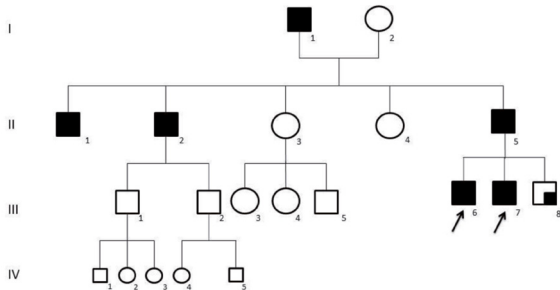
A novel mutation of VCP gene is responsible for Autosomal Dominant (AD) Hereditary Spastic paraplegia (HSP) in a family from Southern Italy.

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Background and aims: Hereditary spastic paraplegias are a group of heterogeneous disorders, with the clinical hallmark of progressive spasticity in the lower limbs. Gene panels and exome/genome-based approaches have provided valid support to diagnosis and have expanded knowledge about the genetic background of these disorders. Variants in VCP gene, known to be responsible for Amyotrophic Lateral Sclerosis type 14 and Inclusion Body Myopathy with Paget Disease and Frontotemporal Dementia type 1, have recently been described in three cases of HSP.

Methods: We describe 2 brothers with slowly progressive spastic gait since their 2nd and 3rd decade of life. The grandfather of the probands, their father and 2 of his brothers have suffered from a similar disorder since their 4th decade, suggesting an AD inheritance.



Pedigree of the family here described with a 3-generation history of progressive isolated spastic gait. Solid symbols indicate affected individuals. Arrows indicate the probands

Results: An extensive diagnostic protocol excluded secondary causes of spastic paraplegia and showed no evidence of lower motor neuron degeneration, myopathy, cognitive deficits or skeletal involvement. Both brothers revealed to carry the novel heterozygous variant c.446-4G>A of VCP gene. Segregation study, performed in the mother and a cousin of the probands, both asymptomatic, confirmed the pathogenicity of the new variant. Significantly, a 3rd sibling of the probands, deceased in his 20^{ties}, suffered from severe skeletal dysmorphism, possibly suggesting a juvenile Paget disease.

Conclusion: We describe 2 cases of HSP due to a novel mutation of VCP gene, within a large family with a history of autosomal dominant gait disorder. Our finding supports the already suggested role of VCP mutations in HSP pathogenesis and further expands the list of known causative variants.

Disclosure: Nothing to disclose

EPO3248

Spastic paraplegia type 7 presenting as subacute cerebellar syndrome

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Background and aims: Mutations in the SPG7 gene encoding a mitochondrial protein called paraplegin are responsible for a recessive form of hereditary spastic paraplegia (HSP). The complicated phenotype of HSP includes cerebellar signs, which is unsurprising since paraplegin is highly expressed in Purkinje neurons. Moreover, recent evidence suggests that SPG7 mutations are a common cause of undiagnosed spastic ataxia.

Methods: A 28-year-old woman was admitted to our clinic for severe gait disturbance and balance impairment with progressive evolution for the last 9 months. She underwent a surgical intervention for endometriosis 5 years prior and had unremarkable family history. Neurological examination revealed gait and limb ataxia, hyperreflexia and bilateral Babinski sign. Brain MRI identified moderate cerebellar atrophy.

Results: Workup for infectious (HIV and syphilis screening), metabolic (including serum ceruloplasmin and copper) and autoimmune disorders (e.g. antineuronal and antiGAD antibodies, oligoclonal bands) was negative. Several genetic tests including spinocerebellar ataxia multigene panel and Friedreich ataxia repeat expansion test were performed. 2 heterozygous SPG7 variants were detected by next generation sequencing and confirmed by classical Sanger sequencing, namely c.233T>A/p.Leu78Ter (pathogenic mutation) and c.2104-2A>C (uncertain significance; splice acceptor). The parents are to be tested genetically in order to confirm the trans configuration of the two heterozygous variants.

Conclusion: Mutation analysis of SPG7 gene should be considered in patients with subacute spastic ataxia. The background of our patient suggests that the c.2104-2A>C variant might be pathogenic, thusly pointing to a novel compound heterozygous SPG7 genotype.

Disclosure: Nothing to disclose

EPO3249

AARS2 mutation-related leukodystrophy: further insight into a rare disorder

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Background and aims: Alanyl-tRNA synthetase 2 (AARS2) gene mutations can present as combined oxidative phosphorylation deficiency 8 (a mitochondrial disease characterized by a lethal infantile hypertrophic cardiomyopathy) and childhood to adult-onset leukoencephalopathy (a neurodegenerative disorder marked by progressive neurologic deterioration and ovarian failure in female patients). Few patients have been reported worldwide so far.

Methods: N/A

Results: A 36-year-old male Portuguese patient, with normal psychomotor development and no known family history of neurologic disease or consanguinity, presented to our outpatient clinic with a progressive cognitive decline during the previous year. It was initially interpreted as a depressive disorder, and he was undergoing antidepressant treatment, albeit with no clinical improvement. 3 months after our evaluation he was also reported to have developed an obsessive-compulsive behavior. On examination there was gait ataxia in tandem walking, brisk reflexes and Babinski sign on the right side, with gaze-evoked horizontal nystagmus. A brain MRI revealed extensive symmetrical white matter changes with a butterfly-shaped pattern and frontal predominance, without contrast enhancement. Blood and CSF analysis were unremarkable. Next generation sequencing genetic testing revealed 2 heterozygous compound mutations in AARS2 gene (c.2255+1G>A; c.595C>T).

Conclusion: Adult-onset leukodystrophies are rare and pose a diagnostic challenge. AARS2 mutation related leukodystrophy is not only rare but still poorly understood, with a variable clinical presentation. We present the 1st Portuguese case of AARS2-related adult-onset leukodystrophy, presenting with neuropsychiatric symptoms, and due to a compound heterozygosity casting further insight into the characterization of this new entity.

Disclosure: Nothing to disclose

EPO3250

Two Cases of X-Linked Adrenoleukodystrophy Confirmed by Genomic Analysis of the ABCD1 Gene: the 1st to be Reported from East Africa

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Background and aims: Non-infectious causes of chronic progressive non-traumatic spastic paraparesis (PNSP) are rarely reported from sub-Saharan Africa (SSA) due to the severe lack of diagnostic services, particularly magnetic resonance imaging (MRI). A rare cause of PNSP is X-linked adrenoleukodystrophy (X-ALD), of which only a few cases have been reported from North Africa.

Methods: We describe 2 unique cases from SSA presenting with PNSP who, after extensive investigations, were found to have X-ALD confirmed through both biochemical and genetic testing.

Results: Case 1: A 36-year-old female presented with a decade of PNSP and urinary urgency, all exacerbated during pregnancy. Neurological examination confirmed spastic paraparesis with extensor plantars, and absent large-fibre sensation to the knees. MRI neuraxis revealed severe thoracic cord atrophy, and serum very long chain fatty acids (VLCFA) analysis revealed increased C26, C24:C22 and C26:C22 levels. Genomic sequencing of the ABCD1 gene showed heterozygosity for p.(Arg617His),c.1850G>A, confirming X-ALD.

Case 2: A 38-year-old male presented with 20 years of PNSP, eventually leading to quadriplegia and bulbar dysfunction in the latter decade, and was now wheelchair-bound. Neurological examination revealed spastic quadriplegia and global ataxia. MRI neuraxis revealed large symmetrical parieto-occipital and splenial hyperintense signals with cervical cord atrophy. VLCFA were similarly abnormal to Case 1, and ABCD1 genetic analysis showed hemizyosity for c.1469_1471dup,p.(val490dup) in-frame variant in exon 5, confirming X-ALD.

Conclusion: Our cases are the 1st to illustrate that X-ALD exists in SSA. Access to appropriate diagnostics provides patients with an explanation for their PNSP and possible implications for their families.

Disclosure: Nothing to disclose

EPO3251

Clinical presentation of adult-onset leukoencephalopathy with axonal spheroids and pigmented glia associated with an A792D mutation in the CSF1R gene.

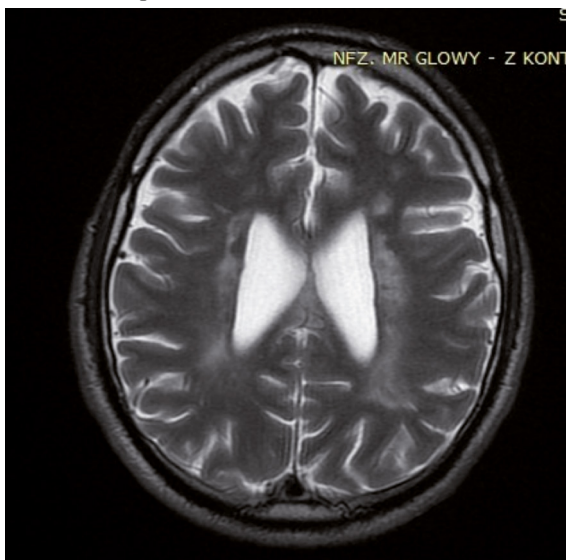
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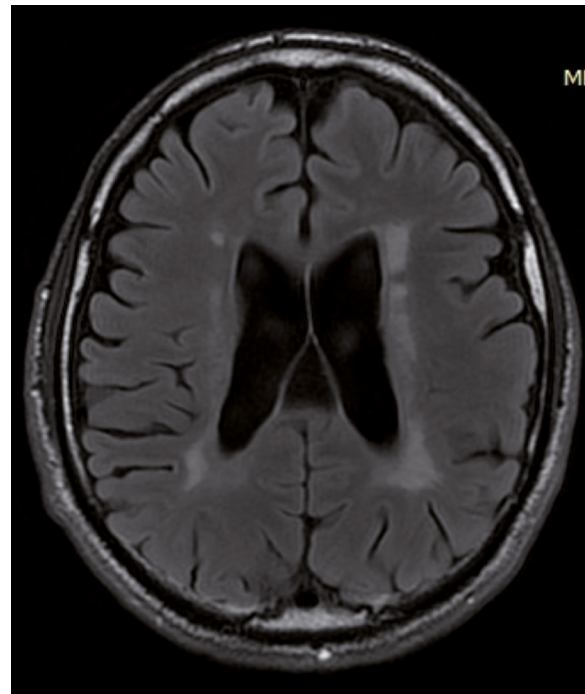
Background and aims: Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia is a rare, autosomal dominant, white matter disease with a wide spectrum of clinical presentation. Here, we report the phenotypic description of a rapidly progressive Caucasian patient with an A792D mutation in the CSF1R gene. This variant has been described in Japanese families and was previously characterized by slow progression and late onset.

Methods: The genotype was identified through sequencing exons of the CSF1R gene.

Results: In 2017, a 38-year-old, Caucasian male with no familial history of neurological disorders, presented with symptoms of dysarthria, bradykinesia and gait disturbances. In 2018 he began to show cognitive dysfunction and became overemotional. In 2019 he presented with urinary incontinence and erectile dysfunction. A brain MRI scan revealed multifocal signal abnormalities in the periventricular and deep cerebral white matter, with a large confluent lesion in the right hemisphere. There was incomplete sparing of the subcortical white matter and multifocal diffusion restricted lesions. Neuropsychological examination showed subcortical cognitive deficits suggesting damage to fronto-subcortical networks. After 3 years of symptoms, the onset EDSS score was 5. In November 2019, the patient received an allogenic bone marrow transplantation.



Multifocal signal abnormalities in the periventricular white matter.



Disease progression after 6 months. T2 FLAIR

Conclusion: This report presents a case study of a 38-year-old Caucasian male who presented with rapid, progressive, adult-onset leukoencephalopathy with axonal spheroids and pigmented glia related to an A792D mutation in the CSF1R gene.

Disclosure: Nothing to disclose

Neuroimmunology 3

EPO3252

Eight-and-a-half syndrome as manifestation of Neurobehçet

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Background and aims: Behçet's disease is a chronic systemic inflammatory disease of unknown cause. Eight-and-a-half syndrome is characterized by the combination of one-and-a-half syndrome (conjugated horizontal gaze palsy and internuclear ophthalmoplegia) with ipsilateral facial palsy. Although rare, it allows precise anatomical location at the lower level of the ipsilateral pontic tegment. Aetiology is usually vascular or demyelinating.

Methods: Case Report: Male, 26-years-old, with history of recurrent oral aphthous ulcers, admitted after acute onset of facial asymmetry, horizontal double vision and fever.

Results: On examination, there was right conjugate gaze palsy and internuclear ophthalmoplegia on left gaze, right facial palsy with Bell's sign, right hypoacusia and slight right hemiataxia. Brain MRI revealed a tumefactive lesion extending from right paramedian pontine territory to right middle cerebellar peduncle, hyperintense on T2 and FLAIR, showing contrast enhancement and normal DWI-MRI. CSF analysis revealed pleocytosis (400cells/ μ l, polymorphonuclear predominance), mild hyperproteinorachie (59mg/dL) and normal glycochorrhachia. In the following days, the patient presented fever, recurrence of oral and genital ulcers and increased inflammatory blood parameters. Neuroophthalmologic evaluation revealed signs of right vitritis and peripheral retinal vasculitis. The diagnosis of Behçet's Disease with CNS involvement was assumed and corticosteroid therapy and monthly cyclophosphamide cycles were started with improvement.

Conclusion: Although CNS disease rarely occurs in Behçet's disease, when this happens there is a predilection for brainstem involvement. This case highlights the eight-and-a-half syndrome as a clinical manifestation of neurobehçet and, being a potentially treatable disease, illustrates the importance of early diagnosis and treatment of this disease.

Disclosure: Nothing to disclose

EPO3253

The influence of catecholamines on Th17-cells in multiple sclerosis

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Background and aims: Catecholamines may participate in multiple sclerosis (MS) pathogenesis by modulating immune cell activity. The aim of this study was to clarify the effects of catecholamines on Th17-cells which play crucial pathogenic role in MS.

Methods: 35 MS patients and 20 healthy controls were examined. Levels of dopamine and norepinephrine in plasma were determined by HPLC. The percentage of Th17-cells was determined by flow cytometry (CD4⁺CD26⁺CD161⁺). CD4⁺-T-cells were stimulated with anti-CD3/anti-CD28-antibodies in the absence/presence of dopamine/norepinephrine at concentrations of 10⁻⁴M, 10⁻⁵M and 10⁻⁶M whereafter levels of IL-17, IFN-gamma, GM-CSF and IL-21 in supernatants were determined by ELISA. Some samples of CD4⁺-T-cells were pre-incubated with antagonists of D1(SCH23390)- or D2(sulpiride)-like dopaminergic receptors (both at 10⁻⁵M) whereafter dopamine (10⁻⁵M) and anti-CD3/anti-CD28-antibodies were added to the cultures. Statistical analysis was performed using Prizm 6 software.

Results: The concentrations of dopamine and norepinephrine in plasma were not different between the groups. The percentages of Th17-cells as well as the production of cytokine were comparable. Dopamine and norepinephrine at concentration of 10⁻⁵M suppressed cytokine production in both groups (p<0.001) without affecting cell viability and proliferative response. At concentration of 10⁻⁴M dopamine and norepinephrine suppressed cytokine production (p<0.001), but reduced cell viability and proliferative responses, while at concentration of 10⁻⁶M, dopamine and norepinephrine had no effect on cytokine production. Blockade of D1-like receptors enhanced the inhibitory effect of dopamine (p<0.001) while blockade of D2-like receptors abolished the effect of dopamine in both groups (p<0.001).

Conclusion: These data suggest an inhibitory effect of catecholamines on Th17-cells in MS.

Disclosure: This study was supported by grant from the Russian Science Foundation (project №19-75-00075).

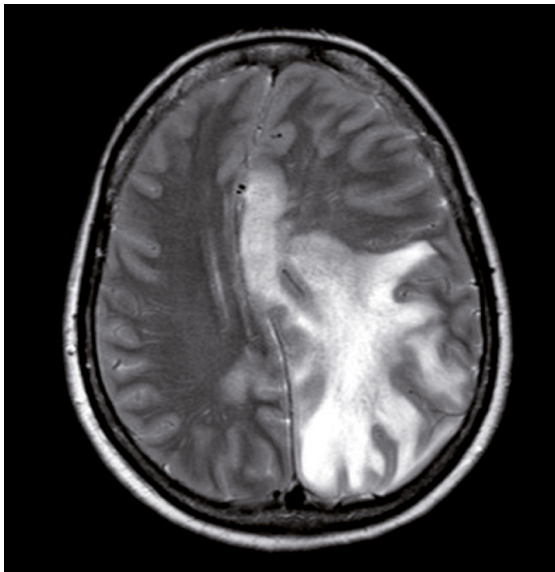
EPO3254

Disseminated necrotizing leukoencephalopathy associated with methotrexate therapy

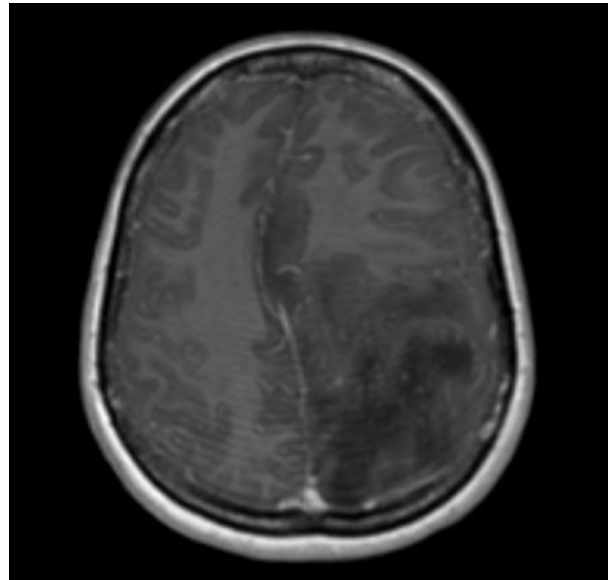
L. Mokosova, J. Haring
Trnava, Slovakia

Background and aims: Leukoencephalopathy is a potentially serious complication of chemotherapy, especially when methotrexate is used. The mechanism of origin is unknown, but may involve a direct toxic effect on axons, oligodendrocytes and progenitor cells, as well as secondary immunological reactions, oxidative stress and microvascular damage. Disseminated Necrotizing Leukoencephalopathy (DNL) is a term reserved for severe, typically progressive and fatal form of the disease.

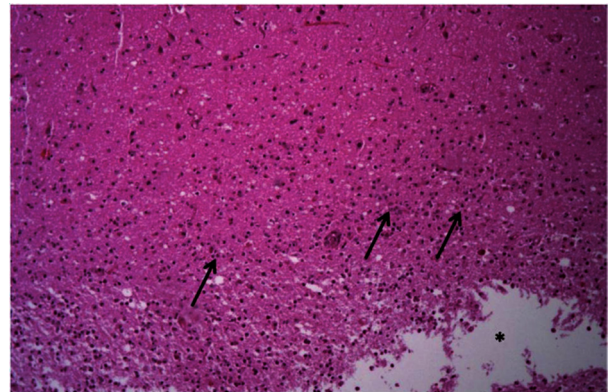
Methods: MRI may be helpful in differentiation lighter forms of leukoencephalopathy and distinguishing them from DNL, which is characterized by hyperintensity lesions in T2-weighted images with a nonvascular pattern, with restricted diffusion, mostly with intense tumor-like enhancement and severe mass effect. Histopathological study was done post mortem.



MRI T2 image



MRI T1 image



Histology, necrotic lesion with disintegration (*) and brain tissue with gliosis (arrows) and edema

Results: In our case report we present a 46-year-old woman on long-term methotrexate therapy for Sjögren's syndrome and purpura vasculitis, who developed acute necrotizing leukoencephalopathy 2 weeks after exposure to influenza virus with dramatic clinical feature with fatal outcome.

Conclusion: The aim of the case report is to highlight a rare fatal disease whose diagnosis is based on high clinical suspicion in the absence of specific imaging or laboratory tests. This disease should be considered in the case of a fulminant clinical course of an expansive intracranial tumor-like process with a history of long-term exposure of the patient to methotrexate.

Disclosure: Nothing to disclose

EPO3255

Anti-Hu-associated paraneoplastic syndromes triggered by immune-checkpoint inhibitor treatment

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Background and aims: Anti-Hu antibodies (Hu-Ab) are associated with diverse phenotypes of paraneoplastic neurological syndromes (PNS), usually in the context of small-cell lung cancer (SCLC). Recently, the introduction of immune checkpoint inhibitors (ICIs) has led to a paradigm shift in the management of many types of cancer. Side effects include neurological immune-related adverse events. Herein we present a sensory neuronopathy and a cerebellar degeneration after ICIs treatment.

Methods: Case series and a review of the literature.

Results: Case 1: A healthy 46-year-old male with SCLC received chemotherapy and 4 doses of pembrolizumab. Twelve weeks later he presented severe 4-limb ataxia and alteration of all sensory modalities. Electroneuromyography demonstrated a non-length-dependent axonal sensory neuronopathy, and Hu-Ab were detected in serum and cerebrospinal fluid (CSF) using immunohistochemistry and Western blot. The treatment with prednisolone and intravenous immunoglobulin (IVIG) temporarily improved his condition, but he eventually died due to pneumonia.

Case 2: A healthy 71-year-old male patient with SCLC was treated with chemotherapy and 3 doses of atezolizumab. 9 weeks after, examination revealed a cerebellar syndrome manifested as gaze-evoked nystagmus, mild dysarthria, and severe gait and trunk ataxia. The diagnostic exams revealed an inflammatory CSF with positive Hu-Ab in both serum and CSF. IVIG were administered, with mild clinical improvement

All previously reported ICI-related Hu-Ab cases were autoimmune encephalitis, and had at best a modest response to immunosuppressive drugs (Table).

Table 1: Paraneoplastic neurological syndromes with anti-Hu antibodies after immune checkpoint inhibitors treatment

Sex , age	Tumor	ICI (doses)	nirAEs	Treatment	mRS evolution	Ref
F, 71	SCLC	Nivolumab+ipilimumab (1)	LE	Methylprednisolone, Natalizumab	4→3	1
M, 46	Myxoid chondrosarcoma	Cemiplimab (4)	LE	Methylprednisolone, IVIG	3→6	2
M, 60	Pleomorphic carcinoma lung	Nivolumab (3)	LE	Methylprednisolone, plasma exchange	5→6	3
M, 58	NSCLC	Nivolumab (16)	AE	Dexametasonone	4→3	4

Abbreviations: AE, autoimmune encephalitis with extralimbic involvement; F, female; ICI, immune checkpoint inhibitor; IVIG, intravenous immunoglobuline; LE, limbic encephalitis; M, male; mRS, modified Rankin scale; nirAE, neurological immune-related adverse event; NSCLC, non-small-cell lung cancer; Ref, reference; SCLC, small-cell lung cancer.

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Paraneoplastic neurological syndromes with anti-Hu antibodies after immune checkpoint inhibitors treatment

Conclusion: We might expect an increased incidence of HU-Ab PNS since the introduction of ICI in SCLC treatment, being imperative to be fully aware of their complex clinical presentation.

Disclosure: Nothing to disclose

EPO3256

Longitudinal extensive transverse myelitis: a new presentation of IgG4-related disease?

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Background and aims: IgG4-related disease is an immune mediated disorder that can involve many organs, including the central and peripheral nervous systems. The most common neurological manifestations are pachymeningitis, hypophysitis and orbital disease.

Methods: Case report

Results: We report a 65-year-old male, that by 39 years of age developed a cerebellar syndrome, right motor and sensory deficits with pyramidal signs. Head-CT disclosed fronto-orbital contusions related to previous trauma. CSF had 5 lymphocytes and proteins 0.65g/dL. Suspecting multiple sclerosis, he was treated with adrenocorticotropic hormone, gradually recovering. At 54 years old he developed a paraparesis with urinary retention, bilateral pyramidal syndrome, pain sensory loss with T4 level and hypopallesthesia. MRI documented a spinal cord T2 extensive hypersignal from C2 to T11, suggesting a longitudinal extensive transverse myelitis (LETM). CSF had pleocytosis (88 lymphocytes, 38 eosinophils), proteins 0.82g/dL, normal IgG index without oligoclonal bands. He presented eosinophilia, high IgE (370U/mL) and IgG4 (231mg/dL), with negative anti-Aquaporin 4/anti-MOG antibodies and microbiological/parasite studies. Other immunological studies were normal. Chest-abdomen-pelvis CT and evoked visual potentials were normal. He was medicated with methylprednisolone (5 days), and 1mg/kg prednisolone afterwards (tapered slowly), maintaining 2.5mg/day in the last 8 years. He fully recovered and has been asymptomatic for 11 years of follow-up. Recently he maintained high IgG4 (319mg/dL), still without systemic involvement.

Conclusion: We report a case of LETM, in a patient with high levels of IgG4, in the absence of other auto-immune disease. To the best of our knowledge this is the 1st description of LETM associated to IgG4-related disease.

Disclosure: Nothing to disclose

EPO3257

Neuromyelitis optica Spectrum Disorders (NMOSD): two cases with atypical presentation

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Background and aims: The association between NMOSD and other disorders have been described. However, peripheral neuropathy or Syringomyelia as complication of NMOSD have been rarely reported.

Methods: Clinical, laboratory and neuroimaging findings of 2 patients with NMOSD (anti-aquaporin-4 seropositive) associated with atypical disorders are described:

CASE 1. A 68-year-old woman had acute transverse myelitis: NMOSD with Syringomyelia-like syndrome was diagnosed

CASE 2. A 79-year-old woman had suddenly cervical pain, loss of strength of lower extremities. Symptoms worsened to severe quadriplegia and sensory loss with high cervical level. EMG findings were compatible with acute polyradiculoneuropathy. Concurrent NMOSD was diagnosed.

Results: In case 1, spinal cord MRI revealed hyperintensities in the cervico-thoracic spine with large cystic lesion (D1-D7).

In case 2, spinal cord MRI revealed hyperintensities in the cervico-thoracic spine (C2-D2). NMO was commonly believed to be confined to optic nerves and spinal cord, with no involvement of the peripheral nervous system (PNS).

Conclusion: CASE 1: Syringomyelia was reported predominantly located in the lower cervical and upper thoracic spinal cord. Non-communicating syringomyelia (NCS) has occasionally been described as an incidental finding pathology in patients with multiple sclerosis (MS). CASE 2: only few reports were reported describing characteristics of neuropathy as rare complication of NMO. Anti-AQP-4 antibody cannot cause neuropathy because AQP-4 is a cell membrane water channel expressed at the astrocyte foot process, and there are not astrocytes in the PNS. Pathogenesis of neuropathy may be T-cell immunomediated and related to epitope spreading from CNS to PNS myelin antigen as occurred in MS.

Disclosure: Nothing to disclose

EPO3258

Seronegative neuromyelitis optica spectrum disorders in a Thai patient

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Background and aims: New diagnostic criteria for Neuromyelitis Optica Spectrum Disorders (NMOSD) have been published. The aim of this report was to discuss the role of new diagnostic criteria in clinical practice with focus in patient without anti-aquaporin-4 (AQP-4) antibody. Differential diagnosis from MS is needed.

Methods: Clinical manifestations, laboratory parameters and neuroimaging findings of a patient with NMOSD but no AQP-4 antibody, were collected.

