ePoster Sessions

Saturday, 16 June 2018

Ageing and Dementia

EPO1001

Impact of White Matter Hyperintensities on progression in Alzheimer's disease

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Background and aims: Cerebral white matter hyperintensities (WMH) have been suggested to contribute to progression in Alzheimer's disease (AD). Quantification of WMH in patients can be performed both manually, where WMH is categorized according to the Fazekas scale, and automatically using software which calculates WMH based on a FLAIR MRI sequence. The aim of this study was to investigate to which extent the WMH-burden affects progression in a mixed population of clinical AD and prodromal AD. Furthermore, we assessed whether manual rating and automatic segmentation of WMH provide equal information on progression.

Methods: Patients with clinical diagnosis of AD and MCI patients suspected of having early AD were included. Evaluation of progression was performed by an experienced clinician at a 12-month follow-up visit. Manual evaluation (Fazekas scale) of WMH was performed by an experienced neuroradiologist and automatic segmentation was performed as previously described (Koikkalainen et al, 2016, Neuroimage). Patients were examined for the association between WMH-burden at baseline and progression in disease after 12 months and stratified by diagnosis of AD without CVD and AD with CVD.

Results: There was no significant difference between WMH-burden and progression status in either AD without CVD (p=0.122) or AD with CVD (p=0.159). However, there was a trend for a higher WMH-burden in progressed vs. stable patients diagnosed with AD with CVD.

	AD without CVD	AD with CVD
n	139	31
progressed: *n*, (WMH mean)	85 (4,33 ml)	16 (23,02 ml)
Stable: *n*, (WMH mean)	54 (6,69 ml)	15 (14,82 ml)
p-value, WMH-burden (stable vs. Progressed)	p = 0,122	p = 0,159

Conclusion: WMH-burden seems to have an impact on progression in AD only when present in large amounts. We are currently investigating the prognostic value of manual and automatic WMH-burden measurements.

Disclosure: Nothing to disclose

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EPO1002

Comparison of Amyloid Biomarkers in Alzheimer's Disease – a Monocentric Study

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Background and aims: According to international criteria, amyloid-biomarkers are diagnostic elements for Alzheimer's disease (AD). Controversies about their accuracy for early and differential diagnosis may be explained by distinct pathological processes or by between-center variability in amyloid-markers. We pretended to compare the agreement between amyloid CSF-biomarkers, [11C]-Pittsburgh Compound Positron Emission Tomography (PIB-PET) and Florbetapir (18F) and the accuracy of these biomarkers for AD diagnosis.
Methods: 96 patients with at least two amyloid markers were included. The clinical course was considered the diagnostic gold standard. We used locally established cut-offs of amyloid CSF-AD biomarkers–Aβ42<610pg/mL; Aβ42/Aβ40 ratio<0.068. PIB-PET and 18F were evaluated qualitatively.
Results: There was entire agreement between PIB-PET and 18F. Amyloid Imaging Markers (AIM) agreed with Aβ42 in 77% cases and with Aβ42/Aβ40 ratio in 74%. Discrepancies were found in 10 clinically non-AD patients (9 with CSF-AD profile and negative AIM; 1 with positive AIM and a non-AD CSF profile) and 12 AD patients (11 with non-AD CSF and positive AIM; 1 with CSF-AD profile and negative AIM). CSF Aβ42 had, in this cohort, a sensitivity of 71% and a specificity of 66% for the diagnosis of AD and MCI-AD, with an overall diagnostic accuracy of 69%. AIM achieved a sensitivity of 85%, a specificity of 92%, with 88% diagnostic accuracy.
Conclusion: Agreement between CSF amyloid and AIM indicates that these measures are not fully equivalent as surrogates of AD-pathology. CSF amyloid seems to have a moderate sensitivity and specificity for AD-related pathologies, while AIM achieves a higher diagnostic accuracy. These results deserve a neuropathological confirmation.
Disclosure: Nothing to disclose

EPO1003

Activation and connectivity of attention networks are preserved in mild AD patients performing a short term memory task