Results: A 55-year-old Thai woman experienced nausea, hiccups and gastric pain. After 1 month daytime somnolence occurred, followed by gait ataxia, urinary retention, blurred vision. Brain magnetic resonance revealed hyperintense lesion in the 1st 2 cervical segments with rostral extension to brainstem. Anti-AQP-4 antibody were negative, CSF analysis showed pleocytosis (74 cells) and oligoclonal bands. Intravenous Methylprednisolone was given with clinical and radiological improvement

Conclusion: New diagnostic criteria for NMOSD have been recently published. Our patient did not fulfilled the 2006 diagnostic criteria. However, she presented 2 core clinical characteristics with neuroimaging findings in accordance with clinical data, as required for the diagnosis of seronegative NMOSD. The CSF findings were partially in agreement. In fact the panel considered CSF pleocytosis (useful for differential diagnosis) and the presence of oligoclonal bands, on the contrary, as a red flag for diagnosis of NMOSD. It is needed a careful monitoring of clinical (further relapse, response to therapy) and humoral (serological retesting) data to strengthen the diagnosis and to better characterize heterogeneity of seronegative NMOSD patients

Disclosure: Nothing to disclose

EPO3259

Agrypnia excitata as main feature in anti-LGI1 antibodies encephalitis: a case report.

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Background and aims: Seizures, faciobrachial dystonic seizures (FBDS), behavioural changes, mnemonic deficit represent the clinical hallmark of Leucine-rich-glioma-inactivated1 (LGI1) autoantibodies associated encephalitis. Agrypnia excitata (AE) is a rare condition, observed in few diseases, characterized by disruption of the sleep-wake cycle, autonomic hyperactivation and episodes of oneiric stupor (EOS). We describe a singular case.

Methods: Detailed clinical, video-polysomnography (video-PS), laboratory and radiological assessment and long-term follow-up were done.

Results: An healthy 58-year-old man arrived at the emergency room because of confusion and generalized tonic-clonic seizure. During last month he had developed insomnia, behavioral change, spasms.

He was disoriented with deficit in episodic memory. During hospital-stay he showed FBDSs but, more significantly, a complete loss of the physiological sleep-wake cycle and dysautonomia with tachycardia and hyperhidrosis. During the day he fluctuated between an awake and a drowsy state and presented curious episodes of complex gestures mimicking various daily activities. Peripheral nerve hyperexcitability was absent.

Prolonged video-PS showed no epileptic patterns but only a mild slowdown of background activity and intermittent generalized delta slowdown without a regular wakefulness or sleep state.

Laboratory exam showed persistent mild hyponatremia. Brain positron emission tomography with fluoro-deoxyglucose showed a hyper metabolism of hippocampi, amygdala and basal ganglia. Anti-LGI1 antibodies were found in cerebrospinal fluid.

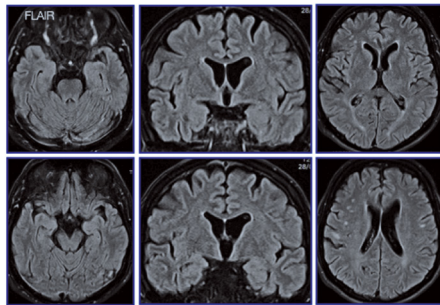
After high dose corticosteroids and plasma exchange a regular sleep-wake cycle was progressively achieved. Episodic memory and executive function deficits still persisted after 6 months of cyclophosphamide and rituximab therapy.

Case Report - EEG



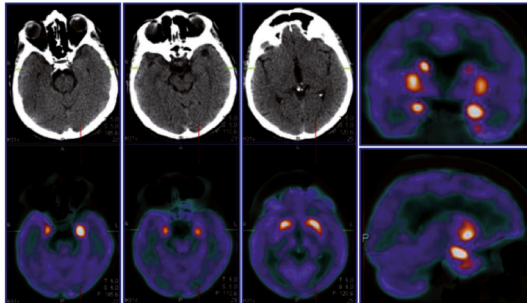
EEG

Case Report - Brain MRI



brain MRI

Case Report - Brain CT/PET/FDG



brain CT/PET with FDG

Conclusion: AE can be the major clinical feature of anti-LGI1 encephalitis. EOS represent a useful diagnostic marker.

Disclosure: Nothing to disclose

EPO3260

Probable autoimmune encephalitis with negative anti-neuronal antibodies: a diagnostic and therapeutic challenge

R. Pinheiro, F. Bernardo, S. Machado, A.N. Pinto,

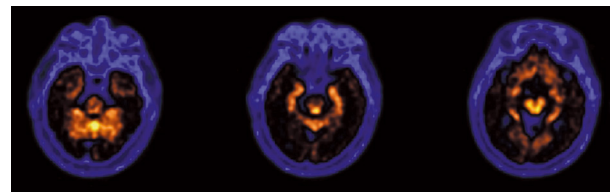
E.P. Parreira

Amadora, Portugal

Introduction: Autoimmune encephalitis (AE) is an increasingly recognized neurological disease. In the presence of a typical clinical presentation, with MRI, electroencephalographic and laboratory findings suggestive of encephalitis, particularly when an anti-neuronal antibody is identified, the diagnosis becomes evident. However, cases with negative anti-neuronal antibodies are a challenge with important prognostic implications.

Methods: (Case report - not applicable)

Results: Clinical Case: A 64-year-old alcoholic male presented with 2-months evolution of progressive cognitive impairment with memory, language and executive deficits, behavioural changes and consciousness fluctuations. The neurological examination revealed disorientation, global aphasia, attention impairment, facial hypomimia, axial and appendicular stiffness. MRI showed bilateral parietal and mesio-temporal atrophy and mild bilateral T2/FLAIR hyperintensity. EEG registered diffuse slowing of electrogenesis. The PET-FDG findings consisted of marked symmetric cortical hypometabolism. CSF analysis, extensive neuronal surface antibodies and occult neoplasia screening were negative. Because of the clinical and imaging findings suggestive of probable AE, he was treated with intravenous methylprednisolone followed by oral prednisolone, 2 cycles of intravenous human immunoglobulin and azathioprine. The patient recovered most of the initial deficits, maintaining slight verbal comprehension impairments.



PET-FDG: marked symmetric cortical hypometabolism

Conclusion: We present a case of possible AE with negative anti-neuronal antibodies and favourable clinical response after immunotherapy. Even in the absence of a specific anti-neuronal antibody, a typical clinical picture associated with imaging changes should raise the suspicion of AE and early immunotherapy initiated to improve functional response and reduce the likelihood of recurrence.

Disclosure: Nothing to disclose

EPO3261

Anti-GAD65 antibody-associated cerebellar ataxia as presentation of lung adenocarcinoma

R. Pinheiro, F. Bernardo, S. Machado, A.N. Pinto,
E.P. Parreira
Amadora, Portugal

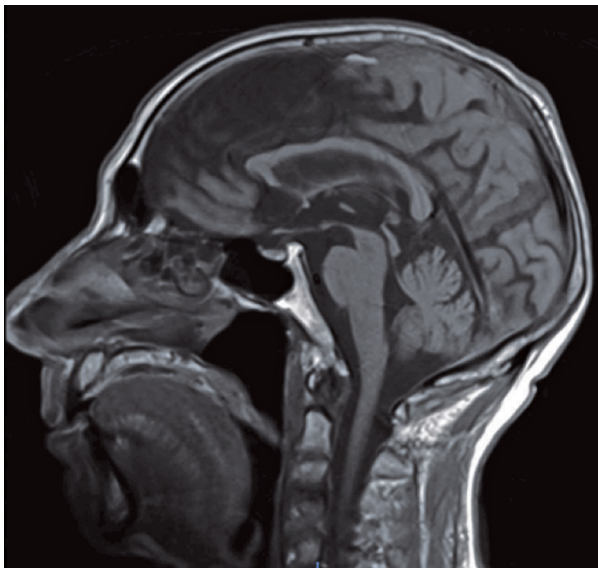
Introduction: Anti-GAD65 antibody-associated cerebellar ataxia is an immune-mediated cerebellar ataxia that occurs commonly in women with type 1 diabetes mellitus. Although not typically related to tumours, recent studies report a possible association of this clinical entity with occult neoplasms, resembling the classic paraneoplastic syndromes.

Methods: (Case Report - not applicable)

Results: Clinical Case: A 75-year-old male with heavy smoking and drinking habits presented with 3-month progressive worsening of gait imbalance, appendicular incoordination, dysarthria, dysphagia and weight loss greater than 10%. The neurological examination revealed moderate dysarthria, opsoclonus, hypermetric saccades, nystagmus and bilateral appendicular and axial ataxia. MRI revealed diffuse cerebral and cerebellar parenchymal atrophy. Spinal MRI, electromyographic and CSF findings were normal. The remaining investigation detected anti-GAD65 antibody, increased neuron-specific enolase and beta2-microglobulin. The search for an underlying tumour with whole body CT/PET-FDG revealed a right perihilar pulmonary mass and mediastinal-hilar adenopathies that were biopsied by bronchial echoendoscopy. The histopathological result was lung adenocarcinoma. The patient was initially treated with intravenous immunoglobulin, with transient improvement of the pancerebellar symptoms. Subsequently, with tumour chemotherapy there was total resolution of the symptomatology.

Conclusion: We present a case of anti-GAD65 antibody-associated cerebellar ataxia in a man with lung adenocarcinoma. Although rarely of paraneoplastic origin, the presence in an older male patient of constitutional symptoms and atypical neurological signs such as opsoclonus, should prompt active screening for occult neoplasm, due to the inherent therapeutic and prognostic implications.

Disclosure: Nothing to disclose



MRI: diffuse cerebral and cerebellar parenchymal atrophy

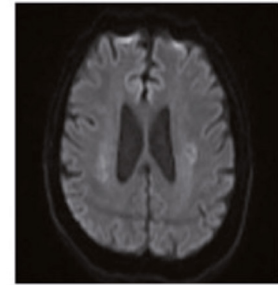
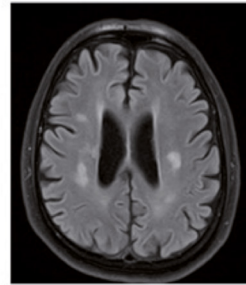
EPO3262

CNS Demyelination after Treatment with Nivolumab for Metastatic MelanomaB. Popinhak¹, G. Fernandes¹, H. Andrade²¹Porto Alegre, Brazil, ²Neurology, Moinhos de Vento Hospital, Porto Alegre, Brazil

Introduction: Immune checkpoint inhibitors (ICPIs) are agents against the ‘inhibitory’ co-stimulatory T-cell molecules currently approved for the treatment of advanced neoplasms such as metastatic melanoma, non-small cell lung cancer and Hodgkin’s lymphoma. However, they may trigger immune mediated neurological disorders, which may be fatal.

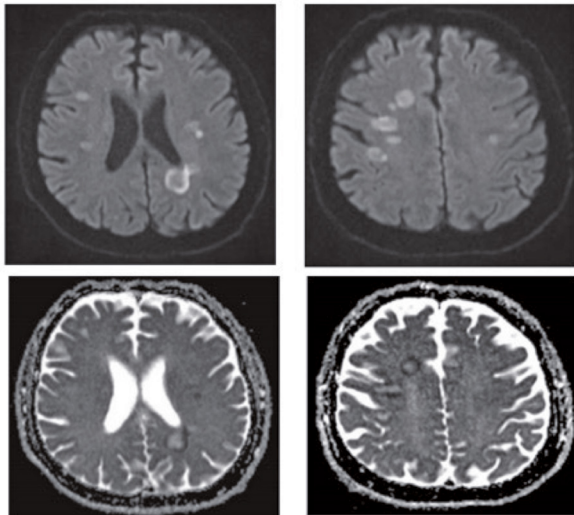
Methods: Case report of a patient diagnosed with central nervous system (CNS) demyelination after treatment with Nivolumab for metastatic melanoma.

Results: 65-year-old caucasian male, admitted with subacute onset of bradyphrenia, anomia and left lower limb paresis. Brain MRI showed multiple supratentorial nodular lesions with peripheral restricted diffusion, complete and incomplete halo of gadolinium enhancement, without significant edema (figure 1). Cerebrospinal fluid analysis showed normal cell count, glucose content and protein level. Oligoclonal bands were positive. A diagnosis of CNS demyelination was made. He was treated with methylprednisolone 1g daily for 5 days followed by intravenous human immunoglobulin 2g/Kg with complete clinical response a few days later. BrainMRI performed 6 months later showed resolution of gadolinium enhancement and significant decrease in the size of the lesions (figure 2). Since severe relapses have been reported, he was continued on azathioprine, still asymptomatic after one year of follow up.



Conclusion: Patients on ICPIs with neurological symptoms should be promptly evaluated for immune mediated disorders. Given its potential severity, we suggest aggressive immunomodulatory treatment with corticosteroids and IVIG in patients with severe symptoms. Continued immunosuppression should be considered.

Disclosure: Nothing to disclose



EPO3263

A fourth category of VGKC positive patients: A retrospective study from a south Indian population.

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Background and aims: Traditionally VGKC (Voltage Gated potassium channel) autoimmune encephalitis (AE) is categorized into LGI1, CASPR2, or both negative. We identified a 4th category of patients, who were positive for both LGI1 and CASPR2 and aim to highlight their clinical characteristics and outcomes.

Methods: We retrospectively selected patients admitted to a university hospital between January 2016 to December 2019 with a serologically proven diagnosis of VGKC positive AE. Patients with encephalopathy secondary to infection, structural lesions, drug/toxin related, nutritional or metabolic were excluded. Data on history, examination, baseline investigations, Cerebrospinal-fluid analysis, neuroimaging and outcomes were collected. Comparative analysis was done between the 3 VGKC autoimmune subgroups A) LGI1 positive B) CASPR2 positive and C) LGI1 and CASPR2 positive.

Results: 16 patients were included in the study, out of which 12 were positive for LGI1, 2 were positive for CASPR2, and 2 patients positive for both. Clinically 77% of LGI1 patients had behavioural changes, 55% had the characteristic facio-brachial dystonic seizures whereas 33% had GTCS (Generalised tonic-clonic seizures). Both the CASPR2 patients presented with behavioural changes, whereas one of them had hallucination, and fasciculation. In contrast patients who were positive for both antibodies, had isolated neuromyotonia. IVIG (Intravenous Immunoglobulin) was required for 2 patients from the LGI1 group, none from the CASPR2 group and for both dual positive patients.

Conclusion: The 4th subgroup highlighted in this study, describes patients with antibody positivity to both LGI1 and CASPR2, presenting with isolated neuromyotonia, with absence of seizure or behavioural disturbances, requiring IVIG, and making good recovery without relapses.

Disclosure: Nothing to disclose

EPO3264

Anti-IGLON5-Syndrom presenting fasciculations and oculomotor palsy associated with renal neoplasia

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Background and aims: Anti-IGLON5-Syndrom is a new and likely underdiagnosed entity. Because of the unspecific symptom presentation patients often experience a grave disease progression until its diagnosis. Even if it is recognized in an early stage a fatal outcome still has a high incidence. The association with a paraneoplastic genesis can lead to the detection of early stage cancers, which offers a causal treatment for both, the neoplasia and the autoimmune encephalitis.

Methods: The following case report is based on clinical, neurophysiological and laboratory investigations as well as diagnostic imaging over a one year period.

Results: A 64-year-old patient presented with generalized fasciculations, incomplete palsy of the left N. abducens and the right N. oculomotorius, unsteady gait, hypo- and apnoea, catathrenia, fatigue, cognitive deficits, areflexia of the legs and ventricular premature beats. Extensive diagnostics led to the diagnosis of an HLA-DQB1*05:01 positive anti-IGLON5-Syndrom with a significantly positive serum titre and the exclusion of competing differential diagnosis. After an initial treatment with high dose methylprednisolone for three days a partial recovery occurred. We initiated an immunosuppressive long-term treatment with azathioprine and intravenous immunoglobulin in 3-month cycles. A tumour screening revealed a left sided clear cell renal cell carcinoma (pT1a NX L0 V0 Ro G2). A complete resection without any complications was performed. Follow-up investigations showed a continuous decline of the serum titre and the symptoms.

Conclusion: Early immunosuppressive and eventually oncologic treatment is likely to reduce the symptoms and possibly leads to the depletion of antineuronal antibodies. A screening for malignancies should be performed repetitively.

Disclosure: Nothing to disclose

EPO3265

Assessment of immunomodulatory properties of Wharton's jelly mesenchymal stem cells in cultures with human oligodendroglia cell line MO3.13 and cerebrospinal fluids - regarding clinical applications in multiple sclerosis.

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Background and aims: Multiple sclerosis (MS) is a peculiar neurological disorder of immunological etiology. Experimental cell therapies using mesenchymal stem cells emerged as a response to the demand of a new treatment options, intrathecal rout of stem cells delivery in being tested. Wharton's jelly mesenchymal stem cells (WJ-MSCs) unique features (e.g. high proliferation rates, immunoregulatory potential) make them a very interesting research and therapeutic model. A model of WJ-MSCs and human oligodendroglia cell line MO3.13 (OLs) cultures incubated with cerebrospinal fluid (CSF) was designed to imitate the conditions of the subarachnoid space and reflect immunomodulatory particular properties of WJ-MSCs.

Methods: Cultures of WJ-MSCs and OLs conducted separately and simultaneously were incubated with 5% CSF collected from MS patients and healthy controls. After 48 hours of incubation supernatants were harvested and analyzed towards released 27 cytokines and trophic factors using Bio-Plex Multiplex Immunoassays (Biorad).

Results: In WJ-MSCs cultures we observed increased levels of cytokines: IL-1b, IL-5, IL-6, IL-8, IL-9, chemokines: IFN gamma, MCP-1, MIP-1b and trophic factors: G-CSF, FGF, VEGF. Addition of MO3.13 and MS CSF resulted in significant higher expression of IL-6, IL-8, eotaxin and MCP. In co-cultures incubated with control CSF IL-6 and IL-8 were hardly detectable.

Conclusion: Immunological and regenerative potential of WJMSCs are strongly dependent on the conditions of particular environment in which they are delivered. This features require further investigation to create a better model of cell therapy for MS patients.

Disclosure: Research was co-financed from a university grant for PhD student, Medical University of Lodz, Poland.

EPO3266

A case of a descending variant of Guillain-Barré syndrome masqueraded by Lyme disease

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Background and aims: Guillain-Barré syndrome (GBS) is an acute immune-mediated polyneuropathy that usually presents with progressive ascending weakness. A descending presentation with onset in the face or arms, dysphagia, ophthalmoplegia and ptosis is less common. While there are many infections associated with GBS, the association with Lyme disease (LD) is rare.

Methods: A 39-year-old man presented with bilateral facial weakness, tingling in his fingers and neck pain. The patient underwent physical and neurological examinations (NE), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the brain and cervical spinal cord, Nerve conduction studies (NCS), Cerebrospinal fluid (CSF) and serological tests for *Borrelia burgdorferi*.

Results: NE revealed bilateral peripheral Cranial Nerve (CN) VII palsy and decreased upper limb reflexes. No pathological changes were detected on the performed CT and MRI. CSF studies showed increased leukocytes and total protein. Due to positive serology and CSF for LD, he was started on antibiotic therapy. But while on therapy, he developed weakness in his hands. NCS showed demyelinating sensorimotor polyneuropathy in the upper limbs while NCS of the lower limbs were normal. A couple days later, due to complaints of tingling in his toes and difficulty walking, repeat NCS revealed demyelinating polyneuropathy in the lower limbs as well. IVIG was started, which halted progression of the weakness.

Conclusion: We aim to accentuate *Borrelia burgdorferi* as an important antecedent infection associated with the development of GBS. A wide spectrum of clinical features necessitates the exclusion of mimics to confirm a diagnosis of GBS.

Disclosure: Nothing to disclose

EPO3267

Use of a vaccinia virus gene product to neutralize interferon-alpha and improve the histopathology of HIV encephalitis in a mouse model

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Background and aims: Interferon-alpha plays a key role in neurocognitive defects associated with human immunodeficiency virus (HIV) and HIV encephalitis. The aim of this study was to assess the effects of a novel inhibitor of interferon-alpha (B18R) in an HIV encephalitis severe combined immunodeficiency mouse model.

Methods: Human macrophages were cultured and infected with HIV-1. Mice (5 week old B6.CB17-Prkdcscid/SzJ) were inoculated with HIV-infected (n=16) or uninfected (n=8) macrophages. The B18R was produced by a modified recombinant procedure. Each B18R treated mouse received 50 mcg per day for 10 days. Brain sections were stained by an immunoperoxidase method. The genes ISG15, IFNA4, and Ifrg15 were analyzed using real-time polymerase chain reaction (PCR).

Results: Gene expression of interferon-alpha signaling was downregulated in the brain by B18R as shown by polymerase chain reaction (PCR). Mononuclear phagocytes were significantly decreased in mice treated with B18R when compared to untreated mice. However, neuronal arborizations were significantly retained in mice treated with B18R when compared to untreated mice. Significant increase in mononuclear phagocytes and loss of neuronal arborization are prominent signs of HIV encephalitis. Findings of this study indicated that the B18R crossed the blood-brain barrier, blocked interferon-alpha signaling in the brain, and improved defects associated with HIV encephalitis.

Conclusion: Findings of this study might suggest that B18R is a potential alternative to monoclonal antibodies used in the management of HIV encephalitis. Further studies are still needed to fully elucidate the effects of B18R in HIV encephalitis.

Disclosure: Nothing to disclose

EPO3269

A Phase 1 study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of HBM9161 in Chinese healthy volunteers

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¹Division of Nephrology, Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong (SAR of China), ²Medicine, Harbour BioMed, Shanghai, China

Background and aims: Blockade of the binding between neonatal Fc receptor (FcRn) and IgG-Fc reduces circulating IgG, and thus emerges as a potential therapy for IgG-mediated autoimmune conditions.

Methods: This was a double-blind, randomised, single ascending dose study evaluating the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of HBM9161 (a fully human anti-FcRn monoclonal antibody) in healthy Chinese volunteers (NCT03971916). Subjects were given a subcutaneous (SC) dose of HBM9161 340, 510 or 680mg and then followed up for 85 days. Study endpoints included incidence of adverse event (AE), serum drug concentration, IgG, and anti-drug antibodies (ADA).

Results: A total of 24 subjects were enrolled. The observed PK profile is consistent with target mediated drug disposition (Figure 1). The median time to peak serum drug concentration was 36 hours (340mg) and 3.5 days (680mg). A dose-dependent IgG reduction started in 2 days and reached nadir within 2 weeks (Figure 2). The maximum mean IgG reductions were 23% (340mg), 35% (510mg), and 40% (680mg). The recovery of IgG started at Week 3 and returned to baseline by Week 8. All reported AEs were mild in severity. The most frequently reported AEs in the HBM9161 groups were influenza-like illness and rash (Table 1). Only 1 subject was tested ADA positive.

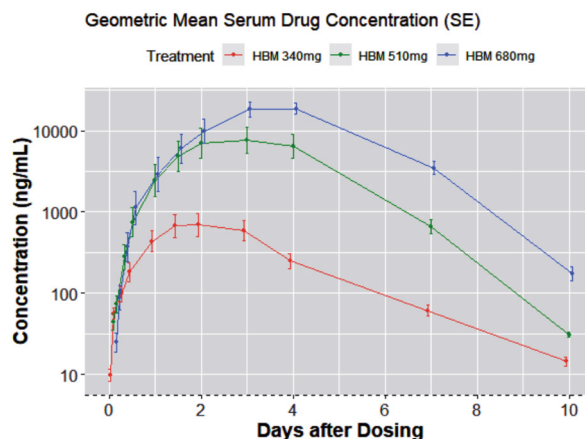


Figure 1. Mean Concentration-Time Profile Following Single Dose SC Administration of HBM9161

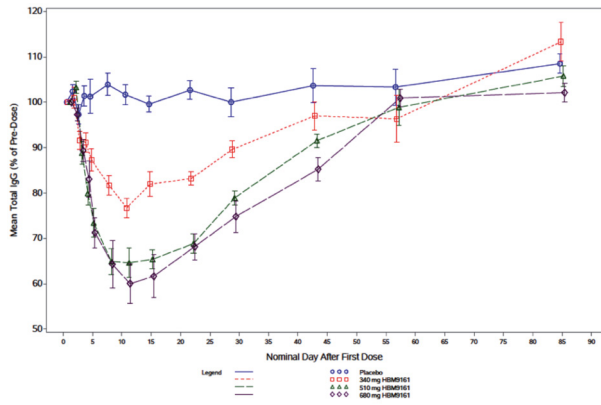


Figure 2. Mean IgG Concentration-Time Profile Following Single Dose SC Administration of HBM9161

	Placebo (N=6)	340 mg HBM9161 (N=6)	510 mg HBM9161 (N=6)	680 mg HBM9161 (N=6)	Overall (N=24)
Overall Total	5 (83.3%) (13)	5 (83.3%) (8)	5 (83.3%) (10)	2 (33.3%) (6)	17 (70.8%) (36)
Neurological disorders	2 (33.3%) (6)	1 (16.7%) (1)	0 (0)	1 (16.7%) (3)	4 (16.7%) (10)
Abdominal pain	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Abdominal pain upper	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Constipation	0 (0)	0 (0)	0 (0)	1 (16.7%) (1)	1 (4.2%) (1)
Diarrhea	1 (16.7%) (1)	1 (16.7%) (1)	0 (0)	1 (16.7%) (1)	3 (12.5%) (3)
Nausea/nausea/gastritis	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Swelling	0 (0)	0 (0)	0 (0)	1 (16.7%) (1)	1 (4.2%) (1)
General disorders and administration site conditions	1 (16.7%) (2)	1 (16.7%) (1)	5 (83.3%) (6)	1 (16.7%) (1)	8 (33.3%) (10)
Influenza like illness	1 (16.7%) (1)	1 (16.7%) (1)	0 (0)	1 (16.7%) (1)	3 (12.5%) (3)
Mucositis	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Immune system disorders	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Hypersensitivity	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Infections and infestations	1 (16.7%) (1)	0 (0)	1 (16.7%) (2)	0 (0)	2 (8.3%) (3)
Asymptomatic bacteriuria	0 (0)	0 (0)	1 (16.7%) (2)	0 (0)	1 (4.2%) (2)
Human contact	1 (16.7%) (1)	0 (0)	0 (0)	0 (0)	1 (4.2%) (1)
Investigations	1 (16.7%) (2)	2 (33.3%) (4)	1 (16.7%) (1)	0 (0)	4 (16.7%) (7)
Alanine aminotransferase increased	1 (16.7%) (1)	2 (33.3%) (2)	0 (0)	0 (0)	3 (12.5%) (3)
Aspartate aminotransferase increased	1 (16.7%) (1)	2 (33.3%) (2)	0 (0)	0 (0)	3 (12.5%) (3)
Gamma-glutamyl transferase increased	0 (0)	0 (0)	1 (16.7%) (1)	0 (0)	1 (4.2%) (1)
Nervous system disorders	2 (33.3%) (2)	0 (0)	0 (0)	0 (0)	2 (8.3%) (2)
Headache	2 (33.3%) (2)	0 (0)	0 (0)	0 (0)	2 (8.3%) (2)
Respiratory, thoracic and mediastinal disorders	0 (0)	0 (0)	1 (16.7%) (1)	0 (0)	1 (4.2%) (1)
Dry throat	0 (0)	0 (0)	1 (16.7%) (1)	0 (0)	1 (4.2%) (1)
Skin and subcutaneous tissue disorders	1 (16.7%) (1)	2 (33.3%) (2)	2 (33.3%) (2)	1 (16.7%) (2)	6 (25.0%) (7)
Pruritus	0 (0)	0 (0)	0 (0)	1 (16.7%) (1)	1 (4.2%) (1)
Rash	1 (16.7%) (1)	2 (33.3%) (2)	1 (16.7%) (1)	1 (16.7%) (1)	5 (20.8%) (5)
Rash pruritic	0 (0)	0 (0)	1 (16.7%) (1)	0 (0)	1 (4.2%) (1)

Table 1. Summary of Adverse Events

Conclusion: A single SC dose of HBM9161 results in sustained and dose-dependent IgG reduction. HBM9161 is safe and well-tolerated at a dose up to 680mg in Chinese subjects. The data warrant further investigation for its effects in IgG-mediated autoimmune disorders including Myasthenia Gravis.