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Background and aims: Alzheimer's disease (AD) has been described as a disconnection syndrome. Network dysfunction has frequently been related to memory impairment, but the involvement of other functional networks in early AD remains a matter of debate.
Objective: The study aimed to explore the effects of early clinical AD on dorsal and ventral attention networks (DAN and VAN) using an activation fMRI protocol.
Methods: Patients with AD and healthy elder controls performed a fMRI short term memory (STM) task. Variation in load (5 versus 2 items) allowed studying DAN and VAN activity and their interaction.
Results: At the behavioral level, STM performance decreased and reaction times increased with increasing task load in both groups. AD patients had poorer performance and were slower than controls, suggesting decreased STM capacities. Imaging revealed common DAN activation for high load in both groups. There was neither significant between group difference nor common activation for low compared to high load condition, even if post-hoc analysis revealed VAN activation for low load in the elder group only. Psycho-physiological interaction analysis showed that there was a negative relationship between DAN and VAN for high versus low load condition in AD patients.
Conclusion: Dorsal attention network remains activated and connected to ventral attention network in early AD patients during (impaired) performance of short term memory tasks. Accordingly, when patients succeed in doing the tasks, they are slower than controls, but this is neither explained by loss of DAN activity nor by disconnection between DAN and VAN in early stage AD.
Disclosure: Funding sources were Concerted Research Action 12/17-0 (University of Liège), InterUniversity Attraction Pole 7/11 (Belgium), and the F.R.S.-FNRS (Belgium).

EPO1004

The role of a cued recall memory test in the prediction of Mild Cognitive Impairment conversion to Alzheimer's disease

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Background and aims: Mild Cognitive Impairment (MCI) due to Alzheimer's disease (AD) requires evidence of episodic memory impairment. Semantic cued recall tests, like the Free and Cued Selective Reminding Test (FCSRT) seem to be a good tool in the early detection of AD. We intend to evaluate how FCSRT, compared with Mini-Mental State Examination (MMSE), CSF biomarkers, Apolipoprotein E (ApoE) genotyping and hippocampal volumetric measures predict the conversion of MCI patients to AD.

Methods: A group of 56 MCI patients with a follow-up≥2 years were included. Memory was assessed using the MMSE and the FCSRT–Immediate Recall (IR) and Delayed Recall (DR). CSF Aβ42, Aβ40, total tau (t-Tau) and phosphorylated-tau (p-Tau) were determined by sandwich ELISA. Patients were genotyped for ApoE status.T1-weighted MRI scans were acquired in a 3T scanner and processed with the FreeSurfer software. Hippocampal volumes were obtained and corrected accordingly to total intracranial volume.

Results: During follow-up 30 patients converted to AD (MCI-AD) while 26 remained stable (MCI-St). A CSF-AD biomarker profile was strongly associated with conversion to AD ($p<0.001$; overall accuracy=82%), followed by an abnormal FCSRT score ($p<0.001$; overall accuracy=80%), ApoE-ε4 genotype ($p<0.001$; overall accuracy=75%) and abnormal MMSE ($p<0.001$; overall accuracy=73%). Hippocampus volume failed to reach a significant difference between MCI-AD and MCI-St. A regression logistic model identified FCSRT-IR score, t-Tau and ApoE as the best predictors of MCI conversion to AD.

Conclusion: We conclude that FCSRT, along with t-tau and ApoE, are good predictors of the conversion to AD in MCI patients.

Disclosure: Nothing to disclose

EPO1005

Incidence of Cancer in Patients with Alzheimer's Disease: A 11-Year Nationwide Population-Based Study

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Background and aims: Alzheimer`s disease (AD) increases with age and is characterized by the premature progressive loss of neuronal cell. In contrast, cancer cells have inappropriate cell proliferation and resistance to cell death. We evaluated the association between cancer and AD and also examined the specific types of cancer.

Methods: This retrospective, nationwide, longitudinal study used National Health Insurance Service–Senior cohort (NHIS-Senior) 2002-2013, which was released by the KNHIS in 2016, comprising 550,000 random subjects who were selected from over than 60. The study included a cohort of 4,408 patients who were first diagnoses as AD between 2003 and 2005. To match each dementia patient, 19,150 subjects were selected from the database by Propensity Score Matching.

Results: We enrolled 4,790 patients for analysis in this cohort and the prevalence of AD was higher in female (19.29%) than in male (17.71%). A higher prevalence of AD was observed in the 70-84 year age group and in the higher income status group. A total of 540 cancers occurred within the observation interval. Overall cancer was less frequent in those with AD (12.25%) than in the control (18.46%), with HR 0.704 (95% Confidence Intervals (CIs)=0.0.64-0.775, p-Value<0.0001).