Disclosure: Dr. Desmond is the principal investigator of this trial sponsored by Harbour BioMed. The travel expense of Dr. Desmond for EAN is sponsored by Harbour BioMed. Xueying Zhou, Michael Lee, Yu Zhang, Meng Wang and Xiaoxiang Chen are full-time employees of Harbour BioMed.

Infectious diseases 2

EPO3270

Locked-in syndrome after bacterial ventriculitis

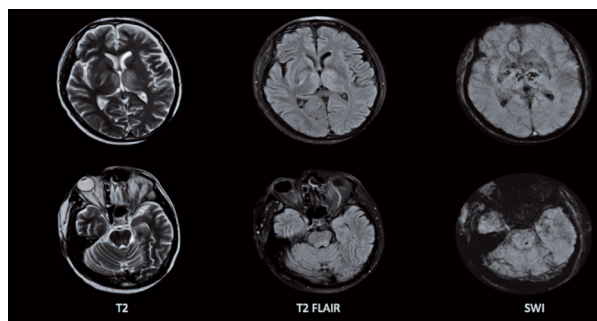
I. Luneva, J. Ryabinkina, M.A. Piradov

*Intensive Care Unit, Research Center of Neurology, Moscow, Russian Federation***Background and aims:** Ventriculitis is the inflammation of the ependymal lining of the cerebral ventricles.**Methods:** This is a case of a 32-years-old male. The debut of the disease with a headache, at the next increase in body temperature to 39,6°C. Brain MRI did not show pathology. Analysis of CSF revealed an increase in protein to 5g/L, cytosis 198/3, glucose 6.5mmol/L. On 7th day of the disease, disorientation, mydriasis and the absence of photoreactions appeared. The next day there was decrease in the level of conscious to coma, the patient was intubated and ventilated. Brain MRI showed ventriculitis, with signs of involvement of the membranes of the brain and spinal cord, and the next day the picture of dynamics in the form of an increase in occulal hydrocephalus, transtentorial wedging. PCR of CSF for *Listeria monocytogenes* was positive. On the 10th day the patient was admitted to our center. We prescribed ampicillin 12g/day plus gentamicin 5mg/kg weight/day. The patient had external ventricular drainage.**Results:** Against the background of therapy, the patient began to slightly shake his right hand, however, other movement his limbs were absent, muscle tone increased with formation of decerebral rigidity. Patient's condition was regarded as a type of locked-in syndrome. On Transcranial magnetic stimulation-EEG, the perturbation complexity index was corresponded to conscious activity. Nowadays, the patient can open eyes, walks with support, can speak, although his speech is dysarthritic.**Conclusion:** Ventriculitis is a serious disease secondary to infection. Timely identification of the agent and shunt placement with increasing hydrocephalus can improve outcomes.**Disclosure:** Nothing to disclose

EPO3271

Influenza-Associated Acute Necrotizing Encephalitis in Adult

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*Intensive Care Unit, Research Center of Neurology, Moscow, Russian Federation***Background and aims:** Seasonal flu is an acute respiratory infection caused by influenza viruses that circulate around the world. Acute necrotizing encephalitis is an extremely severe and rare complication of influenza in adults, with the high mortality rate.**Methods:** This is a case of a 59-years-old male patient. He developed fatigue, malaise, nasal congestion and a fever episode up to 39.1°C. On the 9th day of the disease he developed moderate cognitive impairment and dysarthria, and then his level of consciousness decreased to coma. The cerebrospinal fluid (CSF) analysis showed cytosis and protein 1.52g/L. CSF PCR for viruses was negative. Nasopharyngeal aspiration sample was positive for influenza virus.**Results:** On 17th day of the disease his neurological examination revealed generalized weakness and extreme drowsiness with severe confusion. He demonstrated meningeal syndrome, paresis of the downward gaze, anisocoria S>D, tetraparesis with low muscle tone and low tendon reflexes, myoclonus of the tongue and right hand. The patient was intubated and ventilated. Brain MRI showed hyperintense signal changes in thalami, left midbrain, right lenticular nucleus, internal capsules bilaterally, left para- and hippocampal gyri, and left frontal lobe. Those lesions had unclear margins and contained inclusions of hemosiderin in the thalami and right lenticular nucleus. Small petechial hemorrhages in both cerebral hemispheres were also found. Treatment with an influenza neuraminidase inhibitor was initiated along with IV corticosteroids.

Brain MRI, 17th day of the disease

Conclusion: As a result of the treatment, the patient's condition significantly improved. The patient was transferred to the rehabilitation department and has now fully recovered and returned to work.**Disclosure:** Nothing to disclose

EPO3272

Valacyclovir in the treatment of herpes simplex and varicella zoster encephalitides

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Background and aims: Intravenous (IV) acyclovir is the standard treatment of varicella zoster and herpes simplex encephalitides (VZE and HSE respectively). Despite its high safety profile, IV acyclovir can cause severe nephrotoxicity and neurotoxicity. Yet, there are no clear recommendations in regard to alternative treatment when immediate IV acyclovir discontinuation is required.

Methods: Case report and brief literature review.

Results: An 82-year-old woman presented with delirium and a vesicular rash along left T6-T7 dermatomes. Polymerase chain reaction analysis of CSF was positive for varicella zoster virus (VZV). The patient was started on IV acyclovir 800mg 3x/day for VZE. Rapid improvement of her mental status ensued. However, after 48 hours of treatment, an abrupt 5fold raise in serum creatinine was noted. As acyclovir-induced nephrotoxicity was suspected, the drug was immediately discontinued. The following day, the patient showed psychomotor agitation and severe speech disturbances. Oral valacyclovir, the prodrug of acyclovir, was promptly initiated at a dose adapted to renal function. Mental status, serum creatinine and urine output progressively returned to normal after onset of the alternative antiviral therapy. The patient was discharged after a 10-day course of oral valacyclovir.

Conclusion: We report a case of VZV encephalitis successfully treated with oral valacyclovir after discontinuation of IV acyclovir due to drug-induced nephrotoxicity and discuss the potential of valacyclovir as continuation treatment and first-line treatment of VZE and HSE.

Disclosure: Nothing to disclose

EPO3273

Analysis on gender differences of the nervous system infections in the Moldovan tertiary neurology center

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Background and aims: Scientific data suggests sex (biological) and gender (gender-based roles, behavior and power) differences in the manifestations of infections.

Methods: The study included 201 patients with neuroinfections admitted in the tertiary neurology center from 2007 to 2018. The diagnosis was confirmed based on clinical presentation, CSF, neuroimaging and laboratory testing. The data was analyzed with SPSS package for Windows.

Results: In the study sample 54.7% were men. No sex differences were noted in mean age (44.22±15.85 y), outcome and mortality rate (21.9%). Men were more likely to smoke (9.1% vs. 2.2%, p<0.05), drink alcohol (18.2% vs 6.6%, p<0.05), work outside the country (11.8% vs 1.1%, p<0.01) and have hepatitis (20.9% vs. 7.7%, p<0.01). The main clinical presentation was meningitis, mostly in men (64.5% vs 45.1%, p<0.01), in women – myelitis (16.5% vs 7.3%, p<0.05). Women presented more sensitive manifestations (19.8% vs 5.5%, p<0.01), cranial nerves palsies: n. III (17.6% vs. 8.2%, p<0.05), n.VI (13.2% vs 4.5%, p<0.05), seizures (17.6% vs 8.2%, p<0.05) and tetraparesis (41.9% vs. 19.4%, p<0.001). Neuroimaging shows encephalitic lesions in women (23.1% vs. 10.9%, p<0.05) and abnormalities of the adjacent structures in men (17.3% vs. 4.4%, p<0.01).

Conclusion: The analysis of our data revealed gender-based differences in exposure and clinical profiles in neuroinfections in a prospective cohort.

Disclosure: Nothing to disclose

EPO3274

Neurolisteriosis in a previously asymptomatic patient with serum IgM deficiency

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Background and aims: *Listeria monocytogenes* (Lm), a Gram-positive facultative intracellular bacterium, is an uncommon, highly opportunistic human pathogen. In immunocompetent adults, the infectious process remains subclinical. However, Lm demonstrates a tropism for 2 immunologically tolerogenic sites: the fetoplacental unit in pregnant women and the CNS in elderly individuals or otherwise immunocompromised patients. We present a case of CNS infection caused by Lm (neurolisteriosis) in a previously asymptomatic adult patient.

Methods: Case report

Results: A 62-year-old male who had never experienced severe infections, presented with fever, confusion, irritation and severe occipital headache. The patient was put on empirical intravenous therapy with ceftriaxone, vancomycin, ampicillin and dexamethasone. PCR and culture of CSF showed infection by Lm. A diagnosis of neurolisteriosis was made and dexamethasone and ceftriaxone were discontinued. Further workup revealed reduced serum IgM levels that persisted well beyond the period of acute bacterial infection while levels of IgG and IgA isotypes were largely preserved. After 2 weeks, the patient was afebrile, fully oriented and free of headache. He was discharged in good clinical condition. Intriguingly, flow cytometry revealed a virtually absent membrane-bound IgM on B cells which substantially recovered after 12 months, suggesting that mechanisms other than defective membrane expression are underlying serum deficiency.

Conclusion: Opportunistic infections such as neurolisteriosis warrant thorough immunological examination, even in individuals at increased epidemiological risk. Inapparent predisposing factors such as serum IgM deficiency may underly this risk, as in our case. It is possible that circulating IgM has a role against Lm infection, particularly in the early course of host-pathogen interaction.

Disclosure: Nothing to disclose

EPO3275

Epilepsy in the M'bam Valley: some keys to unlock the mystery

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Background and aims: Epilepsy in oncocercosis endemic African regions is overrepresented. Various types of epilepsy have been described across Africa based essentially on clinical descriptions.

We conducted an epidemiological, clinical and neurophysiologic study of epilepsy in the oncocercosis endemic region of Ntui, Cameroon in order to describe his electro-clinical phenotype.

Methods: Overall, 177 patients were explored based on the high prevalence of epilepsy in their family. Clinical data, standard EEG, and neuropsychological evaluation were recovered

Results: Epilepsy was clinically confirmed in 140/177 (79%) patients among whom 37 (24%) patients had encephalopathy associated epilepsy. A total of 108 EEG were recorded of which 36 (33%) considered abnormal: 27 (73%) revealed atypical specific abnormalities (bifronto-temporal spike and slow waves). Concerning the neuropsychological testings, 29% showed severe global cognition impairment, 28% severe episodic memory impairment and 66% severe frontal cognition impairment. Half of the patients suffered from mental disorder.

Conclusion: We described for the first time the electric and neuropsychologic pattern in oncocercosis associated epilepsy.

Surprisingly, epilepsy was associated with a specific EEG pattern in 73% of abnormal EEG, with mostly frontal and temporal involvement. We confirmed the impact of epilepsy on behavior and cognition with mostly frontal lobe involvement.

Those findings are consistent with a specific oncocercosis neurological tropism. Strong epidemiologic data in literature suggest causality between oncocercosis and CNS symptoms secondary to an autoimmune mechanism. We hypothesize that this mechanism involve mostly the frontal and temporal regions.

Preventing and curing oncocercosis might be a way to prevent immune reaction and reduce epilepsy in some African regions.

Disclosure: Nothing to disclose

EPO3276

Primary Amoebic Meningoencephalitis- A case report and review of literature

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2-year-Background and aims: A 12 year-old-girl with no significant past illness presented with fever, headache and mild disorientation of 3 days duration. On examination she had neck stiffness and mild blurring of nasal margin on fundus examination. There was no other localizing signs. The possibility of acute meningoencephalitis was considered and MRI Brain showed mild meningeal enhancement consistent with the clinical diagnosis. CSF study showed elevated opening pressure with polymorphonuclear pleocytosis, high protein and low glucose consistent with bacterial meningitis. However the CSF wet mount slide showed many mobile trophozoites of *Naegleria fowleri*. Diagnosis of PAM was made and child was immediately started on Amphotericin B, Rifampicin, Fluconazole and Azithromycin along with anti-oedema measures. Miltefosine was not available. She had no history of swimming in fresh water or exposure to any water sports. Guarded prognosis was explained to relatives. The child's sensorium progressively worsened and she succumbed to her illness in 12 hours due to cardiac arrest possibly secondary to brain oedema and central herniation.

Methods: none

Results: none

Conclusion: This is the classical presentation of PAM caused by *Naegleria fowleri*. The clinical picture, imaging and CSF study will very much resemble bacterial meningitis. This case illustrates the importance of routinely looking at the CSF wet mount in all meningitis cases. The mobile trophozoites can be easily visualised in wet mount which will confirm the diagnosis and helps in early initiation of treatment. Other protozoans like *Acanthamoeba* and *Balamuthia* usually presents as subacute meningitis and trophozoites are usually not visualized in CSF.

Disclosure: Nothing to disclose

EPO3277

Intracranial Aspergillosis presenting with multiple cerebral abscesses: A case report

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Background and aims: Fungal brain abscess is a rare but serious condition which generally effects immuno-compromised patients.

Methods: Herein, we present a case of multiple intracranial aspergillus abscess who was treated with steroids after admission to hospital with hyponatremia and nephrotic syndrome.

Results: A 74-year-old female patient admitted to hospital with altered mental status, tendency to sleep and seizures. She had been hospitalized in nephrology department a week before with hyponatremia and nephrotic syndrome and was treated with steroids. In her cranial magnetic resonance imaging, peripheral contrast enhancing lesions and parenchymal oedema were observed in the left parietal lobe, insular cortex, putamen and right superior frontal gyrus, frontal lobe and precentral gyrus (Figure-1). Metastatic brain tumor was considered initially and biopsy was performed. The histopathologic examination was consistent with aspergillus infection (Figure-2). Thoracic and abdominal computed tomography and echocardiography findings revealed bilateral pleural and pericardial effusion, free fluid in the abdomen, diffuse subcutaneous oedema. SS-A and Ro-52 were positive. After the treatment with antifungal agents, Amphotericin B and then Voriconazole, brain oedema diminished and cranial lesions disappeared. Despite treatment the patient died at the 4th month of hospitalization.

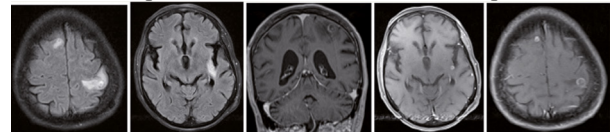


Figure -1

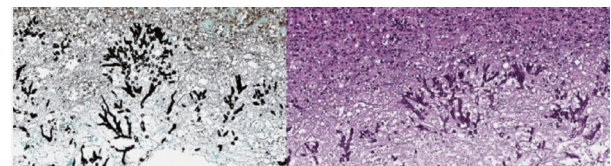


Figure -2

Conclusion: The clinical and laboratory diagnosis of cerebral aspergillosis is problematic and mortality is quite high, even in cases receiving appropriate treatment. Therefore, health professionals should be aware of the symptoms of *Aspergillus* induced brain abscesses, as early detection, accurate diagnosis and appropriate treatment may prove positive patient outcomes.

Disclosure: Nothing to disclose

EPO3278

Central Nervous System Involvement After Herpes Zoster Ophthalmicus: A Case Report

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Background and aims: Herpes Zoster is a common infectious disease caused by the reactivation of latent varicella zoster virus (VZV) in dorsal sensory ganglia. In patients with active zoster infection a variety of neurologic complications may occur.

Methods: Here we report an immune-compromised patient who developed meningitis after herpes zoster ophthalmicus.

Results: A 75-year-old woman with known diabetes mellitus and hypertension admitted to hospital with headache, vertigo, vomiting. She was diagnosed as having ophthalmic herpes zoster and was treated with 3g of oral valacyclovir for 7-days, 2 weeks ago. On physical examination she had scars of herpetic eruption and pigmentation over the left orbita. On neurological examination she had left pupillary mydriasis, left semi-ptosis and limited upward gaze. MRI of the brain and orbita was performed with and without gadolinium contrast. T2-weighted-axial images showed increased signal in extra-ocular muscles on the left and enlargement of retro-orbital fat tissues, compatible with edema. MRI also revealed contrast enhancement of the dura adjacent to the left orbital roof and the left optic nerve sheath (Figure-1). Cytochemical analysis of cerebrospinal fluid (CSF) showed 84 white blood cells/ml and protein level was 104.8mg/dl. Polymerase chain reaction analysis of CSF was negative, Ig G antibody was positive for VZV. The patient was treated with intravenous acyclovir and recovered within one month.

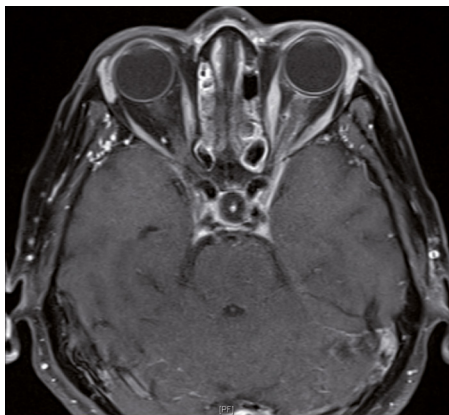


Figure- 1

Conclusion: An uncommon but serious complication of herpes zoster ophthalmicus is zoster meningoencephalitis. Early recognition of neurological complications especially central nervous system involvement is important because it is a potentially life-threatening complication and prompts acute, appropriate antiviral treatment.

Disclosure: Nothing to disclose

EPO3279

Tuberculoma of the central nervous system in the setting of miliary TB in an immunocompetent patient: Case report

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Background and aims: Intracranial tuberculoma is a rare form of tuberculosis with non-specific clinical manifestation. Due to the similarity of its clinical features with many other infectious and non-infectious lesions in the brain, diagnosis is difficult.

Methods: Case report

Results: We report a case of intracranial tuberculoma in a 35-year-old immunocompetent patient, presented with 6 weeks of severe left hip pain and difficulty in walking. On admission, she had 4/5 strength in the left lower extremity and no meningeal signs. Her past medical history was significant for double J stent for 2 times due to ureteral stricture and pulmonary embolism. Cranial MRI revealed multiple contrast-enhancing ring-shaped lesions in supratentorial and infratentorial neuroparenchyma with surrounding oedema. Cerebrospinal fluid analysis revealed no WBC, protein 41g/dL, glucose 75mg/dL, a negative culture and polymerase chain reaction for Mycobacterium tuberculosis complex. In differential diagnosis metastasis and abscess were taken into consideration. MR spectroscopy demonstrated cerebral tuberculomas. Furthermore, thoracic computerized Tomography (CT) was highly suggestive of miliary tuberculosis and abdominal CT revealed tuberculous pyelonephritis as the potential cause of ureteral stricture. The patient had a good initial clinical response to quadruple anti-tuberculous treatment. The follow-up cranial MRI showed that the lesions had become smaller or disappeared.

Conclusion: Tuberculoma should be considered in the differential diagnosis, even in immunocompetent patients with non-specific clinical presentation and involvement of multiple systems such as genitourinary system or central nervous system. The significance of our case is due to the presence of intracranial tuberculomas in the setting of miliary tuberculosis.

Disclosure: Nothing to disclose

EPO3280

Neurological Measles Complications, Encephalitis in an Immunocompromised Host

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Background and aims: In Romania, in the last decade, approximately 10 percent less children were vaccinated against measles, due to parents' refusal to vaccinate their children, as well as insufficient vaccine supply. Outbreaks of measles begin to occur once population immunity threshold decrease below 94%.

Methods: We present the case of a 19-year-old female, known with primary immune deficiency, with history of generalized skin eruption three months before, compatible with measles, admitted to the Neurology ward for vision field loss and balance disturbance, with a febrile episode 10 days before the debut of symptoms.

Results: Brain imaging performed at admission through native MRI revealed left cortical parietal and occipital T2 hypersignal. EEG evaluation was compatible with non convulsive epileptic status.

Subacute measles encephalitis affects both children and adults with defective cell mediated immune responses. The viral infection usually precedes the encephalitis 1 to 6 months and the cerebrospinal fluid may be normal and the levels of measles antibodies do not increase.

The history of measles type eruption, the febrile episode, the progressive deterioration of the neurological clinical status and the evolution of the brain lesions, despite the treatment, in an immunocompromised patient, were highly suggestive for measles inclusion body encephalitis.

Conclusion: Although neurological complications following measles infection are rare, they can be devastating. Measles vaccination is the most efficient prophylaxis against the infection and its complications. Protection of immunocompromised patients and children - before reaching the inoculation age, can be achieved by vaccinating a high percentage of population.

Disclosure: Nothing to disclose

EPO3281

Streptococcus suis meningitis in the Canary Islands: first two reported cases.

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Background and aims: Streptococcus suis (*S. suis*) is a zoonotic pathogen that causes bacterial meningitis, especially in people having occupational contact with pigs or porcine products. The mortality rate is low, but many patients remain with hearing loss or ataxia. Although most cases occur in southeast Asia, human infection has also been described in Europe, less than 15 cases reported in Spain. We present 2 patients with *S. suis* meningitis (SSM) in the Canary Islands.

Methods: Report of 2 cases of SSM occurred in our center between 2014-2019 and literature review.

Results: 2 men, 54 and 56 years old, respectively, were admitted to the hospital. 1 worked as a butcher and had a 1-month-history of fever, hearing loss and gait instability. The other one manipulated raw pork without protection and had skin lesions in his hands. He was brought to the emergency department with a meningeal syndrome and altered mental status. Both cerebrospinal fluid analysis revealed pleocytosis and hyperproteinorrachia, with low glucose level in the 2nd case. *S. suis* was isolated from blood cultures in the 2 of them and they were treated with ceftriaxone for 2 weeks, with a favorable outcome. Repeated blood cultures were negative; however, both ended up with severe neurosensorial hearing loss and gait ataxia as sequelae.

Conclusion: To the best of our knowledge, these are the 1st 2 reported cases of SSM in the Canary Islands. Despite its infrequency in our country, we must remember the importance of recording the occupational history at anamnesis and start early treatment if suspected.

Disclosure: Nothing to disclose

EPO3282

Introduction of Multi-PCR - Impact on the dose of Acyclovir and Antibioti-infectives in adult patients with pleocytosisH. Schmidt¹, B. Wiebalck¹, B. Volkmer²¹Neurologie, Elbe Kliniken Stade, Stade, Germany, ²EKSB Forschungs- und Studienzentrum (FSE), Elbe Kliniken Buxtehude, Buxtehude, Germany

Background and aims: Cerebrospinal fluid (CSF) is needed for the work-up of meningitis, headache, disturbances of conscience, cranial nerve affections or autoimmune-related CNS-processes. Often, the initial treatment of pleocytosis consists of both antiviral and antibiotic agents until lab-results enable final diagnosis. Length of potentially harmful multimodal therapies is determined by the speed to arrival of lab-results. In this observatory, monocentric study, we report the impact of insourcing ME-PCR and Antibody-specific Indices (AI)-measurements for HSV and VZV in comparison to external laboratory analysis on length of hospital stay (LOS), interval to results, cumulative dose/duration of anti-infective agents.

Methods: 280 consecutive patients (m=136/f=144) with pleocytosis (leukocyte count > 4/ μ l) were analysed, N=114 with an external laboratory work-up, 166 with inhouse management. Groups were compared with 2-sided (t-test for normally distributed, U-test for not-normally distributed data) tests. Frequencies were compared with Chi-square-test.

Results: Age (61.6 \pm 1.8 vs. 56.9 \pm 1.6 years, p=0.06), renal-, liver-function-parameters and gender distribution (p=0.07) of did not differ between the groups. Insourcing shortend the interval from LP to PCR- and AI-results significantly. Cumulative ABX and Acyc-use per patient were significantly lower in the inhouse than in the external-lab-group (both p<0.001). Likewise, the length of antibiotic and antiviral therapy was significantly lower in the inhouse than in the external-lab-group (both p<0.001).

Conclusion: Insourcing of ME-PCR and AI-determinations shortened significantly the interval of diagnostic uncertainty. Thereby, LOS and the exposure to anti-infective agents with their potential side-effects was lowered.

Disclosure: The study was sponsored by BioMérieux, Marcy l'Etoile, France

EPO3283

A case of Cryptococcal meningitis in a patient with ANCA-associated vasculitis and glomerulonephritisV. Vasilev¹, J. Samuel¹, M. Dimitrova²¹Sofia, Bulgaria, ²Neurology, UMHATEM "N.I.Pirogov", Sofia, Bulgaria

Introduction: Cryptococcal meningitis (CM) is a deadly systemic opportunistic fungal infection caused by members of the *Cryptococcus neoformans* species. Severe infections of the lungs and skin are common complications of immunosuppressive treatment for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis while CNS infections are relatively rare. Common risk factors for infection are use of high-dose corticosteroids, antibiotics exposure and intrinsic disorders of cell-mediated immunity

Methods: A 44-year-old male with a history of ANCA-associated vasculitis and glomerulonephritis, undergoing daily immunosuppressive treatment with 40mg prednisolone presented to our neurology clinic with complaints of headache, neck rigidity, fever, nausea, vomiting, extreme fatigue, dysuria and periods of confusion. Concomitant diseases included corticosteroid-induced diabetes mellitus, arterial hypertension, and moderate chronic renal failure. He underwent physical and neurological examinations, Computed Tomography (CT) of the brain, ophthalmological tests, Cerebrospinal fluid (CSF) and blood microbial cultures, and consultations with the following specialists: infectious diseases, ophthalmologists and nephrologists.

Results: Neurological examination revealed positive meningeal irritation signs. No pathological changes were detected on the brain CT. CSF studies showed increased levels of leukocytes, total protein and decreased glucose levels. *Cryptococcus neoformans* was isolated from CSF and blood cultures. Ophthalmological tests revealed impaired vision and papilloedema. The patient tested negative for HIV. Initial antibiotic treatment with Ceftriaxone was replaced by combination therapy with Vancomycin and Fluconazole which lead to improvement in the patient's condition. He was discharged on prolonged oral Fluconazole therapy.

Conclusion: We present a successfully treated case of Cryptococcal meningitis in an immunosuppressed HIV negative patient with long-term corticosteroid therapy.

Disclosure: Nothing to disclose

EPO3284

A case of Cryptococcal meningitis in a patient with ANCA-associated vasculitis and glomerulonephritis

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Background and aims: Cryptococcal meningitis (CM) is a deadly systemic opportunistic fungal infection caused by members of the *Cryptococcus neoformans* species. Severe infections of the lungs and skin are common complications of immunosuppressive treatment for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis while CNS infections are relatively rare. Common risk factors for infection are use of high-dose corticosteroids, antibiotics exposure and intrinsic disorders of cell-mediated immunity.