Conclusion: Our data showed a decreased incidence of overall cancers in patients with AD similar to previous studies. Patients with AD had a significantly decreased risk of colon & rectum, lung and stomach cancer. This finding lower than but consistent with Western countries. We need further investigation of genetic evidence linking AD to cancer.

Disclosure: Nothing to disclose

EPO1006

Cerebellar white matter disruption in AD patients: a Diffusion Tensor Imaging study

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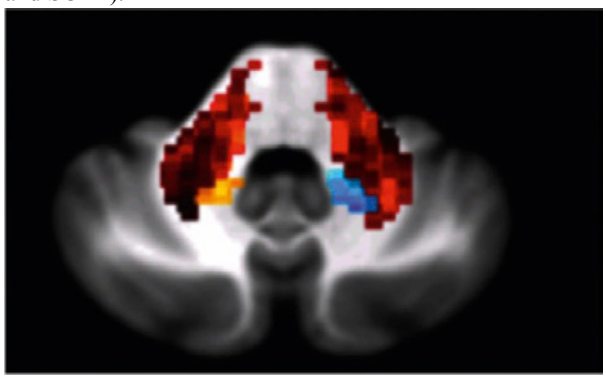
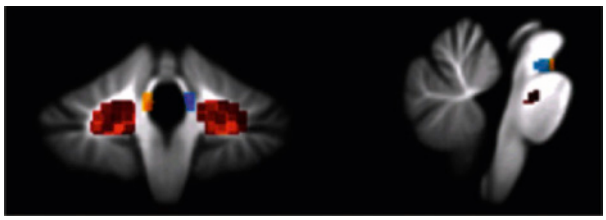
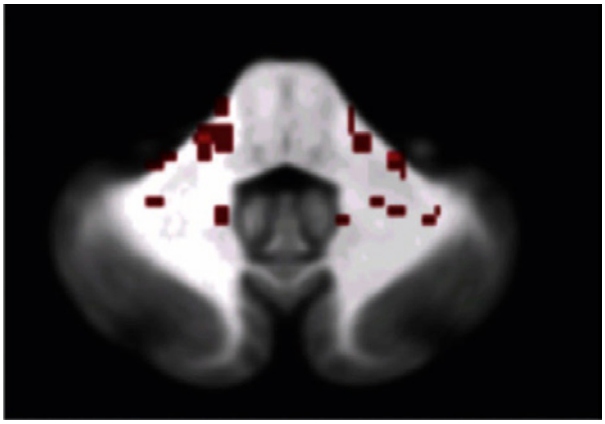
Background and aims: Diffusion tensor imaging (DTI) is an MRI technique sensitive to microscopic changes occurring within the white matter throughout the course of Alzheimer's disease (AD). Given the recent recognition of cerebellar involvement in cognitive functions, the aim of our work is to investigate the DTI microstructural fiber integrity of the cerebellar WM tracts in AD patients compared to healthy controls (HS).

Methods: We enrolled 75 participants, 50 patients with probable AD and 25 age-matched healthy controls. All subjects underwent MRI at 3 T, with the collection of TSE, FLAIR, MDEFT and DTI scans. DTI data were analysed to yield maps of fractional anisotropy (FA), axial diffusivity (Dax), radial diffusivity (RD) and mean diffusivity (MD), and to reconstruct the middle cerebellar peduncle (MCP), and the left and right superior cerebellar peduncles (SCPL and SCPR).





Results: AD patients showed a lower FA and a higher RD compared to HS in MCP, SCPL and SCPR. Moreover, a higher Dax and MD were found in SCPL and SCPR.



Conclusion: This study confirms the pivotal role of WM tracts impairment in AD patients, which could be traced not only in brain regions that are traditionally regarded as highly affected in AD patients, but also in the cerebellum, a yet underestimated cognitively relevant brain region.

Disclosure: Nothing to disclose

EPO1007

Assessement of early cognitive impairment induced by microbleed in male and female mice by Touchscreen automated task

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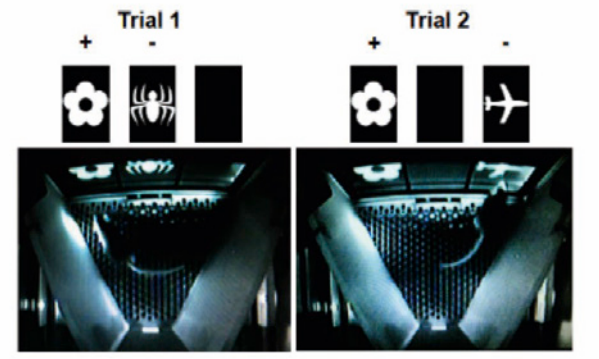
Background and aims: Cerebral microbleeds (CMBs) could contribute to cognitive impairment in the general population and in patients with dementia. We previously presented a novel murine model to induce CMB by stereotaxic surgery. In this study, we aimed to identify an early impact of CMB on the cognitive impairment by object location paired associates learning, which was known to be hippocampus dependant task in rodents.

Methods: Male and female C57Bl6/J mice were stereotactically administered collagenase (0.8 µU/µl) to induce cortical lesion. CMB-mice received atorvastatin (5 mg/kg/day) over the follow-up period. At 6 weeks post-surgery, the visuo-spatial memory was evaluated by the Paired Associates Learning in the Touchscreen test, during 30 daily-sessions. For each trial type, only one visual stimulus was presented in its correct location. Mice were also evaluated for the motor activity and the anxiety level.



The touchscreen automated dPAL task: illustration with two possible trial types. For each trial type, only one visual stimulus was presented in its correct location (denoted '+'); the second visual stimulus was presented in one of its two incorrect locations (denoted '-'), and the third location remained blank.

Results: At 6 weeks, different results were observed in male and female mice in the Touchscreen test. Male CMB-mice expressed a decline of the visuospatial memory, restaured by the administration of atorvastatin. For female CMB-mice, the visuospatial memory was even better than sham-mice. Atorvastatin also improved the visuaospatial memory. There was no difference in motor activity. A slight reduce of anxiety level was observed in male CMB-mice.

Conclusion: The Touchscreen test is less biased than other behavioral tests, and is interesting in its translational approach. We validated in a prospective manner that CMB affected the cognitive performance differently in male and female mice. We will apply the same model with transgenic mice of Alzheimer's disease.

Disclosure: This study is partially funded by the Fondation Recherche Médicale (FDT20170437145)

EPO1008

Neuropsychiatric symptoms in Mild Cognitive Impairment: biological determinants and prediction of conversion

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Background and aims: Mild Cognitive Impairment (MCI) is accepted as prodromal stage of Alzheimer's disease (AD). Neuropsychiatric symptoms (NPS) are frequent in MCI patients, but their impact in prognosis and biological determinants are not fully established.
Aims: To investigate the relationship of NPS with clinical and CSF biomarkers as well as to establish their prognostic impact, in a prospective cohort of MCI patients.
Methods: Data collected besides demographics and rate of conversion at 3 years: cognitive assessment (MMSE and MoCA); staging scales as Blessed and Clinical-Dementia-Rating (CDR); psychopathological assessment, namely Geriatric-Depression-Scale (GDS), Hamilton-Anxiety-Scale and Neuropsychiatric-Inventory (NPI); CSF biomarkers (Aβ42, tau and p-tau); Apolipoprotein E. A univariate, followed by a multivariate analysis for independent predictors of conversion were performed; statistical significance was considered when $p < 0.05$.
Results: We studied 129 patients with MCI, 50 males (38.8%) and a mean age was 68.9 (± 10.9). At 3 years of follow up to 44 (34.1%) patients had converted to AD-dementia. In univariate analysis, GDS and Hamilton were significantly correlated with CSF p-tau and GDS with Aβ42. Conversion was associated with age of onset, NPI-caregiver-burden, Blessed, MoCA, tau and p-tau. In multivariate analysis, Aβ42 was associated with GDS (β=15.435, 95%CI=[5.258, 25.611],p=0.003) and Hamilton with p-tau (β=2.811, 95%CI=[1.111, 4.511],p=0.001). NPI-caregiver-burden was an independent predictor for conversion (OR: 1.093;95%IC;1.007 to 1.186, p=0.033).
Conclusion: Our study demonstrates that in prodromal AD (MCI), NPS are related to cognitive, functional and biological biomarkers and NPI-caregiver-burden emerged as an independent predictor of progression to dementia.
Disclosure: Nothing to disclose