Methods: A 44 year old male with a history of ANCA-associated vasculitis and glomerulonephritis, undergoing daily immunosuppressive treatment with 40mg prednisolone presented to our neurology clinic with complaints of headache, neck rigidity, fever, nausea, vomiting, extreme fatigue, dysuria and periods of confusion. Concomitant diseases included corticosteroid-induced diabetes mellitus, arterial hypertension, and moderate chronic renal failure. He underwent physical and neurological examinations, Computed Tomography (CT) of the brain, ophthalmological tests, Cerebrospinal fluid (CSF) and blood microbial cultures, and consultations with the following specialists: infectious diseases, ophthalmologists and nephrologists.

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Conclusion: We present a successfully treated case of Cryptococcal meningitis in an immunosuppressed HIV negative patient with long-term corticosteroid therapy.

Disclosure: Nothing to disclose

EPO3285

Serological and molecular genetic studies on the involvement of hepatitis E virus in the pathogenesis of neurological diseases

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Background and aims: The aim of the present study was to determine the involvement of hepatitis E virus in the pathogenesis of neurological disorders.

Methods: Blood serum specimens and cerebrospinal fluid were tested for the presence of antibodies against HEV (anti-HEV IgM and IgG) and for infection with other hepatotropic viruses, cytomegalovirus and Epstein-Bar virus for accurate selection of the target population and detection of patients with co-infections and viral infections giving false positive results. Antibodies against HEV were demonstrated by the use of immunoassay methods - ELISA and real-time polymerase chain testing to determine the viral concentration of HEV.

Results: Of the 40 patients enrolled in the study, 21 (53%) tested positive for HEV antibodies (mean age 56 years; 4 females and 17 males), with 8 (40%) positive for anti-HEV IgM and anti-HEV IgG. Only in one anti-HEV IgM and IgG positive patient demonstrated HEV RNA in serum. Also tested for the presence of HEV RNA were 12 CSF, none of which gave a positive result. Of 21 HEV-positive patients, 11 were with Guillain-Barré syndrome, 1 with Miller-Fisher syndrome, 2 with acute motor-sensory axonal neuropathy, 5 with chronic inflammatory demyelinating polyneuropathy, 1 with myelitis and 1 with progressive multifocal leukoencephalopathy. Mild elevation in levels of liver enzymes was discovered only in one-third of our patients.

Conclusion: HEV infection was frequently associated with neurological complications and testing for this infection should be considered in all patients with Guillen-Barre syndrome and any likely inflammatory peripheral nerve disorder especially in cases with elevated liver enzymes.

Disclosure: The project was supported by grant D-104/03.05.2018 of the Medical University, Sofia, Bulgaria

Neuro-oncology

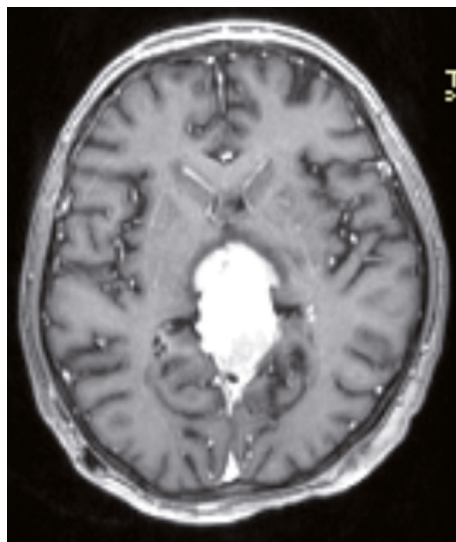
EPO3286

CNS Germinoma with synchronous lesions in the sellar and pineal regions

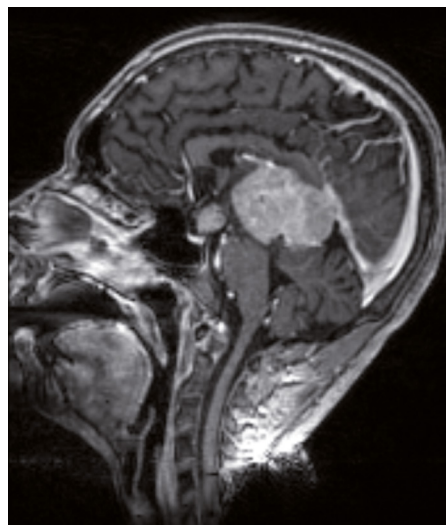
A. Simonyan¹, A. Mikhaylova², L. Lepsveridze¹
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Background and aims: Germinomas comprise approximately 2-5% of all CNS malignancies², and have a favourable prognosis with a greater than 90% overall survival¹. Most of them arise in the pineal and suprasellar region². Synchronous lesions occurs in 5-10% of all cases². Worse outcomes in case of CNS germinomas are relatively rare.

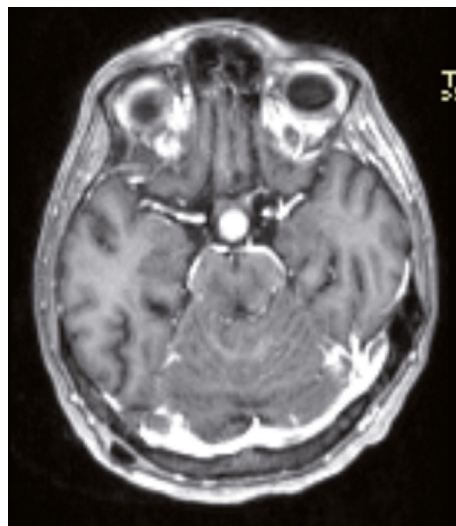
Methods: We report a case of 28-year-old male, presented with motor aphasia, visual impairment, dysphagia and hyperkinesia in left hand. In period of last 15 months patient underwent triventriculostomy, external ventricular draining, ventriculoperitoneal shunting due to occlusive hydrocephalus developed due to compression of cerebral aqueduct. MRI revealed volume formations of the pineal and sellar regions (Fig 1-3). Tumor markers from blood and CSF (AFP, β -HCG) were within the normal range. Tracheostomy was performed for prevention of aspirative pneumonia.



T1 WI C+, Axial MRI shows the strong, homogenous enhanced mass in pineal region with brain invasion



T1 WI, Sagittal MRI shows the mass hiperintens to GM in sellar and pineal regions



T1 WI C+, Axial MRI shows the strong, homogenous enhanced mass in sellar region

Results: Taking into account the severity of the patient's condition (Karnovsky index - 40%, massive bilateral iliofemoral thrombosis with subocclusion of the infrarenal segment of inferior vena cava), and extremely high risks of complications, consilium decided to refrain from surgical intervention and adjuvant therapy. Patient died after 3 months.

Conclusion: Histological changes in tumors corresponds to the germinoma. We don't undertake to judge whether there was diagnostic omission, or incorrect treatment in this case. But in our opinion, in case of suspected CNS germinoma, it is necessary to conduct more "aggressive treatment". Symptomatic treatment should be used in cases, where the treatment of main disease is impossible. We hope that this sad clinical case will help Neurosurgeons in making decisions in a difficult situation.

Disclosure: Nothing to disclose

EPO3287

Loss of IDH1 driver mutation during the progression of an anaplastic oligodendroglioma: an exceptional event associated with an aggressive phenotype

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Background and aims: IDH1/2 mutations are recurrent events typically described as the earliest genetic alteration in lower grade gliomas. Their loss during tumor progression is exceptional

Methods: We performed a longitudinal histomolecular analysis in a patient with anaplastic oligodendroglioma whose tumor lost its IDH1 mutation at recurrence.

Results: A 58-year-old female patient presented in November 2017 with cognitive impairment revealing a right fronto-callous enhancing lesion. She had a partial resection of the lesion and was diagnosed with anaplastic oligodendroglioma, IDH1-mutant and 1p/19q co-deleted. She received adjuvant chemotherapy with PCV from January until June 2018. In July 2019, tumor recurrence motivated a second resection. Surprisingly, the histological examination of the recurrent sample showed 2 distinct components: a sector of IDH1-mutant grade II oligodendroglioma, associated with areas of IDH1-wild-type glioblastoma. Sequencing confirmed the IDH1 mutation loss in the latter area. Radiochemotherapy treatment was started. Unfortunately, the tumor rapidly progressed with the development of subcutaneous metastases, leading to the patient's death only one month after the radiotherapy.

Conclusion: The loss of an IDH1/2 driver mutation is an exceptional event during the progression of gliomas, never reported to our knowledge in oligodendrogliomas. In this patient, 3 main hypotheses are considered: (i) the most likely, loss of the IDH1 mutation within a subclone leading to acquired resistance and recurrence; (ii) existence of an IDH1-wild-type founding clone which evolved in distinct contingents; (iii) development of 2 phylogenetically unrelated gliomas in the same patient. Complementary molecular analyses are ongoing to decipher the specific mechanism in this patient.

Disclosure: Nothing to disclose

EPO3288

The diagnostic journey towards an Osteoid Osteoma: a case presentation

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Background and aims: Osteoid osteoma accounts for 10% of benign bone lesions with a male predilection that usually affects long bones.

Methods: A 30-year-old male patient was admitted for pain started a year ago in the right shoulder which irradiates in the hand. Pain is relieved by NSAID medication. Patient occupation involves heavy physical activity and the neurological examination reveals limitation at the abduction of the right arm.

Results: Electroneuromyography, right shoulder and humerus radiography normal. Cervical MRI showed cervical discopathy. Meanwhile the initial response to NSAID fade away, there was no response to propranolol, and the patient is put on corticoids for a short period of time with limited response. The patient was redirected to rheumatology. After clinical examination and musculoskeletal ultrasound they raise the possibility of a reflex sympathetic dystrophy and a MRI for the right shoulder is recommended. The MRI reveals a signal modification of the proximal humeral diaphysis (Fig.1) and a full upper limb MRI combined with CT are suggested. The upper limb MRI showed a nidus in the upper 1/3rd of the humerus (Fig.2), further confirmed by CT (Fig.3), suggestive for osteoid osteoma. The patient was redirected to orthopedy for surgery and the pathology report confirmed the final diagnostic of osteoid osteoma.

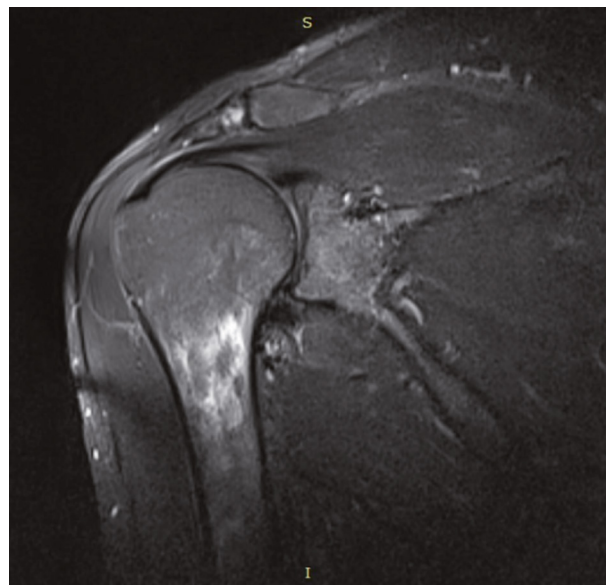


Fig.1

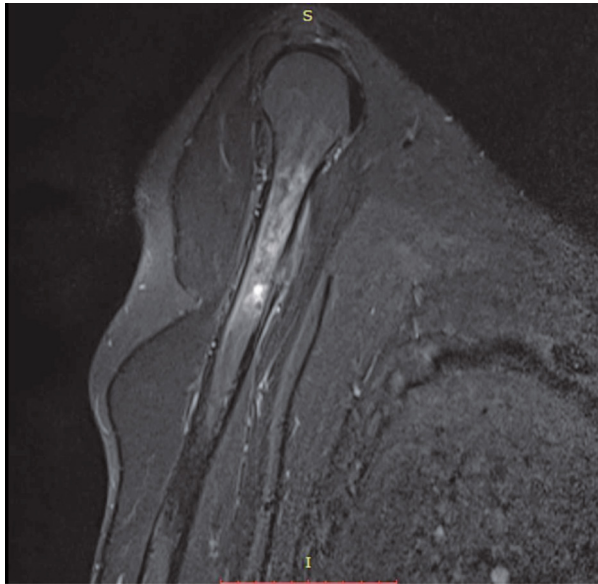


Fig.2

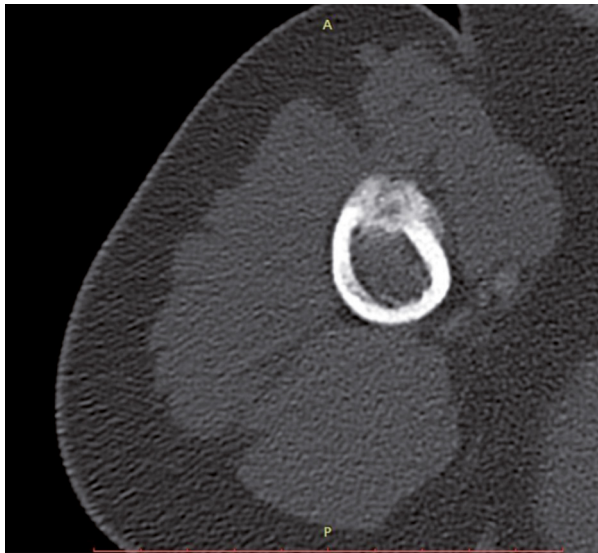


Fig.3

Conclusion: The particularities of the case are the unspecific symptomatology, the patient occupation that misguided our initial diagnostic and the latency of almost one year from initial symptoms to visible lesion on imagistic examination.

Disclosure: Nothing to disclose

EPO3289

Fourth ventricle ependymoma masquerading as Guillain-Barré syndrome

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Background and aims: Ependymomas are relatively rare tumors, accounting for 9% of total gliomas, occurring at any age. They arise from the lining ependymal cells of the ventricular system and the ependymal canal. Topographically, ependymomas are spinal, supra- and infratentorial, the former being more common in adults and the latter in pediatric population. Histologically, WHO classifies ependymomas in 3 grades of malignancy: 1st grade are benign, 2nd either benign or malign and may cause relapse and 3rd are malign, relapses and metastases being frequent.

Methods: We report the case of a 30-year old caucasian male who 14 days prior to admission in our Clinic presented with ascending tetramelic dysesthesias and weakness. He had an undocumented history of posterior fossa tumor for which he underwent surgery 3 years before this admission. Neurological examination revealed tetraparesis and absent osteotendinous and plantar reflexes. Albuminocytological dissociation was found in the cerebrospinal fluid (CSF) examination. The presumptive diagnostic was Guillain-Barré syndrome, but clinical idiosyncrasies and lack of electroneuromyographic findings prompted imagistic evaluation of the cervical spinal cord followed by whole CNS magnetic resonance imaging (MRI).

Results: The MRI studies revealed contrast-enhancing polilobular cystic mass in the IV-th ventricle extending to C2-C3 intervertebral disk, consistent with an ependymoma. A small thoracic spinal cord mass suggesting an intrathecal metastasis was also found.



T2-weighted image sagittal section of the brain stem and upper spine showing a hyper-isointense mass with a cystic component in the 4th ventricle, extending to C2 level. A nodular T2 isointense intradural mass compatible with an ependymoma metastasis at T2 thoracic spinal cord

Conclusion: Temporary inhibition of gamma-motoneurons caused by a rapidly developing spinal cord lesion may result in spinal shock. Subacute presentation without pyramidal signs, more so in the presence of signs suggesting lower motor neuron dysfunction, may pose great challenges.

Disclosure: Nothing to disclose

EPO3290

Bilateral optic perineuritis and recurrent coma

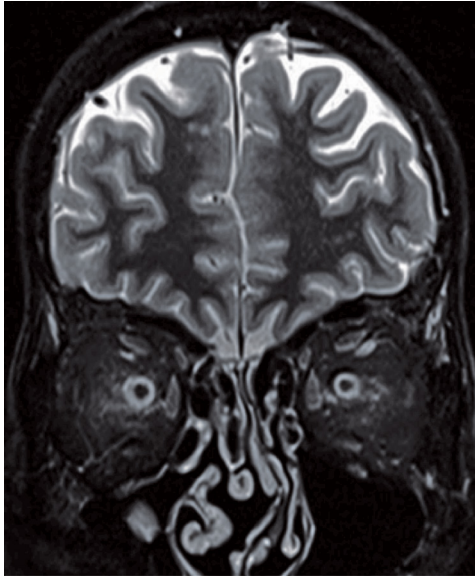
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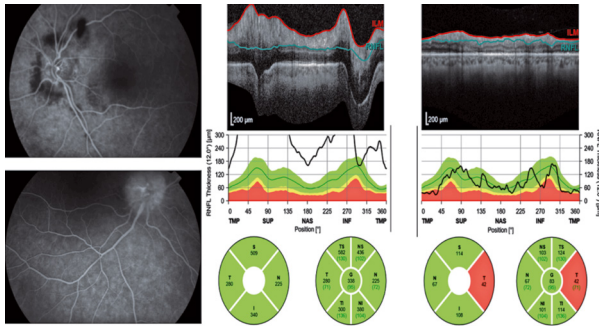
Background and aims: Bilateral optic perineuritis may easily be confounded with inflammatory optic neuropathy. However, this entity has a large differential diagnosis including intracranial hypertension and congenital, genetic and toxic neuropathies.

Methods: We present a clinical case of a 67-year-old man with a diagnosis of signet cell gastric adenocarcinoma submitted to chemotherapy and gastrectomy in the previous year without evidence for disease recurrence.

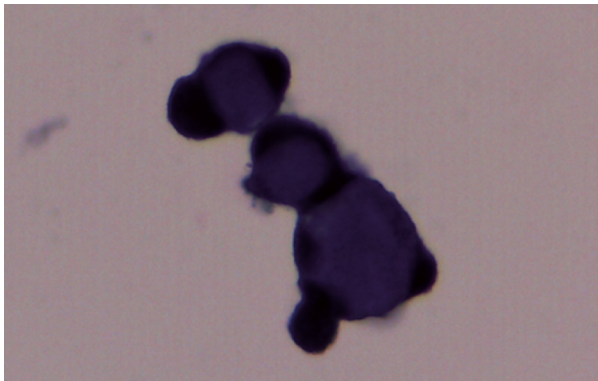
Results: The patient presented in the emergency department with 1 month of progressive worsening of the visual acuity. The neurological exam revealed left pupillary afferent defect and a bilateral optic disk oedema with papillary haemorrhages. The initial blood workup was normal. CT scan showed possible communicating hydrocephalus; spinal fluid analysis, vitamin blood levels, and infectious/autoimmune disease's panel were all unremarkable. Brain MRI showed bilateral optic nerve T2 hypersignal with gadolinium enhancement. The patient was started on prednisolone, only achieving partial response. 2 months later the patient started with headache, behaviour changes and transient episodes of coma with forced bilateral downward gaze deviation. Intracranial CT angiography and electroencephalogram were normal. Repeated lumbar puncture disclosed high opening pressure, pleocytosis and circulating signet cells. Body CT scan did not reveal extracranial neoplastic disease. The patient was started on intrathecal methotrexate with poor clinical response, being referred to Palliative care. He died 5 months after brain involvement.



Optic nerve sheath hypersignal with adjacent tissue involvement.



Funduscopy and optical coherence tomography (right and left eyes, respectively)



Signet cells compatible with gastric adenocarcinoma, according to the WHO classification.

Conclusion: Optic nerve sheath enhancement, adjacent tissue involvement, weak response to steroids and encephalopathy were strong points against an inflammatory disease, supporting a neoplastic process. Repeated lumbar punctures are essential for the correct diagnosis.

Disclosure: Nothing to disclose

EPO3291

Corticotherapy effect on biopsies of lymphoma of the CNS

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Background and aims: Primary lymphoma of the CNS is a rare form of lymphoma. Histopathologic diagnosis through stereotaxic biopsy is mandatory for treatment. Previous use of corticosteroids and amount of available tissue can influence biopsy yield.

Methods: Clinical case.

Results: 43-year-old man, HIV negative. History of subacute headache. MRI showed bilateral intra-axial lesions involving the corpus callosum with significant vasogenic edema, enhancing with contrast, suggestive of CNS lymphoma. The patient was started on dexamethasone symptomatically. Systemic workup was negative. The stereotaxic biopsy of the lesion demonstrated unspecific findings of myelin loss, macrophagic and astrocytic reactive proliferation and presence of T lymphocytes, without pathologic findings of malignancy, and negative for toxoplasmosis. The patient was then admitted on the Neurology ward. Lumbar puncture was contraindicated due to risk of cerebral herniation. Plasmapheresis was started considering the possibility of primary demyelination pathology, but clinical worsening culminated in death. The autopsy showed diffuse proliferation of large lymphoid cells on the cerebral tissue, with immunohistochemistry in accordance with the diagnosis of primary lymphoma of the CNS.

Conclusion: We present a paradigmatic case of the relationship between corticotherapy and the diagnosis of lymphoma of the CNS through stereotaxic biopsy. The cytolytic effect of steroids on lymphoma cells can lead to an equivocal biopsy. The lesion pathology demonstrated a demyelinating process with inflammatory infiltrate of T predominance, without tumor cells, which can't exclude the diagnosis. Therefore, when considering the hypothesis of primary lymphoma of the CNS, steroids must be avoided until after the biopsy, although its use is primarily determined by clinical findings.

Disclosure: Nothing to disclose

EPO3292

Paraneoplastic intestinal pseudo-obstruction as the presenting symptom of a lung malignancy in an elderly womanC. Roy-Hewitson¹, A. Smith², S. Dasari²¹BURLINGTON, USA, ²Neurology, University of Vermont, Burlington, USA

Background and aims: Anti-Hu paraneoplastic syndromes classically present with a sensory neuronopathy or a cerebellar syndrome. We present a patient who was admitted to the surgical service for weeks with a presumed small bowel obstruction as the heralding sign of an underlying lung malignancy.

Methods: A 72-year-old woman presented with weeks of constipation and days of vomiting. An exploratory laparotomy failed to reveal an obstruction. Neurology was consulted when she developed dysesthesias and allodynia in her hands 3 weeks after her admission. On exam she had asymmetric distal >proximal sensory loss in her upper extremities, pseudo-athetosis and areflexia. EMG/NCS showed evidence of an axonal non-length dependent sensory and motor neuropathy. Paraneoplastic panel was positive for antineuronal nuclear antibodies (ANNA-1, Anti-Hu). Imaging showed evidence of a mediastinal mass and the pathology was consistent with a limited stage small cell lung cancer. She was treated with 2 cycles of chemotherapy (carboplatin and etoposide) as well as IV solumedrol followed by IVIG, without improvement. Due to her inability to tolerate treatment and her worsening functional status, the decision was made to transfer to hospice.

Conclusion: We describe the case of a patient with intestinal pseudo-obstruction as the presenting symptom of an Anti-Hu mediated paraneoplastic syndrome associated with small cell lung cancer. Although previously described, this rare presentation lead to delays in diagnosis and initiation of anti-tumour treatment. This presentation should prompt an aggressive search for an underlying malignancy and early treatment initiation while patients still have a favorable functional status.

Disclosure: Nothing to disclose

EPO3293

Metastatic intracranial spread of adenocarcinoma mimicking sporadic human prion disorder: two cases of Creutzfeldt-Jakob disease-like presentationsR. Rusina¹, I. Rektorova², R. Matěj³¹Neurology, Charles University, Third Faculty of Medicine, Thomayer Hospital, Prague, Czech Republic, ²Neurology, Masaryk University, Faculty of Medicine, St. Anne's University Hospital, Brno, Czech Republic, ³Pathology and Molecular Medicine, Charles University, Third Faculty of Medicine, Thomayer Hospital, Prague, Czech Republic

Background and aims: We report 2 patients with rapid progressive dementia evoking sporadic Creutzfeldt-Jakob disease, in whom autopsy surprisingly revealed meningeal carcinomatosis and cortical micrometastases of lung tumors. The clinical diagnosis of human prion disease is in special cases still challenging task, as no causal treatment is available and early introduction of complex palliative care is crucial for the patient and his relatives.

Methods: A 54-year-old female, with a pulmonary adenocarcinoma in remission on biological treatment, developed rapidly progressive dementia, with spasticity and mutism. MRI found parieto-occipital cortical ribboning in diffusion weighted sequences and increased tau protein in the cerebrospinal fluid. She deceased 8 months after the 1st clinical manifestations. A 69-year-old female, with a history of non-small cell lung carcinoma, presented with delirium and myoclonus. The condition rapidly deteriorated towards mutism and severe limb rigidity. Cerebrospinal fluid analysis showed normal cell count, protein and glucose levels. MRI demonstrated right-sided frontal and possible caudate hyperintensities on diffusion weighted sequences. Death occurred after a 2 months disease course.

Results: Neuropathological examination revealed metastatic spread of pulmonary carcinoma in the form of meningeal carcinomatosis and widespread micrometastases in the brain cortex in both cases. Prion deposits were excluded by immunohistochemistry and by western blot.

Conclusion: Our findings confirm the necessity of considering rare manifestations of tumor generalization in atypical cases of dementias in clinical practice and the importance of clinico-pathological correlations.

Disclosure: Supported by grants NV19-04-0090 and NV18-04-0179 (Ministry of Health, Prague, Czech Republic) and DRO TH00064190 (Thomayer Hospital, Prague, Czech Republic).

EPO3294

Methotrexate myelopathy after intrathecal chemotherapy for hematological malignancies: our experience

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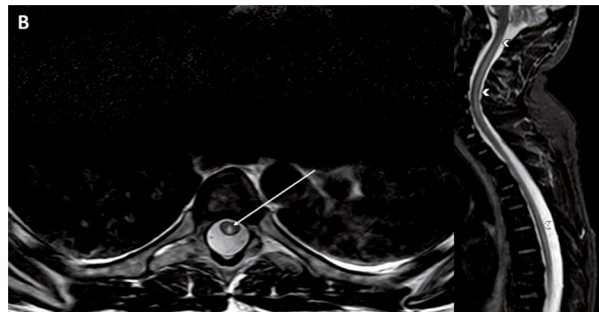
Background and aims: Triple intrathecal chemotherapy (methotrexate, cytarabine and glucocorticoids) is used after hematopoietic stem cells transplant to prevent relapses in the central nervous system. This treatment can produce neurotoxicity. Although the most common form of neurological toxicity is leukoencephalopathy, cases of myelopathy associated with this treatment have been described.

Methods: Retrospective registry of myelopathies after intrathecal chemotherapy

Results: 2 men of 30 and 59 years old were identified, both of them had received triple intrathecal chemotherapy after hematopoietic stem cell transplant for acute lymphoblastic leukemia and extranodal NK/T lymphoma. Subsequently, they developed a subacute paraparesis with hyperreflexia and lower limb hypopalessthesia. Lumbar puncture was performed in which no tumor infiltration was detected. A spinal MRI showed extensive dorsal column myelopathy, from D5 to conus medullaris in patient A and from C2 to conus medullaris in patient B. Both patients had reduced serum folate implicating methotrexate as the cause of neurotoxicity. Blood levels of vitamin B12 were normal. Patient B also developed methotrexate induced leukoencephalopathy in brain MRI. Treatment with folinic acid, cyanocobalamin, methionine, S-adenosylmethionine and even dextromethorphan in patient A was initiated without benefit. Both patients died from complications of immunosuppression.