EPO1009

Genomic studies in early onset Alzheimer's disease (EOAD) in Hungary

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Background and aims: The major Alzheimer's disease (AD) associated genes support the merit of the traditional amyloid cascade hypothesis, since the genes APP, PSEN1, and PSEN2 all directly affect amyloid production or cleavage. Mutation of these genes are mainly responsible for early onset forms of AD (EOAD). The aim of this study was to characterize genotype-phenotype association in the Hungarian patients with EOAD.
Methods: 93 patients diagnosed with EOAD were examined with Sanger sequencing in the case of the coding exons of the PSEN1, PSEN2 and APP genes were investigated. Predisposing genetic factors such as APOE genotypes, MTHFR C677T and TREM2 G140A alterations were analysed. The genetic risk factors were detected in 100 old healthy persons as well.
Results: Five presumed pathogenic mutations (two PSEN1, two PSEN2, one APP) were identified, including one newly detected heterozygous mutation: PSEN1 (c.265 G>C;Val89Leu) which was supposed to be likely pathogenic based on the result of prediction scores and segregation analysis. APOE E4 homozygous, TREM2 heterozygous and MTHFR homozygous status were presented in 7.4%, 5.9% and 13.2%, respectively.
Conclusion: In the EOAD Hungarian cohort likely pathogenic mutations were detected in the three examined genes, with 5.2% frequency. The prevalence of the predisposing genetic risk factors were higher than in the normal population. Our results were suggested that even in the EOAD group the monogenic form was relatively rare. In conclusion, we are hypothesized that in the prevalence of EOAD other gene-gene interactions and relevant genetic and environmental risk factors might be contributing to disease development.
Disclosure: Hungarian Brain Research Program

EPO1010

Role of quantitative MRI measures in prognostic assessment of Mild Cognitive Impairment patients and correlation with Cerebrospinal Fluid biomarkers

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Background and aims: Patients with mild cognitive impairment (MCI) are at greater risk of developing dementia, namely Alzheimer's disease (AD). Limbic atrophy is an early finding of AD and several structures of interest have been investigated as disease biomarkers. The aim of this study was to compare MRI biomarkers between MCI subjects who progressed to AD (MCI-P) and non-progressors (MCI-NP) and to investigate possible correlations with Cerebrospinal Fluid (CSF) biomarkers.
Methods: 78 MCI patients were identified and divided into MCI-NP and MCI-P (53.8%) at a minimum 2-year follow-up. At baseline, hippocampal volume (HV) and cortical thickness of para-hippocampal (PH) and entorhinal (ER) cortices were automatically calculated with FreeSurfer software using T1-weighted volumetric imaging, compared between groups and correlated with CSF total tau (t-Tau), phosphorylated tau (p-Tau) and amyloid-beta1-42 (Aß42) levels.
Results: Significant statistical difference was found for HV and ER, but not for PH between groups (Table 1). Significant correlations were found between ER-[Aß42 (right hemisphere), t-Tau and p-Tau], PH-Aß42, and HV-[p-Tau (right hemisphere) and Aß42] (Table 2). Exploratory receiver operating characteristic curve (ROC) analysis yielded a specificity of 70% and sensitivity of 72% for ER to predict progression to AD.
Conclusion: According to previous studies, these findings suggest that baseline ER could predict progression to AD. Also, variations in HV, ER and PH measures could reflect differences in CSF biomarkers. It would be interesting to further investigate whether the combination of ER measure and Aß42/p-Tau ratio would increase the predictive power to AD progression.
Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EPO1012

Evaluation of platelet-derived microvesicles in patients after thrombotic stroke

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Background and aims: Platelet-derived microvesicles (pMV) are involved in the development of atherosclerotic lesions and are increased in ischemic stroke. The aim of the study was a comparison of pMV in patients after ischemic stroke secondary to large-artery atherosclerosis (LAA) and small vessels occlusion (SVO).
Methods: We recruited patients after ischemic stroke secondary to LAA and SVO. Stroke subtype was determined based on the TOAST classification criteria. pMV were isolated from citrated blood by centrifugation, incubated with the following antibodies: CD61/PerCP (platelet gating Ab), Annexin V/PE (Ab against phosphatidylserine), CD62P/PE-Cy5 (Ab against P selectin), PAC-1/FITC (Ab against active form of GPIIb/IIIa), and CD154/APC (Ab against CD40L) then analysed with an Apogee A50-Micro flow cytometer.
Results: We included 49 stroke patients (mean age 67±9 years): 29 patients (59%) with LAA and 20 patients (41%) with SVO subtype. There was no significant difference in concentration of pMV subtypes between LAA and SVO: CD61+ [1352 (840-1544) n/µl vs 1411 (1048-1945) n/µl, p=0,56], CD61+/AnV+ [174 (118-251) n/µl vs 180 (130-335) n/µl, p=0,77], CD61+/CD62P+ [8 (6-13) n/µl vs 8 (5-12) n/µl, p=0,27], CD61+/PAC-1+ [8 (6-13) n/µl vs 7 (4-12) n/µl, p=0,29], CD61+/CD154+ [6 (5-11) n/µl vs 6 (4-11) n/µl, p=0,88].
Conclusion: We demonstrated that there is no significant difference in the concentration of pMVs or their subtypes determined as an expression of GPIIb/IIIa, PS, P-selectin or CD40L between the thrombotic subtypes of stroke, LAA and SVO.
Disclosure: This study was supported financially by the governmental research grant National Science Centre 2014/15/B/NZ4/00736

EPO1013

Factors associated with short-term mortality after ischemic stroke in Conakry Teaching Hospital

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Background and aims: Stroke is the most debilitating disease in adults and the third leading cause of death worldwide
The aim of this work was to identify the factors associated with mortality in ischemic stroke patients in the neurology department of Conakry Teaching Hospital
Methods: We conducted a prospective study during one year, from January 1st to December 31st, 2016. We included all patients admitted for ischemic stroke in neurology department of Ignace Deen teaching hospital. Clinical, paraclinical and prognostic data were recorded. We compared the characteristics of alive and deceased patients. Data were analyzed using SPSS 20 software. Any p-value less than 0.05 was considered statistically significant
Results: We collected 156 patients hospitalized for ischemic stroke. A total of 43 patients died with a frequency of 28%. The average age was 61±13.5 years. The average NIHSS at reception was 12±4.6. Factors associated with mortality were urinary tract infection (p Value=0.01), sepsis (p-Value=0.01), heart disease (p Value=0.02) and hyperglycemia (p Value=0.01). Half of the deaths (50%) occurred in the first 30 days
Conclusion: Heart disease, hyperglycemia, sepsis are associated with high mortality in ischemic stroke. Better management of these factors could significantly reduce this mortality
Disclosure: Nothing to disclose

EPO1014

Contribution of blood biomarkers to the diagnosis of cardioembolic stroke

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Background and aims: Cardioembolic strokes might be effectively prevented by anticoagulation. Blood biomarkers helping to suggest cardioembolic etiology and to steer the complex diagnostic work-up would therefore be of great advantage. This study addresses the possible contribution of biomarkers associated with thromboembolism (NT-proBNP and D-dimer) to the diagnosis of cardioembolic stroke.
Methods: Over a 7-month period, we prospectively investigated all ischemic stroke patients admitted to our Stroke Unit. All patients underwent a complete stroke work-up including cerebral imaging (CT and/or MRI), neurosonography, electrocardiography, cardiac rhythm monitoring (for at least 24 hours) and echocardiography. Blood to determine NT-proBNP and D-dimer levels was drawn immediately after admission.
Results: Of 188 ischemic stroke patients (age: 69±14 years, female: 38%), 67 had cardioembolic (36%), 73 non-cardioembolic (39%) and 48 cryptogenic strokes (25%), based on extensive work-up. NT-proBNP and D-dimer levels were significantly higher in cardioembolic vs. non-cardioembolic strokes (2543 vs. 707 pg/ml, $p<0.001$; 2.4 vs. 1.4 µg/ml, $p<0.001$). The area under the curve (AUC) of NT-proBNP obtained for the diagnosis of cardioembolic stroke was 0.81. The cut-off point with the highest sensitivity and specificity was set at 525 pg/ml (sensitivity: 82%, specificity: 77%). The AUC of D-dimer in cardioembolic stroke was 0.69, with a cut-off set at 0.75 µg/ml (sensitivity: 67%, specificity: 69%).
Conclusion: In concordance with previous studies, NT-proBNP has reasonable diagnostic accuracy for stroke related to cardiac embolism. Nevertheless, sensitivity and specificity are too low to essentially improve the diagnostic work-up. The contribution of D-dimer levels is even more limited.
Disclosure: Nothing to disclose

EPO1015

"Monocular double vision" – central or peripheral?