Patient A: MRI showed T2 hyperintensity of dorsal column (arrow) from D5 to conus medullaris (arrowheads).



Patient B: MRI showed T2 hyperintensity of dorsal column (arrow) from C2 to conus medullaris (arrowheads)

Conclusion: Dorsal column myelopathy is a rare but distinctive complication with poor prognosis that should be considered in patients who have been treated with intrathecal methotrexate. While there is no effective treatment, early diagnosis can help for prevent further toxicity. Starting intrathecal chemotherapy at minimum effective dose should be considered.

Disclosure: Nothing to disclose

EPO3295

IgG4 positive dural marginal zone lymphoma: a rare cause of focal seizures

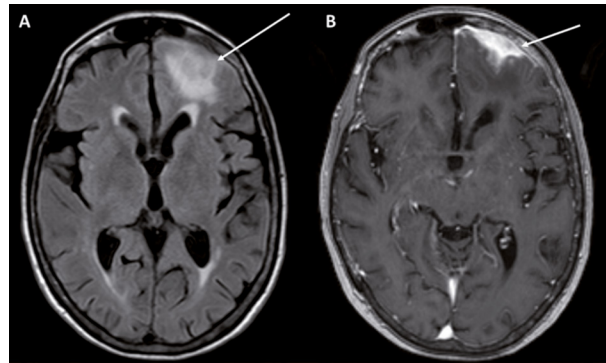
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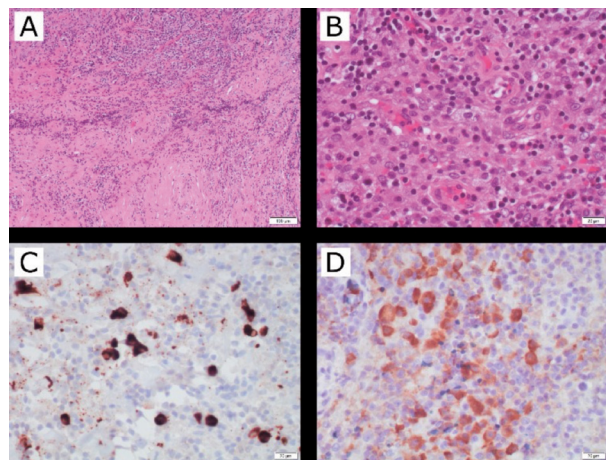
Background and aims: Dural marginal zone lymphomas (MZL) represent an uncommon group of low-grade B-cell neoplasms that radiologically often mimic meningiomas. The expression of IgG4 in these neoplasms has been recently described, posing differential diagnosis with IgG4 related disease.

Methods: A 73-year-old woman with no history of epilepsy was admitted to the emergency department with clustered focal frontal seizures with extension of right arm and flexion of left arm (figure 4 sign) that required intravenous benzodiazepines and phenytoin for control. Neurological examination showed frontal lobe dysfunction such as inattention, language impairment (echolalia and perseveration), anosognosia and difficulty in motor planning, conceptualization, sensitivity to interference and inhibitory control.

Results: Seizures were subsequently controlled with oral phenytoin. An initial MRI showed a leptomeningeal left frontal lesion that was homogeneously enhanced with gadolinium. Based on that findings, the presumptive radiologically diagnosis was “en-plaque meningioma”. Surgery of the lesion was performed and the dural-based solid mass was resected. The histological examination revealed a dense B lymphocyte infiltrate with numerous IgG4 positive plasma cells, clonal rearrangement of the variable IGH region was detected, supporting the diagnosis of MZL. The diagnostic study was completed with PET-CT and bone marrow biopsy which showed no alterations. The patient had an uneventful postoperative course. After follow up for one year she has remained seizure free.



A: FLAIR-weighted magnetic resonance image (MRI) showing a left frontal extra-axial mass with leptomeningeal, parenchymal and bone infiltration (arrow). B: T1-weighted MRI after gadolinium administration showing homogenous enhancement of the mass (arrow).



A. Hematoxylin-eosin, x10. Dense inflammatory infiltrate and storiform fibrosis. B. Hematoxylin-eosin, x40. Inflammatory lymphoplasmacytic infiltration with small lymphocytes, plasma cells and occasional eosinophils. C. Immunohistochemistry versus IgG4, x40. Numerous IgG4 plasma cells. D. Immunohistochemistry versus IgG.

Conclusion: IgG4 positive MZL is a rare meningeal neoplasm. It may manifest as seizure or focal signs and it should be considered in the differential diagnosis of meningeal tumors, since they have excellent long-term survival with local therapy.

Disclosure: Nothing to disclose

EPO3296

Non-Hodgkin lymphoma: an unusual cause of diplopia

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Background and aims: Metastatic infiltration of the extrinsic ocular musculature is an uncommon cause of diplopia. Skeletal muscle is considered an unusual location of secondary growth of solid tumors, however, in lymphomas and leukemia its involvement is frequent and associated with a higher degree of visceral involvement. Herein, we report a case of diplopia in a patient with a previous history of B-cell non-Hodgkin lymphoma (BNHL).

Methods: Case report and literature review.

Results: A 62-year-old male with high blood pressure and a low-grade BNHL in follow-up and expectant attitude since 2015, presents to the hospital with a 3-month history of blurred vision, without pain or other associated symptoms. Physical examination shows hypertropia of the right eye (RE), which conditions vertical binocular diplopia and a slight limitation in the infraduction of the RE. Magnetic resonance imaging of the orbit identifies a mass that depends on the right inferior rectus muscle. Infectious, metabolic, autoimmune and paraneoplastic causes are excluded, as well as meningeal carcinomatosis. Given the medical history of an oncohematologic disease, a muscle biopsy is performed, revealing lymphoid infiltration suggestive of a high-grade follicular lymphoma. Positron emission tomography scan confirms disease progression.

Conclusion: Although lymphomas are the most frequent malignant tumors in the orbit, exclusive involvement of an extraocular muscle is very uncommon. However, the possibility of metastatic infiltration should be included in the differential diagnosis of diplopia, especially in patients with previous history of oncohematologic disease.

Disclosure: Nothing to disclose

EPO3297

Adult-onset primary central nervous system germinoma with atypical neuroimaging findings

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Background and aims: Primary central nervous system germ cell tumours (GCT) are very rare tumours in adult population of Western countries.

Methods: Case report.

Results: A previously healthy 31-year-old man presented with a 3-month history of loss of appetite, polydipsia, polyuria and erectile dysfunction. The neurological examination only revealed a horizontal gaze-evoked nystagmus. Hormonal studies confirmed panhypopituitarism. Brain magnetic resonance imaging (MRI) studies showed enhancement of lateral and fourth ventricles subependymal regions and of midline structures, including the pituitary stalk (Figure 1). Lumbar puncture disclosed elevated protein levels and a mild lymphocytic pleocytosis (polyclonal mature lymphocytes in flux cytometry). Broad microbiological studies in blood and cerebrospinal fluid (CSF) (including PCR for neurotropic viruses and cultures for fungi and mycobacteria) were negative. Autoimmune studies, blood analysis including angiotensin converting enzyme, spinal cord MRI and thorax CT were normal. Whole body F-FDG-PET/CT only showed hypermetabolism in the MRI enhancing areas. The patient was discharged for outpatient follow-up. Months later, he was admitted presenting severe neuropsychiatric symptoms and bilateral internuclear ophthalmoplegia. A new MRI showed volume increase of the enhancement areas. A higher pleocytosis and a positive PCR for Epstein-Barr virus (EBV) were demonstrated in CSF. A brain biopsy revealed reactive polyclonal lymphocytes. Suspecting a persistent EBV-encephalitis, the patient was treated with ganciclovir and corticoids, resulting in a temporary improvement. Upon a new clinical worsening when tapering corticoids, a new brain biopsy confirmed the diagnosis of germinoma. Radiotherapy and chemotherapy were started.

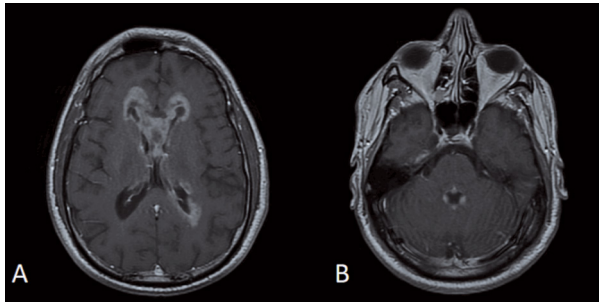


Figure 1

Conclusion: GCT are potentially curable and should be considered in cases of diffuse subependymal and midline enhancement.

Disclosure: Nothing to disclose

EPO3298

Intraventricular dysembryoplastic neuroepithelial tumor: an unusual location

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Background and aims: Dysembryoplastic neuroepithelial tumors (DNET) are cerebral cortical, benign slow-growing tumors of neuroglial origin. They are 1 of the most common surgical indications for epilepsy in younger age patients especially due to the favorable outcomes. Extracortical locations are extremely rare.

Methods: Case report description

Results: A 27-year-old woman had a car accident with no loss of consciousness or involuntary movements. In the emergency department, the patient was alert and with no deficits. Her past medical history was remarkable only for episodic headaches with no medical follow-up. A head CT scan showed an incidental intraventricular calcified lesion in the left frontal horn of the lateral ventricle. The brain MRI revealed a lobulated and well circumscribed lesion, hyperintense in T2/FLAIR, hypointense in T1, and anteriorly hypointense in T2*. It enhanced heterogeneously with gadolinium administration. A complete tumor resection was performed. Pathological evaluation disclosed a tumor with small oligodendrocyte-like cells distributed throughout a mucin-rich background where few floating neurons and scattered astrocytes could be identified. Immunohistochemical staining showed synaptophysin and neurofilament, and GFAP reactivity, respectively within neurons and their processes and astrocytic elements. Oligodendrocytic-like cells were OLIG2 and GFAP reactive. The tumor showed no atypical histological features. The MIB-1 (Ki 67) proliferation index was <1%. ATRX was reactive (non-mutated) and IDH1 and CD34 non-reactive. The diagnostic was a DNET.

Conclusion: We report the case of an incidental diagnosis of an intraventricular DNET. This location is extremely rare and, therefore, determines an accurate differential diagnosis given its good post-surgical prognosis. Thus, we underwent an extensive immunohistochemical evaluation.

Disclosure: Nothing to disclose

EPO3299

Osimertinib activity on leptomeningeal metastasis

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Background and aims: Osimertinib is a 3rd generation epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKI) used as a 2nd-line therapy for non-small-cell lung cancer (NSCLC) harboring activating EGFR mutation and progressing over prior EGFR-TKIs.

Methods: We report here the cases of 2EGFR mutation-positive NSCLC patients, treated with osimertinib for leptomeningeal metastasis (LM) that occurred during first-line EGFR-TKI treatment.

Results: A 49-year-old female treated with afatinib (40mg/d) for 2years then bevacizumab-pemetrexed-carboplatin for 6 months presented an isolated LM confirmed by CSF analysis. The T790M mutation conferring resistance to EGFR-TKI was not detected. Switch to osimertinib (80mg/d) induced regression of leptomeningeal enhancement and normalization of CSF at 4 weeks, persisting at 1year. Osimertinib dosages showed normal blood exposure (142ng/mL) but low CSF penetration (1.4ng/mL), with a CSF:Blood ratio of 1%.

A 71-year-old male treated with erlotinib (150mg/d) for 9 months, then erlotinib-bevacizumab-pemetrexed-carboplatin for 12 months presented an isolated LM likewise diagnosed. T790M mutation was not detected. Osimertinib (80mg/d) was started but his condition worsened, with persistent carcinomatous cells in CSF. Osimertinib dosages showed normal blood exposure (174ng/mL) but low CSF penetration (1.3ng/mL) with a CSF:Blood ratio of 0.6%. A pulsatile schedule of high-dose of osimertinib (320mg every 4 days) failed to increase CSF penetration (ratio at 0.9%). The patient died 1 month later.

Conclusion: Osimertinib CSF penetration was low with CSF:blood ratio around 1%, similar to what was reported with others EGFR-TKIs. Despite this, osimertinib can induce clinical, radiological and biological response in NSCLC with LM. Pulsatile schedule didn't significantly increase CSF:blood ratio.

Disclosure: Nothing to disclose

EPO3300

Myelitis of spontaneous recovery after anti-CD19 CAR T-cells injection

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Background and aims: Anti-CD19 Chimeric antigen receptor (CAR) T-cells treatment for refractory/relapse diffuse large B-cell lymphoma (DLBCL) can develop heterogeneous neurological toxicities, called ICANS (immune cell-associated neurologic syndrome), which remain poorly defined.

Methods: We report here the case of a DLBCL patient treated who developed myelitis 2 weeks after anti-CD19 CAR-T cells therapy.

Results: A 41-year-old woman, diagnosed with DLBCL IPIaa 1, was treated with fludarabine-endoxan conditioned CAR-T cells infusion (tisagenlecleucel) after 3 relapses. 1 day after reinjection (D1), she presented an isolated grade 2 cytokine releasing syndrome (CRS) treated with Tocilizumab.

At D14, she presented urodynamic urges and limbs sensorimotor deficit. Spinal MRI found a D1 to D7 gadolinium-enhanced myelitis with negative etiologic explorations. No specific treatment was implemented due to the delay and spontaneous recovery. The 6 months controls found a disappearance of the gadolinium enhancement and a fading of the T2 hyper signal in the spinal cord, along with a complete response to CAR T-cell treatment.

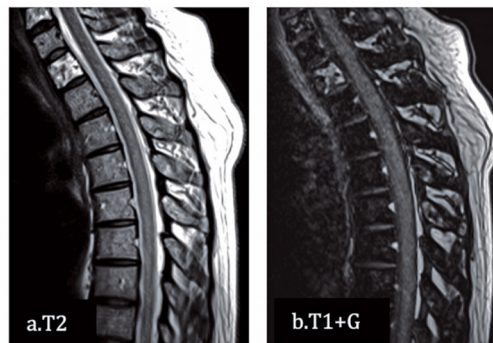


Figure 2: Evolution of spinal MRI pattern (6 months control):
a. sagittal T2 sequence showing a slight persistent hypersignal.
b. sagittal T1 sequence with gadolinium injection (no enhancement).

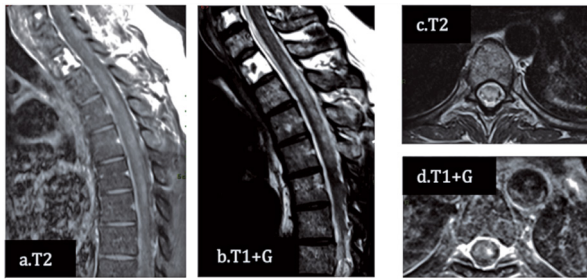


Figure 1: First spinal MRI showing the extensive myelitis:
 a. sagittal T2 sequence showing the heterogeneous intra medullar hyper signal.
 b. sagittal T1 sequence showing gadolinium enhancement.
 c. axial T2 sequence showing the heterogeneous intra medullar hyper signal.
 d. axial T1 sequence showing gadolinium enhancement.

Conclusion: We report here the 1st case of reversible myelitis after anti-CD19 CAR T-cells infusion, thus enriching the spectrum of CAR T-cells neurologic toxicity. Physicians should be aware that CAR T-cells patients can also develop medullar deficits. The spontaneous recovery in our case also suggests that steroids are not always required when developing neurological deficits, what may be interesting in these patients at increased risk of infections.

Disclosure: Nothing to disclose

EPO3301

Primary central nervous system lymphoma: a rare cause of subacute myelopathy

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Background and aims: Primary central nervous system lymphoma with spinal cord localization is a rare, potentially curable disease that requires a timely and rigorous diagnostic process.

Methods: A 76-year-old female, presented with a progressive ataxia during 2 months, followed by flaccid paraplegia within 48 hours, as well as areflexia and sensation loss below T7 level.

The neurological examination also revealed a dysarthria and a cerebellar motor syndrom.

The MRI showed a spinal cord lesion, extending from T5 to conus terminalis with homogeneous contrast enhancement. The brain MRI showed 2 homogeneous gadolinium-enhancing lesions, in the supratentorial and infratentorial spaces. Further research excluded autoimmune, infectious and metabolic diseases. CSF examination demonstrated negative cytology, elevated protein (3g/L), whereas the values of IL-6 and IL-10 were 5000pg/mL and 24pg/mL, respectively. Clonality study and flow cytometry of the CSF were normal, as well as ophthalmologic examination, full body CT scan and FDG-PET scan.

A stereotactic brain biopsy was performed, confirming the diagnosis of a diffuse large B-cell lymphoma.

Treatment consisted of high-dose methotrexate-based chemotherapy based, achieving clinical and radiological improvement.

Results: The clinical and neuroimaging characteristics of this patient's spinal cord lymphoma had a wide range of differential diagnosis including inflammatory disease, CNS infection, paraneoplastic syndromes, vascular cause, or metabolic disease. The presence of associated brain lesions guided towards the diagnosis of lymphoma.

Primary spinal cord lymphoma is a rare cause of subacute myelopathy. The research of cerebral, meningeal, intra-ocular or systemic localization may allow early diagnosis which is essential to start a potentially successful treatment.

Disclosure: Nothing to disclose

EPO3302

Limbic encephalitis: high-grade glioma in disguise?

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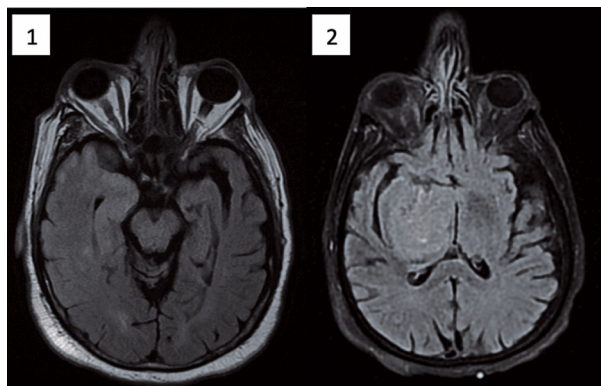
Background and aims: The subacute onset of fever, altered behavior, headache, and seizures should raise the possibility of infectious or para-infectious encephalitis. The differential diagnosis includes toxic, metabolic or immune-mediated parenchymal lesion, whereas tumoral lesion rarely presents with that constellation of symptoms. We present a case of a high-grade glioma mimicking encephalitis presentation.

Methods: N/A

Results: A 69-year-old male patient with no previous history of epilepsy was admitted to the emergency room with generalized tonic-clonic seizures, fever, confusion, and headache. A brain MRI showed the right medial temporal lobe, hippocampus, and insular cortex hyperintensities, without contrast enhancement. CSF examination including cell count, biochemical examination, autoantibody and PCR test for herpes and enterovirus was unremarkable. A diagnosis of viral encephalitis was considered based on clinical and radiological findings, and the patient was started on acyclovir and antiepileptic treatment with complete recovery. A second CSF evaluation performed a week after admission remained normal and the patient was discharged after completing antiviral treatment. 4 months later, he was readmitted with left hemiparesis, gait ataxia and sudden impairment of consciousness. A 2nd brain MRI was performed revealing a large space-occupying lesion in the right mesial temporal region suggestive of high-grade glioma.

high-grade gliomas. In the presence of a persistent innocent CSF examination and infectious and autoimmune workout, a repeated brain MRI should be considered, bearing in mind the possibility of an underlying malignancy.

Disclosure: Nothing to disclose



1 - Brain-MRI, FLAIR. Cortico-subcortical hypersignal at the right insula, frontobasal region and inner part of the right temporal lobe (including the hippocampus). 2 - Brain-MRI, FLAIR. Voluminous right medial temporal lesion, hyperintense, cortico-subcortical, with significant mass effect.

Conclusion: Our case highlights the importance of being aware of the clinical and radiological mimicking features of

EPO3303

Correlation of hypometabolism on brain FDG-TEP and neurotoxicity after treatment with CAR T-cells: a case report.

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Background and aims: CAR T-Cell therapy has recently brought new hope in DLBCL and the number of other indications is expanding. Neurotoxicity is commonly seen after CAR T-cells therapy and is almost always associated with CRS. Cerebral MRI is usually normal, underlying the need for paraclinical examinations that could help the diagnosis and map the cortical lesions.

Methods: A 68-year-old woman with treatment-refractory DLBCL was admitted for anti-CD19 chimeric antigen receptor (CAR) T-cell therapy.

Results: On day 4, a grade 1 CRS was diagnosed and treated with Tocilizumab. The neurological examination evidenced a patient oriented, with cognitive slowness. Symptoms progressively worsened. On Day 9, neurological examination showed a major cognitive slowness associated with ideomotor apraxia, decreased verbal fluency and comprehension disorders, cerebellar syndrome. MRI was normal and EEG showed a diffused slowing. At Day 14, brain FDG-PET showed bilateral diffused low fixation of the cortex, predominant in the parietal and temporal lobes. She was then treated with dexamethasone 10mg twice a day. Cerebellar syndrome and psychomotor slowness improved within 24 hours. At 4 months, neuropsychological tests are within normal limits and FDG-TEP was almost normal with a significant decreased of the parietal and temporal cortical hypometabolism.

Conclusion: Clinical experience for CAR T-Cell neurotoxicity remains limited. MRI does not usually show any abnormality, except in case of severe toxicity, and thus does not allow specific mapping of cortical impairments. Because brain FDG-PET can detect early cortical metabolic alteration, this case suggests that it might be used as a reference exam in CAR T-Cell neurotoxicity.

Disclosure: Nothing to disclose

EPO3304

Neurospecific enolase as serological biomarker of early cerebral complications after surgical removal of meningioma

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Background and aims: The purpose of the study was to investigate the predictive value of neuronspecific enolase (NSE) with respect to postoperative cerebral complications in the patients with meningiomas.

Methods: We observed 70 patients with meningiomas and 62 healthy people. The groups of patients and healthy individuals were comparable by age and gender. NSE level in serum was assessed by enzyme-linked immunosorbent assay in all observed individuals. Clinical, neuroimaging and laboratory examination of the patients was performed upon their admission to the hospital (T0) and in 5–6 days after tumor removal (T1). Continuous variables were expressed as median [quartiles].

Results: There was no statistically significant difference between the NSE levels in patients with meningiomas at T0 (3.1 [2.1-6.2] ng/ml) and healthy individuals (4.1 [2.3-7.1] ng/ml).

Cerebral complications such as severe cerebral edema in the area of surgery and/or 2ndary focal ischemia, tumor bed hematoma, epidural hemorrhage, meningitis were revealed in 13 of 70 (18.6 %) patients in the early postoperative period after craniotomy.

The NSE level at T1 statistically significantly increased compared to T0 in the patients with early postoperative complications, while in patients without such complications it has not changed significantly.

ROC (receiver operating characteristic) analysis suggested that the optimum NSE cut-off point for cerebral postsurgical complications was 9.8ng/ml with 71% sensitivity, 87% specificity.

Conclusion: Neurospecific enolase may be used as serological biomarker of early postoperative cerebral complications after surgical removal of meningioma.

Disclosure: Nothing to disclose

Neurorehabilitation 2

EPO3305

Electrostimulation of suprahyoid muscles in swallowing disorders after stroke (poster)

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Background and aims: The aims of the study was to evaluate changes in swallowing, general neurological state, self-sufficiency and quality of life of patients after stroke with dysphagia after 4 weeks of orofacial rehabilitation with or without electrostimulation of suprahyoid muscles.

Methods: A prospective randomized study of dysphagic patients early in the stroke was performed from 1/2013 to 12/2016, with 54 patients (26 males, mean age 70 years) with standard orofacial rehabilitation and electrostimulation of suprahyoid muscles, and in the control group a group of 54 patients (31 males, mean age 69 years) underwent orofacial rehabilitation without electrostimulation.

Results: The difference in the changes after 4 weeks of therapy was statistically and clinically significant.

Conclusion: Electrostimulation of suprahyoid muscles improves swallowing, neurological status, overall self-sufficiency and quality of life of post-stroke patients with dysphagia.

Disclosure: This study was supported by The Junior Grant of Palacký University Olomouc (No. JG_2019_004) and the Internal Grant Agency of Palacký University Olomouc (No. IGA_FZV_2020_008)

EPO3306

Evaluation of motor rehabilitation using augmented reality in patients with ischemic stroke

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Background and aims: Motor disorders are the most severe consequences of stroke and the cause of disability. Augmented reality (AR) is a new approach of using physiological stimuli during training with biofeedback.

We analyze the impact of visual stimuli created by AR on motor function paralyzed upper extremity in patients after stroke. We developed specialized software for assessing motor function during motor rehabilitation.

Methods: 59 patients in early recovery period of ischemic stroke (average age 63 (57 - 65)). The course of motor rehabilitation was 10 days. The course of motor rehabilitation - 10 days, 1 training session - 60 minutes.

We used spectral criterion as a method characterizing the variability of movements when following a given trajectory. The normalized ratio of the power of the fundamental harmonic of the spectrum to the other harmonics is calculated, which is considered as a characteristic of the accuracy of the main trajectory.

Results: Accuracy of movements - found a significant increase in the value of spectral criterion with an increase in the number of training sessions. It indicates a decrease in number of excess movements during the main task. We find significant increase in number of completed movements with each subsequent session. It indicates an increase in the speed of task over the course of rehabilitation, and reduction in rest period between the approaches performed during one training session.

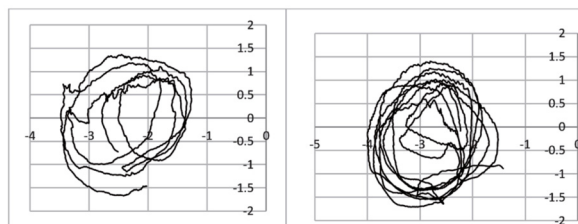


Illustration of the task in 1 and 8 training sessions

Training session	Value of the spectral criterion	Number of completed moves	Maximum duration of a series of tasks (seconds)
1	0.94[0.74:0.96]	23[9:30]	25[10-32]
2	0.95[0.74:0.97]	28[12:30]	27[12-30]
3	0.96[0.88:0.96]	34[20:38]	35[19-40]
4	0.96[0.71:0.97]	45[39:49]	38[20-44]
5	0.95[0.94:0.96]	46[38:52]	37[22-48]
6	0.95[0.92:0.96]	50[39:55]	43[30-49]
7	0.96[0.93:0.97]	53[45:58]	43[33-50]
8	0.96[0.95:0.97]	55[34:59]	45[38-68]
p	0.032	0.002	0.012

Calculated parameters reflecting the dynamics of changes in motor activity during training hands with paresis, Me [Q1; Q3]

Conclusion: The results of the study revealed a significant increase in accuracy of movements and an increase in endurance, which indicates the effectiveness of the approach used in the process of motor rehabilitation.

Disclosure: This study was supported by the Russian Science Foundation (RSF), grant No. 18-15-00082 "Laboratory for robotic rehabilitation"

EPO3307

Botulinum toxin A therapy of post-stroke hand spasticity in combination with brain-computer interface + exoskeleton

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Background and aims: Post-stroke spasticity (PS) is one of most common motor disorders. PS limits the possibility of rehabilitation. The aim: to study the effectiveness of rehabilitation with brain-computer interface that controls the exoskeleton of hand (BCIE) in patients with PS paresis with the inclusion of botulinum toxin type A therapy (BTA).