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Background and aims: The monocular diplopia usually implies a peripheral etiology related with intraocular pathology. More uncommon are the central nervous system causes that included visual illusory phenomenon, epileptic disorder or aura of migraine. We described a case of central monocular diplopia related with visual illusory phenomenon named polyopia.
Methods: Case report.
Results: A 39-year-old right-handed woman presented to the emergency department with complaints of double vision as seeing separated or overlapping images and vertigo sensation that began abruptly. She was smoker. She had no history of headaches, epilepsy or stroke. On admission, she was afebrile, her blood pressure was 157/114 mmHg. The neurological examination disclosed a horizontal diplopia, in all directions of gaze, maximal on the right gaze. The diplopia persisted when she closes only one eye, both right or left. The ophthalmologic examination was normal. She had no pupillary involvement, nystagmus, cranial nerve palsy, visual campimetry deficits or visual extinction. She had a right algic hypoesthesia. Brain MRI shows an acute ischaemic left parietal lesion.
Conclusion: This case shows the clinical challenge of localizing a subjective complaint of double vision, which can localize to the eyes, oculomotor systems, visual pathways, and as in our patient, central structures of visual perceptual processes. A careful history and examination were the key. The patients, often have associated other signs of occipital or parietooccipital region lesion, such as homonymous hemianopia or visual agnosia. In our patient these signs were absent, and the sensitive loss was the clue to consider a central cause for her monocular diplopia.
Disclosure: Nothing to disclose

EPO1016

Is it possible to identify acute ischemic stroke patients with large-vessel occlusions using clinical screening scales?

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Background and aims: For acute ischemic stroke caused by large-vessel occlusion (LVO), intravenous thrombolysis followed by thrombectomy is the most effective treatment. Since endovascular thrombectomy is only performed in specialized centers, successful prehospital screening would be of great importance. A number of screening tools for LVO exists, however, these have been tested retrospectively in patients with an established stroke diagnosis. Few studies have investigated the predictive values in patients presenting with acute stroke symptoms.
Methods: The Stroke Unit at Akershus University Hospital is the largest in Norway with a catchment area of about 10% of the total population in Norway. In 2012, a stroke fast track with direct access to neurologist on call, for patients with acute stroke symptoms < 4.5 hours considered as prehospital candidates for intervention was established. Initial CT scan and CT angiography are conducted at the hospital, and all patients are evaluated with the National Institutes of Health Stroke Scale by the neurologist before possibly intervention. We have conducted a retrospective review of all stroke fast tracks for the period 2012-2017 in order to validate the use of screening scales to detect LVO in a population with acute stroke symptoms of<4.5 hours.
Results: More than 2600 patients have been included in the stroke fast track. Approximately 650 have received intravenous thrombolysis, and about 6-7% of the total population had LVO detected by CT angiography at admission. As the year 2017 will be included, all data are not yet available.
Conclusion: The results will be presented at the meeting.
Disclosure: Nothing to disclose

EPO1017

Etiology of ischemic stroke in young patients: Findings from the HISTORY study

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Background and aims: Ischemic stroke (IS) in young adults is relatively less frequent, however recent data reporting an increasing incidence up to 10-15% of all IS. Moreover, the cause of IS often differs from older patients and may require a cause-specific management. Our aim was to determine the etiology of IS in young 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). In all patients, the brain ischemia was confirmed on CT or MRI. Admission ECG, serum specific cardiac and thrombophilia markers, neurosonology, TEE, 24-hour and 3-week ECG-Holter were performed in all patients to assess IS etiology according to the TOAST classification.
Results: Out of 1348 patients enrolled in the HISTORY study, 218 (16%, 122 males, mean age 40.9 ±7.9 years) were<50 years. Large-vessel atherosclerosis was detected in 15 (6.5%) patients, cardio embolism in 26 (12%) patients and arterial dissection in 15 (6.5%) patients. Eight (3.5%) patients had hypercoagulable state, and only one patient had genetic disorder and one non-infectious vasculitis. 161 (72.5%) were identified as cryptogenic. Recurrent IS occurred in 4.5% of all IS patients.
Conclusion: The cause of IS in young adults remains often unclear, in our study were identified 72.5% patients as cryptogenic. The most common cause of IS was cardiac embolism (12%), arterial dissection (6.5%) and large-vessel atherosclerosis (6.5%).
Disclosure: Study was supported by the grant IGA LF UP_018_2018 and by the grant of Ministry of Health Czech Republic, nr. 17-30101A.