Methods: There were included 84 post-stroke patients aged 18-85 who received rehabilitation with a brain-computer interface that controls the exoskeleton of the hand (BCIE). In 56 patients (group 1), BTA was applied 3-4 weeks before BCIE, in the group 2 (n=28) - only BCIE without BTA. We assessed neurological deficits before, after BTA, and after BCAA on Ashworth, Fugl-Meyer and Action Research Arm Test (ARAT) scale.

Results: After BTA, group 1 showed a statistically significant decrease in spasticity on the Ashworth scale ($p < 0.05$), after BCIE – a further decrease in spasticity ($p < 0.05$). In group 2, there was no decrease in PS after BCIE ($p > 0.05$). Improvement of motor function of the hand on the Fugl-Mayer and ARAT scale after BCIE was found in patients of group 1 ($p < 0.0001$) and group 2 ($p < 0.05$), but the improvement in patients of group 1 was statistically significantly greater ($p < 0.01$).

Conclusion: The use of BTA allowed to begin the rehabilitation process with a lower PS of the hand. The results in group 1 demonstrates significant effectiveness in reducing spasticity. It was significant improvement in the motor function of the hand after BTA. Reducing of PS allows to expand the window of rehabilitation opportunities and to increase the effectiveness of BCIE.

Disclosure: Nothing to disclose

EPO3308

Dynamics of EEG power during motion imagery in post-stroke patients

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Background and aims: The recovery of movements after stroke is based on neuroplasticity. The brain-computer interface that controls the exoskeleton of the hand (BCIE), and the movement imagery (MI) have the greatest neuroplastic effect.

Methods: We examined 5 right-handed post-stroke patients and used the dynamics of the EEG power (EEGP) during the period of MI in the paretic right arm before and after rehabilitation. The control group - 5 healthy people.

Results: Initially, in the C3 lead, mu-rhythm event-related desynchronization (ERD) was registered for 1-3 seconds, then from 7 seconds - event-related synchronization (ERS), strong exciting interaction with frontal-parietal regions in both hemispheres was detected. After rehabilitation, it was found the restoration of EEGP in the primary motor cortex, reducing the pathological influence of the contralateral hemisphere. In the control group, normal ERD was observed in the C3 lead. There were registered a slight decrease in the power of the alpha rhythm and statistically insignificant fluctuations in the power of the beta and theta rhythm in the anterior and posterior frontal, upper-parietal leads of both hemispheres.

Conclusion: The reorganization of neural networks as a result of rehabilitation was manifested in the restoration of the interhemispheric balance of bioelectric activity. The strong exciting interaction of the primary motor cortex and the frontal-parietal regions in the affected and “intact” hemispheres after a stroke was probably a reflection of the dynamic reorganization of neural networks. Significant decrease in EEGP after course of rehabilitation coincided with a partial restoration of the impaired motor function of the right hand.

Disclosure: The work was supported by the Russian Foundation for basic research, RFBR grant № 19-015-00192\19a.

EPO3309

Assessment of serum BDNF and NGF in patients after motor rehabilitation in early recovery period of ischemic stroke

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Background and aims: Brain-derived neurotrophic factor (BDNF) and Nerve growth factor (NGF) are neurotrophins that activate neuroplasticity after motor rehabilitation.

Aim: to detect clinical-laboratory correlation after motor rehabilitation in early recovery period of ischemic stroke.

Methods: The study involved 68 patients with ischemic stroke (average age 65 (59-68) years; Rankin scale 3 (2-3); NIHSS=4 (3-6) after early rehabilitation in Tomsk regional vascular center. 2 groups of patients: 48 moved to the 2nd stage of rehabilitation in Research Institute of Balneology; 20-rehabilitation without. Points of view: I-14th, II-45th days of stroke. Neurological examination was completed by Fugl-Meier Assessment (FMA). BDNF was determined by MAGPIX multiplex analyzer (Luminex, USA) using xMAP® Technology, NGF by SEA105Hu «Cloud-Clone Corp.» (USA)

Results: 1 group: FMA I=205 (192-211); FMA II=205 (192-213); p=0.753

BDNF I=2745 (1855-4686) pg/ml; BDNF II=1110 (679-1484) pg/ml; p=0.005

NGF I=2,1(1.6-2.3) pg/ml; NGF II=2,0 (1.9-2.1) pg/ml; p=0.225

2 group: FMA I=191 (177-201); FMA II= 199 (190-212); p=0.00

BDNF I=2768 (2009-3652) pg/ml; BDNF II=2175 (1730-2739) pg/ml; p=0.807

NGF I=1,5 (1,4-1,8) pg/ml; NGF II=3,0 (1,5-3,3) pg/ml; p=0.002

Strong positive correlation was found between NGF level and values on FMA (after motor rehabilitation in early recovery period of ischemic stroke ($r=0.583$, $p=0.012$).

Conclusion: The results are demonstrated the effectiveness of 2nd stage of motor rehabilitation in early recovery period of ischemic stroke in Research Institute of Balneology.

Disclosure: This study was supported by the Russian Science Foundation (RSF), grant No. 18-15-00082 “Laboratory for robotic rehabilitation”

EPO3310

The effectiveness of repeated courses of training using ExoAtlet exoskeleton for patients with multiple sclerosis

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Background and aims: One of the directions in the recovery of consequences of multiple sclerosis is rehabilitation using robotic devices.

Purpose: To evaluate the effectiveness of repeated courses of training using Exoatlet exoskeleton for patients with multiple sclerosis who have impaired walking function.

Methods: The study included 9 patients in remission and with the presence of motor deficit in the lower extremities. To assess the severity of functional deficit were used the Kurtzke extended scale of disability and MSFC (MS functional composite) test before and after the 1st course and after 6 months (beginning of the next course) and in the end of the 2nd course. Each course consisted of 10 classes.

Results: The study of the index of dysfunction of the pyramid system showed a significant decrease in the degree by 1 point (31.2%) compared to the initial value ($p<0.05$). Assessing the level of disability on the EDSS scale cyclical changes were observed with positive dynamics by the end of the rehabilitation course and returning to the initial value by the beginning of the next course. The improvement after each course was an average of 5%. According to the MSFC test there were positive changes in dynamics after the course of neurorehabilitation in relation to cognitive part. The dynamics of the test result compared to the initial value was 2.3%, 38.6%, 50% during the study.

Conclusion: The presented results showed the prospects for further studies of the effectiveness of robotic mechanotherapy for patients with multiple sclerosis and with motor disorders.

Disclosure: Nothing to disclose

EPO3311

Evaluation of the safety and effectiveness of the ExoAtlet robotic complex for patients in the early recovery period of ischemic stroke

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Background and aims: The aim was to study the possibility of restoring movement and cognitive functions of patients in the early recovery period of ischemic stroke using robot therapy (ExoAtlet complex).

Methods: We used the ExoAtlet Pro Rev. robotic system for 40-80 minutes once per day during 10 days for 5 patients. To assess the dynamics, before and after treatment we used the estimative score scales of: muscle strength, Ashforth spasticity, Berg balance, Rankin, Bartel index (BI), Montreal Cognitive Assessment (MoCA), stabilometric study.

Results: Improvement of motor functions and functional state were achieved during classes with ExoAtlet Pro Rev. There was an increase of 1 point in muscle strength of 1 patient and functional activity on the Rankin scale of 2 patients. A more sensitive method was to evaluate daily activity using BI (positive dynamics of 15 points for 1 patient and 5 points for 3 patients). Positive trend was also detected in the whole group as an increase in the value of the Berg Balance scale indicator from 4 to 10 points - the increase in stability. 4 patients had an improvement in stabilometric parameters in the form of the decrease in length, speed, and area of the statokinesiogram. The data correlate with the Berg balance score. Positive dynamics was revealed in the form of regression of cognitive disorders on the MoCA scale.

Conclusion: The use of robot therapy for patients with ischemic stroke in the early recovery period contributes to the restoration of movement function, regression of cognitive disorders and is safe and effective.

Disclosure: Nothing to disclose

EPO3312

Clinical progress of individuals in minimally conscious state plus and minus. Description and comparison of the level of consciousness and disability

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Background and aims: To describe and compare the clinical progress of a sample of patients diagnosed with Minimally Conscious State Plus (MCS+) and Minus (MCS) based on specific items of the Coma Recovery Scale-Revised (CRS-R).

Methods: 68 patients, 17 women and 51 men, with a mean age of 42.0±16.2 years old, who had sustained a traumatic (n=37) or non-traumatic brain injury (n=31) were included for analysis. All patients were monthly assessed with the CRS-R and the Disability Rating Scale (DRS) for at least 12 months after the injury or until recovery of consciousness.

Results: At admission, 23 patients were in MCS+, had a mean CRS-R of 15.3±1.8 and a DRS score of 21.9±1.8. 45 patients were in a MCS- and had a mean CRS-R of 9.5±1.8 and a DRS of 23.8±1.6. Both groups significantly differed in both CRS-R (p<0.01) and DRS score (p<0.01). 12 months after the injury, 45 patients had recovered consciousness (after a mean period of 169.9±83.2 days). A statistical significant effect of the clinical condition was found in the emergence of consciousness: while all patients in MCS+ recovered consciousness, only 22 patients in MCS- did. Patients who recovered consciousness had significantly higher CRS-R at admission (12.6±3.2 vs 9.1±1.9, p<0.01) and lower DRS (22.7±1.8 vs 23.9±1.9, p<0.05). No other significant differences were found.

Conclusion: Diagnostic criteria for MCS+ and MCS- defined based on CRS-R items was associated to different functional disability and recovery of consciousness.

Disclosure: This study was funded by Conselleria de Educació, Cultura y Deporte of Generalitat Valenciana of Spain (Project SEJI/2019/017) and Universitat Politècnica de València (Grant PAID-10-18).

EPO3313

Functional reciprocal electromyostimulation in adaptive kinesitherapy of post-stroke patients

V.V. Ponomarev, U. Lukashevich

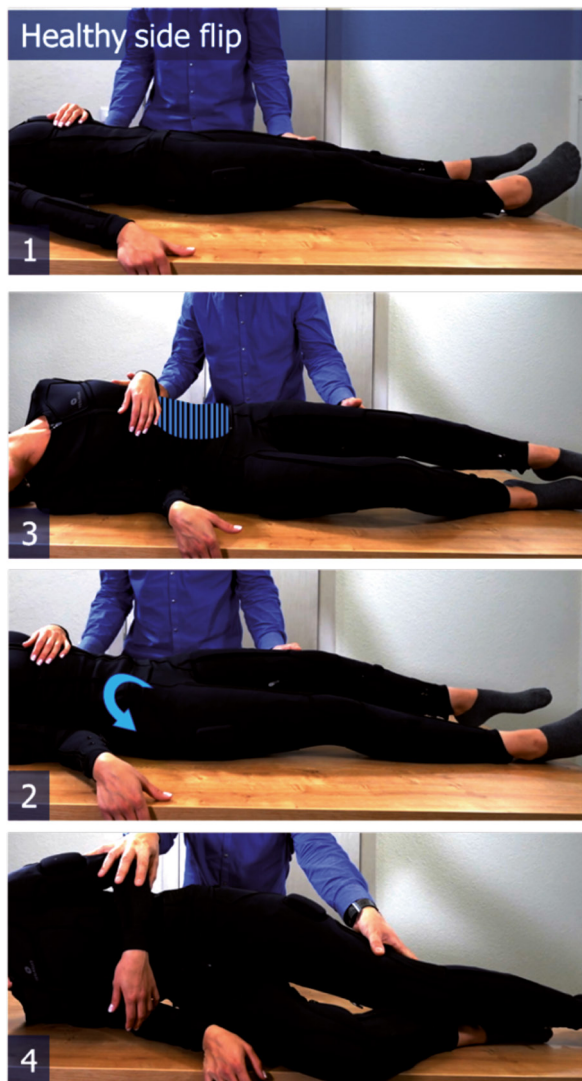
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Background and aims: Various neuromuscular and musculoskeletal diseases lead to impaired human interaction with the environment (process of motor adaptation). Comprehensive medical rehabilitation program for this group of patients consist of numerous technologies and techniques, one of which is adaptive kinesitherapy(AK).

Methods: The study involved 24 male patients after a stroke with hemiparesis. The time after a stroke was 3-6 months. 10 patients received a standard rehabilitation program (group#1). 14 patients underwent AK using TESLASUIT smart suit (group#2). Using TESLASUIT technology, reciprocal electromyostimulation(EMS) of various muscle groups was performed. The AK program used 27 exercises to correct postural, vestibular, proprioceptive function, as well as mobility of joint functions, involuntary movement reaction functions, control of voluntary movement functions and gait pattern functions. Average AK time-3 weeks. The essence of the approach is that with active or passive movement, the motion capture system recognizes the performed locomotion and implements a specific pattern of muscle stimulation of agonists and antagonists in the form of functional EMS. For assessment were used: Modified Renkin Scale(MRS), Barthel Index(BI), Scandinavian stroke scale(SSS), 10 Meter Walk Test(10MWT).



Exercise example: THREE-STAGE HIP FLEXION



Exercise example: HEALTHY SIDE FLIP



Exercise example: TRUNK TURNS

Results: Results were obtained (before treatment : after treatment)

Group#1:

MRS -3,6:3,0;

BI - 56,1:46,8;

SSS - 17,9:23,5;

10MWT: 1,7 - 2,9

Group#2:

MRS -3,4:2,1;

BI - 54,7:36,4;

SSS - 18,7:27,9;

10MWT: 1,5 - 4,2

Conclusion: Application of TESLASUIT technology with the function of reciprocal EMS in the comprehensive AK program increases the effectiveness of rehabilitation after-stroke patients.

Disclosure: Nothing to disclose

EPO3314

Rehabilitation in Virtual Reality (VR): determinating number of exercises for simple arm movement

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Background and aims: Rehabilitation after ischemic stroke is a long and difficult process. In addition to standard physio- and occupational therapy, patients may perform tasks in VR. Aim of our study was to determine how many session using haptic device Bimeo is needed to improve reaching movement.

Methods: We included 13 patients 3 weeks after ischemic stroke. Patients had standard physio- and occupational therapy and performed reaching movement in VR using haptic device Bimeo. All patients held Bimeo in the affected arm and had 10 rehabilitation sessions doing reaching movements in the period of 14 days. mRS and modified Box&Blocks test score were evaluated at the beginning and the last session. Reaching parameters (movement quality index (MQI), velocity, smoothness and accuracy) were measured using Bimeo. Mean scores were compared using t-test and ANOVA.

Results: Patient's neurological conditions significantly approved after 14 days of rehabilitation. Final mean mRS score (1.5 ± 0.6 vs 1.2 ± 0.4) and mean time of modified Box&Blocks test improved (27.92 ± 16.81 s vs 20.31 ± 7.62 s). Similarly, several parameters of reaching measured with Bimeo improved. Our results indicate that MQI improves after 6 consecutive exercises, while smoothness, velocity and accuracy approved after 10 consecutive exercises.

Conclusion: We may conclude that Bimeo may be used for rehabilitation of the upper limb in patients with mild to moderate motor impairment ($mRS \leq 3$). Patients need to practice with the device at least ten times in 14 days for optimal results.

Disclosure: Nothing to disclose

EPO3315

Factors influencing efficiency of rehabilitation in patients after ischemic stroke

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Background and aims: Prediction of the success of rehabilitation treatment in the post-stroke period is determined by the factors of rehabilitation potential (RP). The aim is to study the factors influencing the effectiveness of rehabilitation treatment in patients in the acute period (AP) of ischemic stroke (IS).

Methods: 72 patients in the AP of IS in the Regional vascular center in Ufa were examined. The average age of patients is 63.8 ± 1.3 years. The following scales were used: NIHSS, Renkin, Barthel, Rivermead mobility index, Montreal cognitive assessment, Spielberger-Khanin's anxiety scale, Beck's depression scale, Wayne A.M. and Ehlers questionnaire, the method of Schubert. Assessment of the RP was carried out using data analysis of the "Rehabilitation sheet".

Results: The majority of patients in the AP of IS, cognitive impairment (CI), anxiety-depressive disorders (ADD) and autonomic dysfunction were detected. During the treatment period, the number of patients with mild neurological deficit (MND), mild disability and mobility significantly increased. 82.9% of patients at the beginning of treatment had a medium to high degree of motivation for success. According to Ehlers, a success-oriented person prefers medium or low risk. Such patients were the majority 95.1%. Based on a combination of factors, 78% of patients had medium and high levels of RP.

Conclusion: A comprehensive and individual approach to the correction of various pathological disorders in patients in the AP of IS taking into account RP is the key to the effectiveness of rehabilitation treatment at the stages of rehabilitation.

Disclosure: Nothing to disclose

EPO3316

Using pressure algometry in the assessment of post-stroke shoulder pain

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Background and aims: Post-stroke pain syndromes are difficult to rehabilitate. In connection with the formation of speech and cognitive impairments an objective assessment of pain in the post-stroke period is a certain problem. Pressure algometry is considered to be the relevant method for objectivization of pain syndrome in various studies.

Aim of investigation: to determine the correlation between the degree of pain syndrome (visual-analogue scale, VAS) and the factor of the pain threshold under pressure (PPT) in patients in the post-stroke period.

Methods: 120 volunteers were recruited (mean age: 68), 62 men. Inclusion criteria: a history of stroke (from 1 to 6 months after acute stroke); degree of arm paresis (from 1 to 4 points according to MRCS); pain syndrome in the shoulder area; signed informed consent.

To assess the effectiveness VAS was used. The indicator PPT is determined by applying controlled pressure to the trigger painful point in the certain muscle.

Results: In accordance with VAS 3 groups of patients were found: 30% (n=36) VAS under 4; 37.5% (n=45) VAS from 4 to 6; 32.5% (n=39) VAS above 6.

The PPT indices in the groups were distributed as follows: $3.04 \text{ kg/cm}^2 \pm 0.38$ in the first group, $2.97 \text{ kg/cm}^2 \pm 0.27$ in the second, $2.89 \text{ kg/cm}^2 \pm 0.24$ in the 3rd. Spearman's rank correlation coefficient $r = -0.71252$.

Conclusion: The use of pressure algometry makes it possible to objectify the assessment of pain after a stroke, and can be useful for patients with speech and cognitive impairment.

Disclosure: Nothing to disclose

EPO3317

Endocannabinoid (Recompensatory) system. Bridging the gap between Cannabis plant molecules, cell metabolism, cognitive function and emotional experience. Mechanisms, healing pathways and multiplicity of health domains.

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Background and aims: A literature review paper that provides a bird's eye view of the Endocannabinoid System functions and presents the potential, which lies in the alchemy between Cannabis plant molecular compounds and the human body's innate abilities, to heal symptoms of maladies and/or to reverse undesired health disorders.

The main objective is to simplify and to organise (schematise) the multiplicity of aspects of human health and holistically present this interrelatedness to make an understanding of healing pathways easier to grasp.

Methods: The review paper is built on a framework of three domains of health. Physical health - Cell metabolism. Inflammatory processes, cancerous mutations, neural degeneration, and pain. Mental health – Cognition and consciousness. Neural function, stress management, learning and creativity improvement, increased awareness and modulation of neuropathic pain. Spiritual health – Emotional resilience, experience perception, enhancement of spiritual feelings of appreciation, love, peace, etc.

Results: Much of the scientific research data of Endocannabinoid System and molecular compounds of Cannabis, available today, clearly demonstrates therapeutical benefits of the plant. This review provides an overarching understanding of the function between the plant and the human body.

Conclusion: The knowledge of pathways of multifunctional mechanisms is paramount for successful therapy, its design, and education. Yet even more so important is the culture of consumption, dosage, ways of administration and legal status of the plant itself. Without much rhetoric, this also is briefly addressed.

Disclosure: Nothing to disclose

EPO3318

Goal-oriented therapy planning in neurorehabilitation: Adherence to personalized treatment pathways in subacute stroke – a feasibility study

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Background and aims: Therapy planning in neurorehabilitation is usually based on expert opinions instead of standardized assessments and/or clinical guidelines. We therefore developed a novel procedure integrating multidisciplinary and discipline-specific assessments, long-term goals and best clinical practice recommendations to define personalized treatment pathways. The aim of this feasibility study was to investigate whether such personalized treatment planning can be implemented within the major neurorehabilitation disciplines.

Methods: 23 patients with subacute stroke were included and 84 completed weeks of in-patient neurorehabilitation were analysed. The primary outcome was adherence to target treatment plan. Feasibility was assumed if deviations were <5%. The 2ndary outcome was participant satisfaction with the new procedure assessed 72 hours prior to discharge. Univariate descriptive analysis and multiple comparisons were performed.

Results: Relative deviations of the target treatment plans were +7.8% in physical therapy (p=0.480), -47.6% in neuropsychology (p=0.061), -49.8% in occupational therapy (p=0.003) and -83.1% in speech therapy (p=0.003), indicating that only physical therapy met the feasibility threshold of the novel procedure. Participants rated the novel procedure on a 5-point Likert scale as “very good” to “excellent” (mean 1.59, SD=0.73).

Conclusion: This study indicates that the adherence to personalized treatment pathways is challenging due to multidisciplinary resource allocation and implementation of efficient treatment settings. While physical therapy profits from efficient group settings and established technology-assisted therapies, other disciplines seem limited to cover requirements due to more individualized patient needs. Future work needs to refine the multidisciplinary prioritization and integrate efficient treatment solutions among disciplines.

Disclosure: Nothing to disclose

EPO3319

Efficiency of exercises on the “Exarta” kinesitherapeutic technology in patients with cervical osteochondrosis.

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Background and aims: To achieve reducing cervical pain and improve movement in cervical zone with exercises “EXARTA” kinesitherapeutic technology (EKT).

Methods: 28 patients with cervical osteochondrosis, from the age of 25 to 45 years were examined. They were divided into 2 groups: Main Group (10 patients) and Control Group (18 patients). The main group has done special exercises based on the EKT for cervical zone to reduce pain syndrome with classical physiotherapy, during 14 days. The control group has done classical physiotherapy only. To evaluate the functionality, we used: Visual Analogy Scale (VAS) and Neck Disability Index (NDI).

Results: At the end of 14 sessions of EKT patients underwent to a further evaluation aimed to compare the results. According to results, the VAS conducted in main group from 5.24±1.42 to 2.68±1.29, in control group 5.36±1.16; the NDI in main group from 11.61±3.9 to 7.13±4.14, in control group 11.50±3.86. A significant difference between the main and control groups $p < 0.05$.

Conclusion: EKT special exercise is considered effective a program that improves the functionality of the body in the form of reducing pain, fatigue; function improvement and quality of life in patients with osteochondrosis of the cervical spine. Nevertheless, the data collected indicate that the use of EKT with classical physiotherapy at the same time gives effectiveness in a shorter time.

Disclosure: Nothing to disclose

EPO3320

Potential Role of tDCS in increasing balance complexity to facilitate motor recovery in chronic stroke

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Background and aims: Alterations in neuroplasticity and cortical excitability are important pathophysiological factors in stroke. Promising outcomes on motor performance have been identified in individuals with stroke following cortical stimulation. In this study, we aimed to examine the potential of tDCS in nonlinear dynamic postural stability in individuals suffering from chronic stroke. The hypothesis that tDCS can modify the efficacy of balance training in these individuals was tested.

Methods: In the present study, 22 individuals were included in this double-blind randomized controlled clinical trial. The anodal tDCS was applied to the leg motor cortex for 5 consecutive sessions concurrent with intensive balance training. we recorded: (1) functional outcomes using the Timed Up and Go test, as well as the Timed 10-Meter Walk Test and Berg balance score (2) Postural stability was assessed by a nonlinear approach using complexity index. Measurements were taken at baseline, after the 1st treatment session, and after the last treatment (5th) session.

Results: The results indicated that the active tDCS group showed significant differences in Timed 10-Meter Walk Test Scale ($P < 0.05$). The multi-scale entropy analysis and complexity index provide significant differences between the 2 groups in closed eyes condition. Participants exhibited increased complexity of standing COP dynamics from baseline during eyes closed trial after 5 sessions of training ($P < 0.05$).

Conclusion: Considering the results of the current study, it seems that tDCS affects the domain of stroke rehabilitation by increasing system complexity and provides a valuable adjunct therapy to boost ambulation recovery in individuals with chronic stroke.

Disclosure: Nothing to disclose

EPO3321

Rehabilitation of patients after stroke with use of Robotic Mechanotherapy Technology.

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Background and aims: The level of disability of patients after a stroke ranges from 76 to 85, and 25-30% remain disabled for the rest of their lives. Hardware and robotic rehabilitation are actively being introduced into practice. However, among experts there is no unanimous opinion on the effectiveness of the use of robotic systems.

Objective of research to study the effectiveness of robot mechanotherapy in the rehabilitation of post-stroke patients with motor disorders.

Methods: The results of treatment of 69 patients after ischemic stroke were analyzed. Of these, 42 (61%) are women and 27 (39%) are men. Patients were divided into 2 groups. Group 1 consisted of 35 patients who received robotomechanotherapy in addition to pharmacotherapy. Group 2 included 34 patients who received only basic therapy. Analysis of treatment results was carried out according to the following parameters: restoration of neurological functions, level of social and domestic adaptation, psycho-emotional state and quality of life of patients. The Barthel scale evaluated motor function and household adaptation.

Results: In group 1, a sufficient complete degree of restoration of neurological functions was observed in 66.3% of patients, and in group 2, 38.5% ($p < 0.001$). In the 1st group, a fairly complete degree of household adaptation was noted in 64.2% of cases, and in the 2nd group in 36.2% of cases ($p < 0.001$).

Conclusion: The use of robotic mechanotherapy in addition to pharmacotherapy significantly affects the effectiveness of the recovery potential of treating patients after a stroke.

Disclosure: Nothing to disclose

EPO3322

Dance steps as exercise treatment in patients with the late cerebellum ataxia

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Background and aims: There are no special physical exercises for the patients with the late cerebellum ataxia. The aims of the study were selection and evaluation of the clinical effect of the new exercise treatment based on dance steps for the balance and gait in the patients with the late cerebellum ataxia.

Methods: The group 1 (12 males, age 49.3 ± 8.8 years) and the control group 2 (10 males, age 50.1 ± 10.0 years) with the diagnosis of the late cerebellum ataxia were included in this study. The daily program for the group 1 was composed of the training lessons with the doctor every day and the independent task-repetitions to 5-6 times a day during 12 days. The evaluation of the clinical effect was conducted in the scale SARA before and on 12th day of the therapy.

Results: In the course of the study for the patients with the late cerebellum ataxia was compiled the program of the physical exercises based on the techniques of the steps of the dance. The total scores SARA, the scores of gait and stance in the group 1 decreased and did not change in the group 2.

Conclusion: The selection of the special physical exercises based on dance steps is important for the therapy of the late cerebellum ataxia.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

EPO3323

Functional prognosis among the variants of Guillain-Barré Syndrome in a Mexican Population

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Background: Guillain-Barré Syndrome (GBS) is an acute polyradiculoneuropathy mediated by immune mechanisms. It is heterogeneous in terms of severity and prognosis.

Objective: We compared functional prognosis at 30 days of the neurophysiological variants of the GBS.

Material and methods: We conducted a retrospective cohort study. We included patients with diagnosis of GBS with nerve conduction velocities (NCV) and lumbar puncture. We divided our population in axonal and demyelinating variant. We calculated Hughes, MRC, EGRIS and ERASMUS scales and followed the patients for 30 days. We made a comparison of the functional prognosis (defined by MRC Scale after 30 days) with the x2 test for comparison of proportions between both groups with a level of statistical significance $p < 0.05$.

Results: We included 51 patients. The axonal variant was present in 90.2% and 5.88% were demyelinating. The most frequent clinical variant was AMAN (n=32). About 60% had modified ERASMUS > 5 and 68% of patients had functional stage 4, according to Hughes score. Patients with axonal variant had worse functional outcome (32.39% Vs 4.22%) ($p = 0.0121$).

Conclusion: Patients with axonal variant had worse functional prognosis assessed by MRC scale, compared with the demyelinating variant. There are important differences in the clinical presentation of our cohort when compared to others.

Disclosure: Nothing to disclose

EPO3324

Spastic paraparesis and periodic paralysis in siblings: the extensive phenotype due to MT-ATP6 mutations.

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Background and aims: Defective oxidative phosphorylation is described as a potential genetic cause of hereditary spastic paraparesis (SPG). In the literature, the case of 3 siblings with SPG phenotype and periodic paralysis has been published. We report a 2nd family with siblings presenting distinguished phenotypes due to MT-ATP6 mutation.

Methods: Sibling n°1 (S1) is 36 years old and he has presented since the age of 20 a severe SPG associated with an axonal sensitivo-motor neuropathy. The 1st screening for genes related to SPG was negative.

Sibling n°2 (S2) is 26 years old and she has reported since childhood episodes of periodic paralysis associated with an axonal sensitivo-motor neuropathy. The screening of genes encoding ion channels was negative.

Sibling n°3 (S3) is a 19 years old man with 1 episode of transient lower-limb weakness. No neuropathy was displayed.

S1, S2 and S3 has different fathers, all are small and have a slight cognitive impairment. No medical history was reported.

MT-ATP6 and MT-ATP8 genes were screened.

Results: We detected a known pathogenic variant (m.9185T>C (p.Leu220Pro, L220P)) in MT-ATP6 gene, with homoplasmic aspect. S2 dramatically improved with acetazolamide treatment.

Conclusion: MT-ATP6 mutation are known to cause Leigh syndrome or optic neuropathy. Yet, in case of Charcot-Marie-Tooth-like or SPG phenotypes with negative gene testing, physician should think about this mitochondrial disease. Indeed, when the patients report transient motor weakness, the episodes of periodic paralysis could be mistaken with functional worsening. Oxidative stress due to MT-ATP6 mutations can lead to several phenotypes like axonal neuropathy, SPG and periodic paralysis.

Disclosure: Nothing to disclose

EPO3325

A tale of nodes and paranodes

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Background and aims: To describe a case of pan-neurofascin antibody-mediated neuropathy

Methods: Case presentation: A 78-year-old man, with no significant past medical history, presented to ED with gradual-onset symmetrical arm numbness, loss of hand muscle power and imbalance. On examination there was mild dysarthria, distal weakness and absent reflexes in the upper and lower limbs. He had normal eye movements. He had glove and stocking sensation loss to sharp touch and temperature, impaired sensation to vibration and marked sensory ataxia. He was started on IVIG on admission, but deteriorated and required ventilatory support. He recovered strength and was extubated within 2 days. However, he gradually deteriorated again on the ward and had to be reintubated, despite a repeated course of IVIG. He underwent plasmapheresis and received a third course of IVIG in consultation with the Immunology service.

Results: Investigations: CSF analysis on admission showed elevated protein (53mg/ml) with normal WCC and glucose. Initially, nerve conduction studies showed a demyelinating sensory-motor neuropathy. A subsequent study in ICU showed motor axon loss and denervation of all muscles sampled. MR spine imaging, CT TAP and antiganglioside antibodies were negative. A cell-based assay for nodal and paranodal antibodies was performed. This revealed the presence of an autoantibody cross-reactive with 3 isoforms of neurofascin (NF140, NF155, and NF186). Once the antibodies were identified, the patient received Rituximab, which led to a significant improvement in muscle power.

Conclusion: Pan-neurofascin antibodies are associated with severe neuropathies which often have an acute/sub-acute onset.

Disclosure: Nothing to disclose

EPO3326

The clinical and electrophysiological characteristics of Charcot Marie Tooth disease: A hospital cohort

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Background and aims: Charcot Marie Tooth disease (CMT) is the most common sensitivomotor neuropathy of hereditary nervous system pathologies. Different forms of CMT are distinguished by the electro-clinical data. We propose to study the clinical and electro-physiological characteristics of patients with CMT.

Methods: This was a cross-sectional study including all the patients who had been followed for CMT in the neurology department at Fattouma Bourguiba Hospital in Monastir. All patients had an electroneuromyogram (ENMG).

Results: 10 patients (7 men) were collected. The average age at onset symptoms was 17.11 years [2.30]. 6 patients were born from an inbred marriage with the presence of similar family cases in 5 patients. Gait disorders were the most frequent reason for consultation. A distal amyotrophy was observed in 60% of cases.

5 patients had sensory symptoms (hypoesthesia in gloves and socks). 8 patients presented with bone deformities (hollow feet, an equine varus, scoliosis). 2 patients had unusual associated signs (an intellectual impairment and areflexia with bilateral Babinski). Neuropathy was axonal in 70% of cases, demyelinating and axonodemyelinating in 20% and 10% of patients respectively. A conduction block with temporal dispersion was present in only 1 patient. Sensory-motor neuropathy was the most common form (80%) followed by the pure motor forms (20%). 50% of patients with early onset CMT had an axonal form. The severity of motor deficit was not correlated with the onset age ($p > 0.05$).

Conclusion: CMT remains common in countries with high inbreeding. New therapeutic approaches are needed for these patients with functional disabilities.

Disclosure: Nothing to disclose

EPO3327

Distal limb weakness and interosseus atrophy. A case of Multifocal Motor Neuropathy

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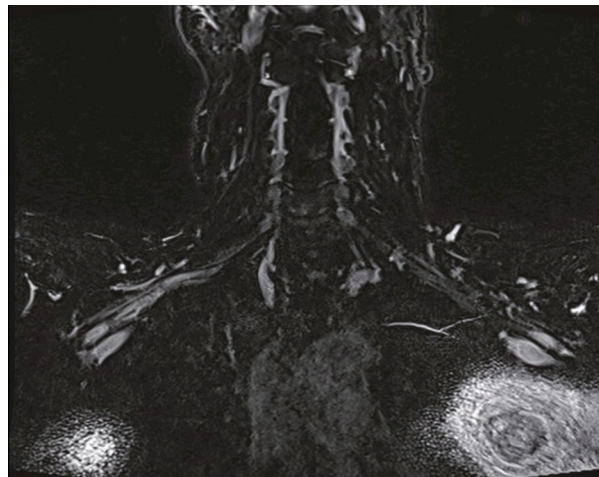
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Background and aims: Multifocal motor neuropathy (MMN) is an uncommon and purely motor neuropathy with predilection for upper limb involvement, that predominantly affects young males. It is believed an underlying autoimmune etiology of MNM, and it is associated with anti-GM1 antibodies and with a robust response to immunomodulatory treatment.

Usually it appears as a slowly progressive weakness that is asymmetric and involving at least 2 separate motor nerve distribution. It is important to distinguish from motor neuron disease because both present with asymmetric, progressive, distal weakness without numbness.

Methods: We describe a case report of a 53-year-old male patient, ex-smoker, who refers pain located in right shoulder and 2 weeks later presents right hand weakness. In neurological examination it is found right hand paresia in the carpal extension, finger flexion, first finger abduction and interosseus atrophy with no associated sensory deficit.

Results: Electromyography shows 2 conduction blocks in right motor median (elbow) and right motor radial (forearm) nerves. Sensitive nerve conduction was normal. The anti-GM1 antibodies were negative. Magnetic Resonance Imaging (MRI) showed a T2 high signal of the Brachial Plexus Inferior Trunk. The patient was treated with intravenous immunoglobulin for 3 intervals with improvement of symptoms. No side effects were reported.



T2 Hyperintensity of the Brachial Plexus Inferior Trunk

Conclusion: MMN is an important treatable cause of neuropathy. MRI can demonstrate abnormalities of cervical root and plexus T2 hyperintensity and enlargement between 35 to 50% of patients. Its early recognition is vital as MMN must be differentiated from other mimicking conditions for which immunomodulatory therapy is ineffective.

Disclosure: Nothing to disclose

EPO3328

Vinca-alkaloids induced small nerve fibre impairment in young patients with malignant lymphomaA. Rajdová¹, E. Vlckova², J. Bednarik¹¹Department of Neurology, University Hospital Brno, Brno, Czech Republic, ²Brno, Czech Republic

Background and aims: Chemotherapy-induced peripheral neuropathy is a frequent adverse consequence of anti-cancer treatment that severely impacts upon the quality of life of cancer survivors.

To assess the impact of the neurotoxicity of vinca-alkaloids (V-A) on small nerve fibres including autonomic nervous system in patients with malignant lymphoma.

Methods: A cohort prospective study included 18 patients with malignant lymphoma (12 men, 6 women, median age 36, range: 23–51 yrs). Detailed clinical examination, pain questionnaires, quantitative sensory testing (QST), lower leg skin-punch biopsy, corneal confocal microscopy (CCM) and spectral analysis of heart rate variability (SAHRV) were performed before chemotherapy including V-A and 6 months after the end of it.

Results: In the course of chemotherapy, 14 patients (78%) reported sensitive symptoms, mainly in distal extremities; these led to V-A dose reduction. QST abnormalities were found in 13 patients (72%) compared to 8 patients before chemotherapy, while intra-epidermal nerve fibre density in skin biopsy and corneal innervation did not differ significantly from initial examination. However, nerve thinning and fragmentation in skin biopsy were observed in 4 patients. Most of the patients (75%) developed no significant autonomic dysfunction persisting for 6 months after V-A treatment, as confirmed by SAHRV.

Conclusion: Skin biopsy and CCM did not demonstrate significant reduction of small fibres, also autonomic dysfunction was not confirmed. However, some structural changes in intra-epidermal innervation were detected, which appear to indicate incipient degeneration of the terminals of small-nerve fibres. These changes could contribute to sensitive abnormalities induced by V-A as detected by QST.

Disclosure: Nothing to disclose

EPO3329

CIDP and positive neurofascin-155 antibodies: description of two casesM. Rodríguez Camacho¹, R. Piñar Morales¹, A. Carvajal Hernández², J.L. Ruiz Del Amo¹, M. Carrasco Garcia³, F.J. Barrero Hernandez¹¹Neurology, Hospital San Cecilio, Granada, Granada, Spain, ²Neurology, Hospital Universitario Virgen de las Nieves, Granada, Spain, ³Neurology, Hospital Clínico San Cecilio, Granada, Spain

Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated demyelinating disorder characterized by the presence of sensorimotor deficits, predominantly proximal, subacute onset, and wide clinical variability. Autoantibodies against adhesion molecules on Ranvier node (neurofascin-155/140/186, contactin-1, contactin associated protein-1) have been described.

Methods: 2 cases of CIDP and positive anti-NF155 are described.

Results: 55-year-old female presenting with progressive weakness of lower limbs and gait disturbances. Elevated proteins, and normal cell count on CSF. Demyelinating sensorimotor polyneuropathy pattern on electrophysiological tests. Positive anti-NF155 antibodies. No response to corticosteroid treatment nor intravenous immunoglobulins. Weekly Rituximab (375mg/m²) was administered for 4 weeks with remarkable clinical improving.

41-year-old male presenting with progressive and predominantly distal paresthesias of 4 limbs, and gait instability. Elevated CSF protein with normal cell count was found. Electroneurography informed about severe demyelinating predominantly sensitive polyneuropathy. Intravenous immunoglobulin and plasmapheresis were not effective. Improvement and clinical stabilisation were possible after corticosteroid treatment.

Conclusion: AntiNF-155 antibodies (IgG4 subclass) directed to cell adhesion proteins of the Ranvier node have been described in up to 5.5% of patients with CIDP. Phenotypically, they present at a younger age with disabling tremor and sensory ataxia. Response to intravenous intravenous immunoglobulins is poor, and variable to corticosteroids, with remarkable response to Rituximab in some cases. Therefore, determination of these antibodies is an important consideration in patients with CIDP since it is a useful biomarker for diagnosis, prognosis and selection of treatment in these type of patients.

Disclosure: Nothing to disclose

EPO3330

Treatment-related fluctuations in GBS: stabilization with high-dose steroids

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Background and aims: Treatment-related fluctuations (TRF) may reflect a mismatch between the magnitude and duration of the immunological attack and the efficacy of therapy in GBS. We report a patient who had several TRF's that only stabilized after high-dose steroids.

Methods: Case report.

Results: A 24-year-old male presented with distal paresthesias, rapidly progressive ascending weakness, and universal areflexia, with MRC sumscore (MRCS)=21 (normal=60), receiving IVIG (2grams/Kg over 5 days). On day 7, he was intubated. NCS's showed demyelinating features. CSF showed albuminocytologic dissociation. Clinical course was characterized by 3 TRF's over a 2 month period, for which he received PLEX (5 sessions), IVIG (2gram/kg), IVIG (1gram/kg), respectively (figure 1). Follow up NCS's showed diffuse motor inexcitability (figure 2) and active denervation. After the 3rd TRF, acute-onset-CIDP was suspected, and he received IV methylprednisolone 500mg/day 5 days, followed by prednisone 60mg/day with rapid improvement (MRCS=30). 2 weeks later he was able to stand with assistance (MRCS=49), and had a sustained improvement during a prolonged steroid taper over 18 months. 3 years later, he remains symptom-free with normal NCS. The clinical course is not considered consistent with CIDP.

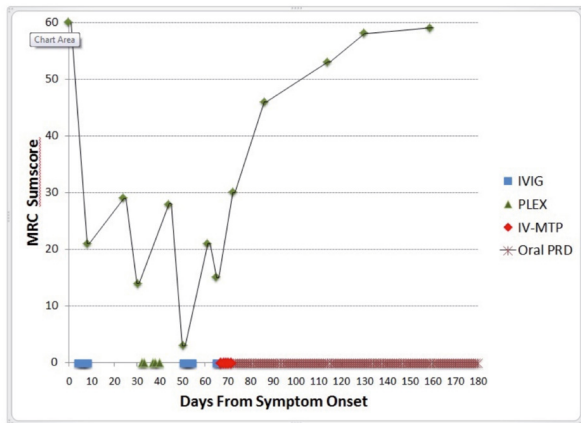


Figure 1: Clinical course and treatments received.

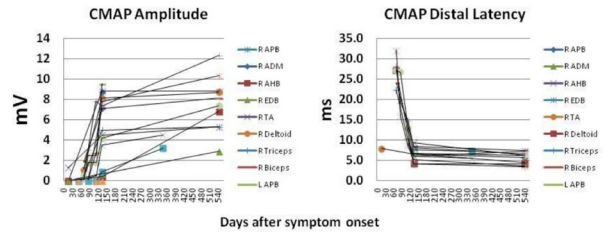


Figure 2: Electrodiagnostic data.

Conclusion: This case is noteworthy for several reasons: The patient had protracted symptoms with several TRF's that only stabilized with steroids. This suggests that some of the pathophysiologies underlying AIDP may be steroid-responsive. Universal motor inexcitability has poor prognostic value in some AIDP cases. Quick clinical and electrophysiological recovery suggests persistent distal motor conduction block not easily explainable with current axonal or demyelinating pathophysiologies.

Disclosure: Nothing to disclose

EPO3331

Neurological complications in women with breast cancer after radical mastectomy

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Background and aims: The urgency of the problem in Russia is obvious: breast cancer occupies a leading position among malignant tumors in women (20.9%) and occupies 3rd place in the causes of the death of the female population from cancer processes.

Methods: We examined 124 women aged 33-79 years after a radical mastectomy for breast cancer. All patients underwent a detailed neurological examination and needle myography of the upper extremities.

Results: Burning pain bothered 86 patients, 52 people noted numbness on the inner surface of the shoulder or forearm. Anesthesia on the posteromedial surface of the shoulder and axillary region was detected in 25 people. Motor disturbances could clearly be identified only by 7-10 days after surgery. ENMG results showed the following disorders: anterior scalene syndrome, including vascular disorders, and middle scalene syndrome, which is manifested by neurological disorders; syndrome of the dorsal scapular nerve, long nerve of the chest and suprascapular nerve; axillary nerve syndrome; rib-clavicle syndrome (Folkoner-Weddell syndrome); minor pectoral muscle syndrome (Wright-Mendlovich syndrome); intercostal nerve syndrome. Autonomic disorders on the side of the mastectomy occurred in 65 patients no earlier than 7-10 days after the surgery: vascular hyperemia or pallor of the skin, dry skin, brittle nails.

Conclusion: Thus, neurological disorders in women undergoing surgery for breast cancer are characterized by polymorphism of the syndromes and are found in 70% of patients. However, our data revealed a clear correlation between the use of the nerve-sparing modification of the surgical aid and the decrease in the number of patients with peripheral nerve damage.

Disclosure: Nothing to disclose

EPO3332

Peripheral neuropathy and livedoid vasculopathy

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Background and aims: Livedoid vasculopathy (LV) is a rare thrombotic disease of the skin microcirculation resulting in painful ulcers, mainly affecting the lower legs. Recently, cases of peripheral neuropathy, most often mononeuritis multiplex, have been reported in association with LV.

Methods: We describe 4 cases of peripheral neuropathy associated with LV, and review the literature.

Results: All patients were female, ranging in age from 51 to 80 years old. Time between 1st cutaneous manifestations and diagnosis of neuropathy ranged from 2 to 9 years. No body weight loss was observed in any patients. Nerve biopsies in 3 cases revealed multiple axonal loss suggestive of ischemic processes without significant inflammation or necrotizing vasculitis. 1 patient presented with necrotizing vasculitis in nerve and muscle specimens and had been treated with corticosteroid.

Conclusion: Although LV was formerly considered a vasculitic disorder, recent advances have suggested primary hypercoagulable state rather than inflammation as a more likely primary cause of ischemic damage and cutaneous manifestations. A French study reported that 10 of 20 LV patients for whom results of neurophysiological investigations were available showed peripheral neuropathy, with 2 patients demonstrating specific thrombo-occlusive vasculopathy. 3 of our cases showed vasculopathy, but 1 developed vasculitic features in nerves and muscles. Our presentation will discuss the significance of LV with neuropathy along the spectrum of vasculitides based on the Chapel Hill Consensus Conference nomenclature.

Nerve biopsy is beneficial for confirming diagnoses and selecting adequate treatments in LV associated with peripheral neuropathy.

Disclosure: Nothing to disclose

EPO3333

Guillain-Barré syndrome and acute hepatitis E virus infection.

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Background and aims: To analyze a possible association between acute hepatitis E virus (HEV) infection and Guillain-Barré syndrome (GBS), which is identified as an emerging extrahepatic manifestation of infection due to HEV.

Methods: Retrospective study of patients with GBS and its variants, diagnosed in the Department of Neurology of a University Hospital. Cases were identified by searching ICD codes in medical records from January 2015 to December 2018. Medical charts were reviewed and following data were collected: age, sex, prodromes, liver damage markers, hepatotropic viruses, serology and others.

Results: A total of 36 patients were included. Mean age 47.3 years (SD 23.2), 52.8% males. Prodromic gastrointestinal symptoms were reported in 41.7%, with jaundice in only 1 patient (2.8%). The median time from prodromes to neurological symptoms was 7 days (range: 1-30). Increased levels of Aspartate transaminase (AST) and Alanine transaminase (ALT) were recorded in 19.4% and 27.8% respectively, only 2 patients (5.6%) presented high bilirubin levels. The frequency of evaluation of hepatotropic viruses was HBV (72.2%), HCV (72.2%), HAV (27.8%) and HEV (8.3%). CMV serology was analyzed in 86.3% and EBV in 83.3% being positive in 2 cases each. Despite HEV was the 1 less frequently analyzed, it was the 1 with the higher percentage of seropositivity (33.3%). It was observed statistically significant relationship between the increase level in AST ($p=0,044$) and ALT ($p=0.001$) with the seropositivity for the viruses studied.

Conclusion: HEV infection is possibly underdiagnosed in patients with GBS symptoms, since it is the hepatotropic virus in which the determination is made less frequently.

Disclosure: Nothing to disclose

EPO3334

Transient, recurrent Central Nervous System clinical manifestations of X-linked Charcot-Marie-Tooth disease presenting with very long latency periods between episodes. Prolonged sun exposure a provoking factor?

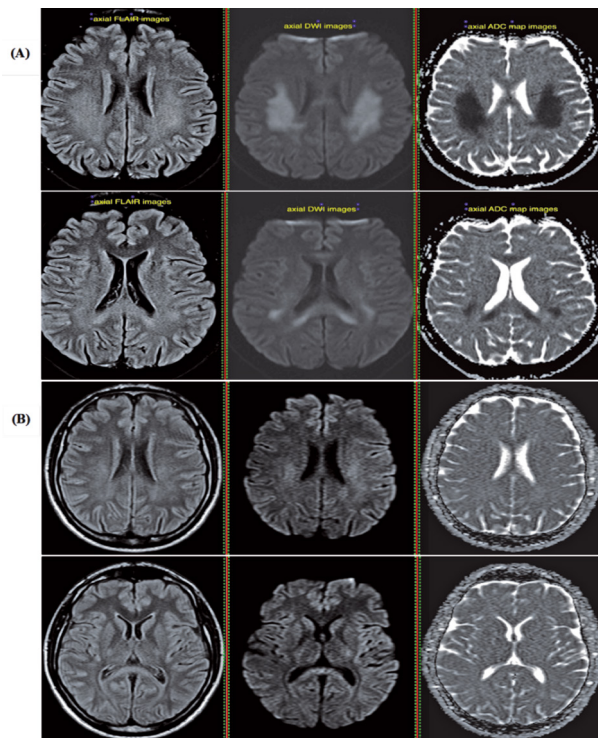
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Background and aims: Charcot-Marie-Tooth disease is one of the most common inherited neurological disorders affecting the peripheral nervous system. Common clinical manifestations include distal muscle weakness and atrophy, often associated with a characteristic steppage gait and foot deformities. An X-linked type of CMT (CMTX1) is known to cause transient acute and recurrent, or chronic CNS (central nervous system) symptoms, predominantly dysarthria, dysphagia, motor weakness and ataxia. CMTX1 is caused by mutations affecting the GJB1 gene encoding for the gap junction protein connexin32 (Cx32) which is mainly expressed in the myelinating Schwann cells of the peripheral nerves, causing the typical polyneuropathy symptoms. Growing evidence suggest that dysfunctional gap-junction mediated coupling in the CNS accounts for the stroke-like manifestations of the disease. Predisposing factors such as exercise, fever and returning from areas of high altitude have been described as triggers of the CNS manifestations, however in many cases a substantial cause remains undetermined.

Methods: In this report we describe a patient with 3 attacks of transient CNS deficits at the ages of 11, 21 and 38 years, which were also accompanied by transient white matter abnormalities on MRI.

Results: The CNS symptoms preceded both the diagnosis and the clinical manifestation of the polyneuropathy in our patient and a novel relationship between prolonged, intense sun exposure and the attacks was detected.



(A) MRI FLAIR and DWI at symptom presentation: diffuse symmetric deep white matter involvement of the centrum semiovale. T2/FLAIR hyperintensity, restricted diffusion (1st row), extending to the splenium of the corpus callosum (2nd row). (B) 1 month follow-up MRI: significant symmetric improvement both in volume and intensity

Conclusion: In our knowledge this is the first documented case with such long latency periods between CNS attacks, and the only report describing intense sun exposure as a possible provoking factor.

Disclosure: Nothing to disclose

EPO3335

Unravelling the mechanisms of hyperreflexia in Guillain-Barré syndrome: A single-case study.

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Background and aims: We report a previously healthy patient who presented with symmetric ascending weakness without sensory loss following *Campylobacter jejuni* enteritis. He had bilateral hyperreflexia, bilateral Hoffmann's sign, and Babinski's sign on the right side. Electrodiagnostic studies concurred with an acute motor axonal neuropathy (AMAN) variant of Guillain-Barré syndrome (GBS). Following a standard regime of intravenous immunoglobulin the patient regained the ability to walk within 12 weeks. Hyperreflexia persisted throughout the course of the disease.

Methods: Electrophysiological studies were performed to assess central motor pathways and spinal segmental reflex activity.

Results: Spinal hyperexcitability was evidenced by disinhibition of soleus H reflex (increased Hmax/Mmax amplitude ratio, facilitation of excitability recovery). Contrary to previous reports, transcranial magnetic stimulation did not reveal prolonged central motor conduction time to distal limb muscles. Since no impairment of descending motor control was evident, enhanced segmental reflex activity was presumably due to a dysfunction of spinal inhibitory interneurons. Pre-synaptic inhibition of Ia afferents was indeed impaired, based on absent vibration-induced soleus H reflex suppression. Furthermore, peroneal nerve conditioning of the soleus H reflex documented defective reciprocal Ia inhibition from ankle dorsiflexors onto plantar flexors. Delayed and shortened cutaneous silent periods in soleus muscle following noxious sural nerve stimulation also concurred with spinal disinhibition.

Conclusion: Although spinal magnetic resonance imaging did not demonstrate structural alteration, neurophysiological findings highlighted a damage to the inhibitory interneuronal network and subsequent spinal hyperexcitability. The immune-mediated attack likely extended into the spinal anterior horn, which may be the etiopathogenetic mechanism underlying hyperreflexia as occasionally encountered in GBS patients.

Disclosure: Nothing to disclose

EPO3336

Characteristics of neuropathic pain and its impact on quality of life in patients with diabetic polyneuropathy

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Background and aims: To determine characteristics of neuropathic pain and its impact on quality of life (QoL) in patients with diabetic polyneuropathy (DPN).

Methods: We examined 140 patients with DPN. 58 patients (41.4%) had clinical diagnosis of neuropathic pain based on the criteria of Haanpää et al. (2011). These patients were tested with 3 questionnaires for neuropathic pain (Pain Detect Questionnaire, Leeds Assessment of Neuropathic Symptoms and Signs and Douleur Neuropathique en 4 questions). We selected 32 patients who were positive on all 3 questionnaires (experimental group), and 32 patients with DPN who didn't have clinical diagnosis of neuropathic pain, and were negative on all 3 questionnaires (control group). Hamilton depression and anxiety rating scales and SF-36 questionnaire were also applied. Patients who had other significant comorbidities were excluded from the study.

Results: Patients with neuropathic pain (experimental group) had significantly severe form of DPN measured by The Lower Limb Neuropathy Impairment Score - NISS-LL score. The most distinctive feature of neuropathic pain was allodynia. Patients with neuropathic pain had significantly higher depression score, as well as worse QoL compared to the control group. The worst items on the SF-36 questionnaire were Role physical and General health. The most important predictors of quality of life in patients with DPN are the presence of depression ($p < 0.01$) and neuropathic pain ($p < 0.05$).

Conclusion: The most important feature of neuropathic pain was allodynia. Patients with neuropathic pain had worse QoL compared to the control group in physical and mental domains.

Disclosure: Nothing to disclose

Sleep disorders

EPO3337

Blood pressure in obstructive sleep apnea syndrome: implications for stroke risk

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Background and aims: Obstructive sleep apnea (OSA) is one of the most prevalent sleep disorders associated with higher risk of cerebrovascular (CV) disorders, being an independent risk factor for stroke. Blood pressure (BP) is an important CV risk factor. We aimed to assess CV risk among OSA patients using OSA severity and BP.

Methods: Polysomnographic (PSG) and home sleep apnea testing (HSAT) data and one-time blood pressure (BP) measurements of patients who attended a tertiary sleep center were retrospectively analyzed. OSA diagnosis was based on apnea-hypopnea index (AHI) using American Academy of Sleep Medicine scoring criteria. A sample of 67 participants (M/F-10.45%/89.55%) was divided into 2 groups according to AHI: mild-to-moderate OSA group (MOSAG) (AHI<30/h) and severe OSA group (SOSAG) (AHI≥30/h). Mann-Whitney U test was used for statistical analysis.

Results: Descriptives. MOSAG: n=29, mean age-46.8, F-10.3%; SOSAG n=38, mean age-52, F-10.5%. BMI for MOSAG/SOSAG-29.2/35.9kg/m². Mean PSG-HSAT parameters for MOSAG/SOSAG groups: arousal index-27.2/46.3, AHI-15.5/69.6, ODI-16.1/70, oxygen saturation-92.6%/86.7% (p<0.05 for all), heart rate-68.5/73.3 (p>0.05). BP measurements: systolic BP, diastolic BP, mean BP and pulse findings in MOSAG/SOSAG groups: 121.2/119.7, 80/76.3, 174.5/170.6, 75.6/79 respectively (p>0.05). Despite expected worse PSG-HSAT results in SOSAG group, BP measurements and heart rate did not significantly differ between groups.

Conclusion: According to our data, we can presume that not only severe OSA, but also patients with mild-to-moderate OSA have high CV risk and equally need early diagnosis and treatment.

Disclosure: Nothing to disclose

EPO3338

Regional differences in factors affecting insomnia: A cross-sectional study in South Korea

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Background and aims: Insomnia is influenced by multiple biological and socio-environmental factors. As rapid changes in industrial structure are a global phenomenon, there appears to be considerable gap between metropolis and rural areas not only in Korea but around the world. Herein, we compared the differences in factors affecting insomnia in large cities and rural areas.

Methods: A questionnaire-based cross-sectional survey was conducted among Koreans aged above 19 years on a national basis. We used the Insomnia Severity Index (ISI) to assess the clinical significance of sleep-related problems. I was regarded as having insomnia, if the ISI score was 8 or higher. We evaluated the risk factors of insomnia in urban and rural areas respectively by univariable and multivariable regression analysis.

Results: Of the total 1,590 subjects, the prevalence of insomnia was 16.2% in urban area, and 18.1% in rural area. Female gender, anxiety, depression and monthly income less than 3,000 USD were risk factors for insomnia in both urban and rural areas. Unemployment (Odds ratio [OR], 1.310; 95% CI, 0.995-1.724) was a risk factor in urban area, while age above 50 (OR, 1.728; 95% CI, 0.983-3.038) was associated with insomnia in rural area.

Conclusion: These results suggest that female gender, anxiety, depression and low income are common risk factors of insomnia in both urban and rural areas. Unemployment and older age are independent risk factors of insomnia which have a significant impact only in urban and rural area, respectively.

Disclosure: Nothing to disclose

EPO3339

Prediction of sleep disordered breathing in acute stroke patients: The accuracy of screening questionnaires

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Background and aims: Sleep disordered breathing (SDB) is highly frequent in stroke patients and negatively affects its outcome. How to best screen for SDB in this setting is a matter of debate. The objective of this study was to evaluate the performance of 5 SDB screening questionnaires after acute stroke.

Methods: A total of 438 acute stroke patients underwent a prospective sleep breathing assessment with polygraphy or apnealink within days of the event. 5 SDB screening tools (which have been validated in the general population) were used. The Berlin Questionnaire was completed by patients; the STOP-BANG, NoSAS, SACS, and NoApnea scores were calculated. Sensitivity, specificity, positive predictive values, negative predictive values and the area under the receiver operating characteristics (ROC) curve (AUC) were calculated for different SDB severities (according to the apnea-hypopnea and oxygen-desaturation (ODI) indexes).

Results: In this cohort, the Berlin questionnaire showed the poorest performance, with an AUC for the ODI thresholds of >5/h, >20/h or >30/h between 55-57%. The other 4 questionnaires performed significantly better and similar to one another. The best performance was found for the prediction of severe SDB (ODI >30/h) with an AUC ranging from 72% (STOP-BANG) to 74% (NoSAS).

Conclusion: Established questionnaires for SDB are moderately accurate in the prediction of SDB in acute stroke patients. The 2-item NoApnea test (neck circumference & age) showed a comparable performance to more complex screening tools. Further analyses will show whether the addition of other variables may improve the accuracy of current screening tools in this clinical setting.

Disclosure: This project was funded by the Swiss National Science Foundation

EPO3340

The role of comorbidities and risk factors in cognitive functioning in patients with obstructive sleep apnea

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Background and aims: It is a well documented fact that obstructive sleep apnea (OSA) results in cognitive impairment. OSA is associated with many comorbidities. Some of them are independent risk factors for cognitive decline and that is the reason why the role of comorbidities could not be clearly differentiated.

Objective: To find association between cognitive decline in patients with OSA and the presence of comorbidities and risk factors.

Methods: The cognitive deficit in a group of 103 patients with OSA was assessed by using neuropsychological battery. Comorbidities were analysed and then the patients were divided into groups consisting of individuals with or without certain comorbidity or harmful habit. The results from the neuropsychological tests were then compared between the groups with Independent Samples T-Test.

Results: The most frequent comorbidities accompanying OSA were arterial hypertension, diabetes mellitus and dyslipidemia. Smoking, obesity and alcohol use were analysed as lifestyle risk factors. Data analysis showed that 70.9% of all patients had arterial hypertension, 27.2 % had diabetes mellitus, 50.5 % had hyperlipidemia. Patients with arterial hypertension show deficit on SDMT test, Stroop test, TMTA and B. Patients with diabetes had more depressive symptoms and impairment on Stroop test when compared with non-depressive patients. Obesity was a main risk factor. We discovered statistical significance between obese and non-obese patients on all administered cognitive tests.

Conclusion: Hypertension, diabetes and obesity have significant impact on the cognitive function of patients with OSA. The effects of other risk factors remains to be established.

Disclosure: Nothing to disclose

EPO3341

Sleep Difference between Urban and Rural region of elderly population

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Background and aims: Elderly population is rapidly increased after 20th century. Also urbanization is increasing, regional influence may influence to sleep status. Elderly population have more sleep disorder than younger population and vulnerable to regional environment. We study the sleep status of elderly population and compare with regional site.

Methods: The present study used data from the nationwide, cross-sectional study on sleep status among elderly Koreans aged 65 to 86 years. Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI) were used to classify sleepiness. Insomnia Severity Index (ISI) was used for evaluation of insomnia symptoms and the Berlin Questionnaire for high risk of sleep apnea. Cambridge-Hopkins diagnostic questionnaire (CH-RLSq) was used to get prevalence of restless leg syndrome.

Results: We divided the region with metropolitan city, city and rural area. Total sleep time of weekday and weekend day are no difference. ESS and PSQI score were no difference between regions. But average of ISI score and poor sleepers were higher in rural region. Risk of obstructive sleep apnea and prevalence of restless leg syndrome were similar in each group.

Conclusion: This results showed in rural area poor sleeper and high ISI are common. We try to find out the causes and proper treatments.

Disclosure: Nothing to disclose

EPO3342

TAK-925, an orexin 2 receptor-selective agonist, has a threshold plasma concentration to induce arousal in a narcolepsy mouse model.H. Kimura¹, T. Ishikawa¹, H. Hara¹, K. Aoyama², H. Yukitake¹, M. Suzuki¹

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Background and aims: Orexin 2 receptor (OX2R) agonism may represent a promising approach for the treatment of narcolepsy type 1 (NT1). TAK-925 is an OX2R-selective agonist with >5000-fold selectivity over orexin 1 receptor and ameliorates narcolepsy-like symptoms including fragmentation of wakefulness and cataplexy-like episodes in orexin/ataxin-3 mice, a narcolepsy mouse model with orexin deficiency. TAK-925 also increased wakefulness in patients with NT1. In this study, we conducted in vitro kinetic binding analyses and measured time-dependent changes in plasma concentration and wake-promoting effects in orexin/ataxin-3 mice, to understand the pharmacokinetic (PK)/pharmacodynamic (PD) relationship of TAK-925.

Methods: The dissociation rate of TAK-925 from OX2R was characterized using OX2R selective radioligand. TAK-925 was administered subcutaneously (SC) to orexin/ataxin-3 mice at zeitgeber time 12, and the sleep/wakefulness states were evaluated based on electroencephalogram/electromyogram measurements. In a separate PK study, blood samples were collected at various time points after SC administration of TAK-925 in mice. Plasma concentration of TAK-925 was quantified with high-performance liquid chromatography-tandem mass spectrometry.

Results: TAK-925 showed fast dissociation from OX2R. In orexin/ataxin-3 mice, TAK-925 significantly increased wakefulness time, and ameliorated fragmentation of wakefulness during active phase. In these mice, comparison of change over time in PK versus wakefulness found that the wake-promoting effect of TAK-925 was observed when plasma concentration exceeded a threshold concentration.

Conclusion: TAK-925 showed fast dissociation from OX2R, suggesting minimal residual OX2R stimulation after elimination from plasma. TAK-925 induced wake-promoting effects when its plasma concentration exceeded a threshold concentration in orexin/ataxin-3 mice.

Disclosure: Nothing to disclose

EPO3343

Alterations of white matter integrity including thalamus, brainstem, and cerebellum are associated with worse cognitive function in untreated obstructive sleep apnea

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Background and aims: A major consequence of obstructive sleep apnea (OSA) is impaired cognitive functioning. To investigate the relationship between fiber tract abnormalities and cognitive deficits, we applied diffusion tensor imaging (DTI) tractography for the white matter tracts of subcortical structures in patients with untreated OSA.

Methods: We enrolled 106 patients with OSA and 104 controls, who were diagnosed by polysomnography. Fractional anisotropy (FA) and mean diffusivity (MD) maps were obtained from whole-brain DTI including white matter tracts of thalamus, brainstem, and cerebellum. All participants underwent a battery of neuropsychological tests. To evaluate the association between FA/MD values and clinical, polysomnographic, and neuropsychological parameters in the OSA group, correlation analyses were performed after controlling age and BMI.

Results: OSA group showed significantly reduced FA values in the subcortical white matters in corpus callosum, thalamus, and brainstem. FA values of thalamic radiations, which are connected to parietal, prefrontal, and premotor area, were significantly decreased in OSA group ($p=0.044$, $p=0.007$, and $p=0.027$, respectively). FA values of OSA patients decreased in medial lemniscus, middle longitudinal fasciculus, and superior longitudinal fasciculus ($p=0.049$, $p=0.040$, and $p=0.040$). The composite score of visual memory revealed a positive correlation with FA values in the rostrum of corpus callosum ($p=0.016$).

Conclusion: Untreated OSA could impact negatively on the white matter integrity of corpus callosum, thalamus, and brainstem. Fiber tract abnormalities of the rostral corpus callosum were significantly associated with the impairment of visual memory.

Disclosure: Nothing to disclose

EPO3344

Self-Reported Short Sleep Duration and Lipid Profile: Data from the Epidemiological Study

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Background and aims: Dyslipidemia is one of the main cardiovascular risk factors. Fat metabolism might be affected by lack of sleep as sleep plays an important role in modulating energy metabolism. In this analysis, we evaluated the relation between self-reported sleep duration and lipid profile in the population-based sample.

Methods: Among 1600 participants (population-based sample of the epidemiological study ESSE-RF), we selected 1433 subjects without previously known cardiovascular events, who reported their sleep duration, underwent blood tests and did not take lipid-lowering drugs (35% males; mean age-46.2±11.7years). All subjects underwent a structured interview about lifestyle, medical history, complaints, sleep duration (How long have you been sleeping per night during last month?). Sleep duration <6h/night was considered short. Lipid assessment included total cholesterol, low-density and high-density lipoproteins (HDL), Apolipoprotein AI (ApoAI) and ApoB and ApoB/ApoAI ratio. For statistical analysis we applied parametric statistics, frequency and contingency analyses (Chi-square), correlation analysis.

Results: Only 5.1% (n=73) reported sleep duration <6h. Short-sleepers and those sleeping ≥6h did not differ by age, gender, body mass index. Short-sleepers demonstrated lower HDL (1.17 (0.7-3.4) vs 1.38 (0.5-2.9) mmol/l, $p=0.005$) and ApoAI (1.44 (0.25-4.19) vs 1.57 (0.32-4.27) g/l, $p=0.015$) compared to those with sleep duration ≥6h. There were no differences in any other lipid parameters between the groups. Correlation analysis did not show association between sleep duration (as continuous variable) and any of the lipid indices.

Conclusion: In our population-based sample, self-reported sleep duration is not directly associated with lipid metabolism disturbance.

Disclosure: The analysis is supported by the grant of the Russian Foundation of Fundamental Investigations RFFI, project #20-013-00874 A.

EPO3345

Prevalence of sleep disorders and determinant of sleepiness in a multicentric cohort of Italian physicians

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Background and aims: In Italy 60% of hospital employees are engaged in shiftwork. Sleepiness in hospital physician can be a risk factor for decreased cognitive performance, leading to potential increase of risk of medical errors. So far no studies had investigated this issue in Italian physicians. The objective of our multicenter study is to assess the prevalence and the determinants of somnolence in a cohort of Italian hospital physicians.

Methods: 196 physicians were recruited. Participants filled two questionnaires: the AIMS “questionnaire for the evaluation of alertness for the occupational medicine”, investigating sleep habits and disturbances, shift working routine, and the Epworth Sleepiness Scale (ESS) for somnolence. With non parametric tests we explored the association between personal characteristics, history of nightshift work and ESS.

Results: The population was composed for 62% of females, mean age 46.9 years (SD 11.1). All participants had been working 2-4 nightshifts/month, no fixed rotation scheme, with an average 35 nights/year (SD 12.1). The prevalent chronotype was intermediate (58%); 19% were larks, 23% owl chronotype. Being older than 50, overweight, and having a lark chronotype were significantly associated with an increase in the ESS score ($p < 0.001$). A history of 15 or more years of nightshift work engagement was also more likely to result in a higher ESS score ($p = 0.04$).

Conclusion: Our results might provide clues useful for the definition of selection criteria for fitness to nightshift work and design shiftwork schedules, in order to reduce its impact on the performances and health of hospital physicians.

Disclosure: Nothing to disclose

EPO3346

The relationship between Restless Legs Syndrome and Hypertension, Diabetes mellitus, Ischemic vascular disease.

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Background and aims: Restless legs syndrome (RLS) can change sympathetic activation and blood pressure. But the association between RLS and hypertension (HTN), diabetes mellitus (DM) and ischemic vascular disease (IVD) remains contradictory results.

We investigated the prevalence of RLS and its association with HTN, DM and IVD in a cross-sectional nationwide sample of adult population.

Methods: This was a cross-sectional questionnaire-based study including 2,836 nationwide Korean adults aged 19 years or more.

We identified subjects who met the four essential International RLS study group (IRLSSG) criteria were defined as the RLS group.

The presence of HTN, DM, and IVD was defined as a self-reported history of physician-diagnosed diseases.

Results: Among the 2,836 subjects, 157 (5.5%) were found to have RLS symptoms.

The prevalence of self-reported HTN was 38 (24.2%), DM was 15 (9.6%) and IVD was 14 (10.4%) respectively.

The RLS group was associated with old age (Odds ratio [OR], 2.306; 95% CI, 1.703-3.271), the women gender (OR, 1.431; 95% CI, 1.033-1.984), HTN (OR, 2.273; 95% CI, 1.550-3.334), DM (OR, 2.140; 95% CI, 1.221-3.752) and IVD (OR 2.088; 95% CI, 1.171-3.724).

In multiple logistic regression analysis adjusted with age, it showed that odds ratio for self-reported HTN in the RLS group was 2.104 (95% CI, 1.428-3.099), DM was 1.783 (95% CI, 1.009-3.150) and IVD was 1.399 (95% CI, 0.764-2.562) compared to controls.

Conclusion: RLS symptoms is age independently associated with a high prevalence of HTN, DM and IVD in the adult population.

Disclosure: Nothing to disclose

EPO3347

Sleep alteration and anxiety behavior in a modified post-traumatic stress disorder (PTSD) rodents modelY. Lo¹, P.-L. Yi², F.-C. Chang¹¹National Taiwan University, Taipei, Taiwan, Chinese Taipei,²Department of Sport Management, Aletheia University, Taipei, Taiwan, Chinese Taipei

Background and aims: Post-traumatic stress disorder (PTSD), a typical syndrome of chronic stress induced by high intensive and emotional stimulation, causes the persist hyper-arousal, anxiety, poor sleep quality, and nightmares for over 1 month. Although several PTSD-like models can successfully simulate the decreased sleep efficiency and elevated anxious behavior on rodents, the limited time of these exhibiting symptoms causes question about the animal model. Therefore, in this study, we modified and extended fear behavior to establish an ideal PTSD-like animal model.

Methods: In order to extend stress behavior, the model of single-prolong stress (SPS) was modified by elevating the intensity and the uncontrollability of the containing stressors. The male Sprague-Dawley rats were randomly receiving seven days in a series of stressors. Then the bodyweight alteration, fear memory retrieval ability, sleep-wake activity, and anxious behavior were assessed in the short-term (3 weeks) and long-term (7 weeks) periods.

Results: Our results showed a significant stress expression during the SPS procedure and that the fear memory could be retrieved after 7 weeks of giving the modified SPS. The declined bodyweight, increased corticosterone secretion, and freezing behavior, which occurred during the SPS and fear memory recalling process, have successfully been prolonged. In addition, the high anxiety level evaluated by the theta oscillation power and behavior tasks after the memory recall were also obtained. Furthermore, REM sleep was suppressed, which reflects the phenomenon of chronic stress-induced sleep alteration.

Conclusion: In sum, increasing the intensity and the uncontrollability of the stimulations can prolong the psychological and physiological symptoms to simulate the PTSD.

Disclosure: Nothing to disclose

EPO3348

Factors associated with excessive sleepiness in patients with Parkinson's diseaseM.A. Nikitina¹, N.G. Zhukova¹, V.M. Alifirova¹, E.Y. Bragina², K.F. Nurzhanova¹, E.S. Kolupaeva¹, I.A. Zhukova¹¹Department of Neurology and Neurosurgery, Siberian State Medical University, Tomsk, Russian Federation, ²Population Genetics Laboratory, Research Institute of Medical Genetics, Tomsk, Russian Federation

Background and aims: Excessive daytime sleepiness (EDS) is a common non-motor symptom in Parkinson's disease (PD) and affects up to 55% of people with PD [Chahine LM,2017]. The aim is to identify the factors associated with the presence of EDS in PwPD in Tomsk region.

Methods: A cross-sectional study was performed involving 296 PwPD (women:men=169:127, average age – 63.9±18.3, PD average duration – 12.7±11.3, average stage – 3.86±3.73). The research consisted of demographic details, disease related parameters (PD duration, PD type, H&Y Scale, LEDD, sleep disturbance duration, influence of sleep disturbance on life quality, MDS-UPDRS (III part), HADS, Beck depression inventory II, Epworth Sleepiness Scale, Parkinson's disease sleep score (PDSS), SAQ (Sleep attack scale), Apathy Scale, Montreal Cognitive Assessment (MoCA-test), Questionnaire for Impulsive-Compulsive Disorders (QUIP-RS), PDQ-39, Columbia-Suicide Severity Rating Scale(C-SSRS). The study protocol was approved by Ethics Committee.

Results: EDS was observed in 59.4% of PwPD (176). Main related factors were the presence of cognitive impairment ($r=0.489$, $p<0.0001$), depressive disorders ($r=0.476$, $p<0.0001$), apathy ($r=0.429$, $p<0.0001$), anxiety ($r=0.375$, $p<0.0001$), dysphoria ($r=0.381$, $p<0.0001$), MDS-UPDRS – motor score ($r=0.336$, $p<0.0001$), suicidal thoughts/actions ($r=0.332$, $p<0.0001$), impulsive-compulsive disorders ($r=0.315$, $p<0.0001$), life quality ($r=-0.401$, $p<0.001$), compared with patients without sleepiness in following indexes of the PDQ-39: mobility ($p<0.01$), activity ($p<0.001$), cognitive ($p<0.001$), advanced disease ($p<0.001$).

Conclusion: EDS is a common symptom in PwPD, and other factors, different from general population observed, seem to have a greater importance in this patients group.

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EPO3349

The study of psychophysiological indicators in short sleep states for during monotonous cognitive load

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Background and aims: The state of sleep and capabilities are still of considerable interest. It is already reliably known that sleep periods of slow wave activity are especially important, the presence of which correlates with the subjective feeling of “sleepiness”, as well as restoration to the cognitive functions maximum level. We evaluate the dynamics of the cognitive attention function during the occurrence of short periods of drowsiness, including episodes of slow wave activity, in subjects, caused by evening time and an artificial uniform monotonous load.

Methods: We studied electroencephalography for a group of participants (5F, 10M; 33.6±7.3 years old years; 32 EEG channels). All experiments took place in the evening in a darkened room. For 60 minutes, subjects observed cognitive stimuli (bistable images) to which they responded by pressing a button.

Results: Based on wavelet time-frequency analysis we demonstrate a pronounced predominance of slow-wave activity in the occurring short sleep periods. Before going to bed, the subject shows a sharp increase in reaction time. After the spontaneous end of the sleep period, the subject’s cognitive ability is restored to its maximum level. The cognitive functions of subjects not experiencing sleep episodes experience a trend of gradual decline during the entire experiment.

Conclusion: We describe a period of sleep that is abnormal in the level of observed slow activity with prolonged monotonous cognitive load. After these sleep states, subjects demonstrate a significant increase in cognitive attention function indicators. Subjects without short-term drowsiness experience a trend of slow decline in attention rates throughout the experiment.

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EPO3350

Sleep disorder symptoms improvement after the 12-week mindfulness therapy sessions in myofascial facial pain syndrome patients

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Background and aims: Sleep disorders impair the body’s functioning, resulting in more severe pain, longer pain duration, greater levels of anxiety, depression, and worse impairment in physical and psychosocial functioning. The study aims to assess the effectiveness of mindfulness therapy in myofascial facial pain syndrome (MFPS) patients according to sleep disorder symptoms.

Methods: The prospective randomized study included 64 patients with MFPS, who attended the Pain clinic in Sept. 2018–Aug. 2019 and were divided into 2 groups (32 patients each) by the sealed envelope method. All patients received venlafaxine 75mg/day and tizanidine 4mg/day during 12 and 4 weeks respectively. The study group was additionally educated with mindfulness meditation techniques (weekly 2-hour group sessions with following daily outside preparation during 12 weeks and individual session for every participant). Treatment effectiveness was evaluated at admission, 6 and 12 weeks after treatment by measuring pain intensity using a subjective visual analogue scale (VAS) and sleep disorders characteristics—total wake time (TWT) and Insomnia Severity Index (ISI).

Results: At admission the VAS score was 4.8±1.5 and 5.4±1.6 points, TWT – 57.6±18.4 and 54.2±19.8 minutes and ISI total score – 17.1±2.2 and 16.8±1.4 points in the study and control groups, respectively. 6 weeks after treatment measurements showed significant VAS score (2.1±0.9 vs. 3.4±1.1), TWT (31.5±16.1 vs. 48.2±15.7) and ISI (10.9±1.8 vs. 15.5±1.7) score reductions in the study group compared to controls. 12 weeks follow-up show tendency to upcoming VAS score decreasing (1.7±0.5 vs. 3.2±0.7), TWT (21.7±11.4 vs. 45.6±14.3) and ISI score (5.2±2.6 vs. 16.4±1.9) in the study group compared to the controls.

Conclusion: Mindfulness therapy can significantly improve sleep disorders in MFPS patients.

Disclosure: Nothing to disclose

EPO3351

LMOD3 gene mutation in a patient with familial periodic hypersomniaE. Wenz¹, M. Tafti², C. Bassetti¹¹*Department of Neurology, University Hospital Bern, University Bern, Berne, Switzerland,* ²*Department of Biomedical Sciences, University of Lausanne, Lausanne, Switzerland*

Background and aims: Kleine-Levin syndrome (KLS) is a debilitating disorder with a prevalence of 1-2 per million characterized by episodes of hypersomnolence associated with cognitive, psychiatric and behavioral disturbances. The diagnosis of KLS is based on clinical findings. Recently, LMOD3 mutations were described in a family with KLS in Saudi Arabia and in 7 sporadic cases.

Methods: Review of a patient's clinical record and the relevant literature.

Results: We report a case of a 35-year old female patient, who over 17 years received different sleep diagnoses including those of idiopathic hypersomnia, non organic hypersomnia and periodic Hypersomnia. Her history is also positive for psychiatric/psychological disturbances (depressive symptoms, worsening of hypersomnia going along with psychosocial stress). A positive family history for periodic hypersomnia and psychiatric symptoms was noted. Current diagnostic criteria for KLS were not satisfied. We were recently able to prove a mutation in the LMOD3-gene in this patient, a Proline for Histidine substitution at codon 552. The p.P552H mutation was previously reported in 2 sporadic KLS patients.

Conclusion: This report illustrates the current difficulty in differentiating different forms of non narcolepsy central disorders of hypersomnolence. In addition, it documents the association of a LMOD3 gene mutation with a familial, incomplete form of KLS.

Disclosure: Nothing to disclose

EPO3352

A possible link between current restless legs syndrome and surgical interventions in the pastG. Yeganyan¹, Z. Tavadyan², S. Khachatryan²¹*Sleep and Movement Disorders Center, Somnus Neurology Clinic, Yerevan, Armenia,* ²*Department of Neurology and Neurosurgery, National Institution of Health, Yerevan, Armenia*

Background and aims: We had shown before, that patients with restless legs syndrome (RLS) report significantly more surgical interventions (SI) in their medical history compared with health population. It was hypothesized that specific types of SI could be risk factors for RLS. Our aim was to investigate the prevalence of appendectomy and tonsillectomy in medical history of RLS patients who had surgery in the past.

Methods: Patients from a sleep clinic population were involved. Based on international diagnostic criteria participants were divided into RLS (+) and RLS (-) groups. Detailed SI history was obtained. Appendectomy and tonsillectomy were identified as most common types of SI. Chi-square test was utilized for statistical analysis.

Results: We included 161 adult patients (F=51.5%, mean age=41.0) who had previous surgical anamnesis. RLS was diagnosed in 37.0% (52) of them. We divided them into subgroups: RLS (+) (mean age=49.5) and RLS (-) (mean age=35.7). Prevalence of appendectomy and tonsillectomy in total group was 29.2% (47) and 33.5% (54) respectively. Prevalence of appendectomy in RLS (+) was 38.5% (20), while in RLS (-) was 24.8% (27) (p=0.07). In RLS (+) prevalence of tonsillectomy was 32.7% (17) versus 33.9% (37) in RLS (-) (p=0.87).

Conclusion: There is no significant difference in prevalence of appendectomy and tonsillectomy between patients with RLS and non-RLS population. However, we found a trend towards more appendectomies done in RLS population. This hypothesis needs further investigation for a possible link.

Disclosure: Nothing to disclose

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