EPO1019

Clinico-radiological correlation of anterior cerebral artery stroke presenting as unilateral ataxic syndrome

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Background: Frontal lobe gait disorders, also termed frontal lobe (pseudo)ataxia, are commonly linked to insidious conditions such as frontal lobe tumors or extensive cerebrovascular disease. Its anatomical substrate is still poorly defined, though a disruption of cortico-cerebellar fibers and medial frontal wall involvement have been hypothesized.
Aims: Characterize clinical–anatomical correlation of anterior cerebral artery stroke (ACAS) with and without ataxia at presentation.
Methods: Consecutive cases of ACAS presenting with axial ataxic syndrome (atypical ACAS), out-of-proportion to motor deficits were clinically characterized. Classical (crural paresis/hemiparesis) ACAS were used as controls. All patients underwent MRI. Vascular lesion topography was compared between groups by two Neuroradiologists blinded to the diagnosis
Results: We obtained four atypical and five classical ACAS cases. All four atypical ACAS cases had right ACAS. Four patients presented with acute instability while standing and three patients also while sitting. All had left lateropulsion but no limb paresis or dysmetria. All atypical ACAS had caudal cingulate zone (CCZ) infarction on MRI (part of Brodmann's area 24, posterior to the vertical anterior commissure line), with variable involvement of other medial frontal wall areas. Among controls, only one patient had CCZ involvement.
Conclusion: We report the first case series of ACAS presenting with lateralized axial ataxic syndrome, interestingly all right-side ACA, with particular involvement of CCZ, when compared to classical ACAS. This is in agreement with previous case reports and the available evidence of a fronto-thalamic-cerebellar connection that may involve the cingulate cortex. The evidence that ACAS may present with cerebellar-like symptoms has relevant clinical implications.
Disclosure: Nothing to disclose

EPO1020

Ischemic stroke in patients with malignant solid tumors: a descriptive analysis

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Background and aims: The relationship between stroke and cancer is complex and not yet well characterized. The aim of this study is to describe ischemic stroke in cancer patients.
Methods: Retrospective review of the clinical files of adult patients of our centre with malignant solid tumors who suffered ischemic stroke between 2012 and 2017. Demographic, cancer-related and stroke-related data was collected. A descriptive statistical analysis was then performed.
Results: 55 patients were identified (39 male and 16 female), mean age 65.1±12.3 years. Digestive system tumors were the most frequent (29.1%). The median time between cancer diagnosis and stroke was 9.0 (interquatile range=[2.0;36.0]) months. By the time of stroke, 34.5% of patients had metastization and 36.4% were under chemotherapy (platinum-based regimens in 80.0% of cases). 10.9% of patients had no traditional vascular risk factors, and 20.0% had only one, mostly hypertension (67.3%). 41.8% of the strokes resulted from an apparently embolic mechanism. The cancer treatment was interrupted or suspended in 60.7% of the patients who were under chemo and/or radiotherapy.
Conclusion: Embolic mechanisms seem to play an important role in the pathophysiology of stroke in cancer patients. Our data suggest that platinum-based regimens may have a role in the occurence of stroke in patients under chemotherapy, and inferential studies shall be performed in order to verify this association. Ischemic stroke represented per se an unfavourable prognostic factor in the oncologic disease, because it interfered with the performance of the previously proposed oncologic treatment.
Disclosure: Nothing to disclose

EPO1021

Cerebrovascular disease In antiphospholipid syndrome: 20-year experience in a University hospital

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Background and aims: Antiphospholipid syndrome (APS) is an autoimmune disorder for which optimal clinical management remains controversial. Specific immunologic profiles may have prognostic relevance.
Methods: We conducted a retrospective analysis of the electronic database of our stroke centre university hospital Neurology Department and included patients admitted due to APS related cerebrovascular disease from 1997 to 2017. Clinical, immunological and therapeutic variables were registered.
Results: Seventeen patients (82% female, mean age of 48±17 years) were included. Seven patients (41%) were receiving antithrombotic therapy because of previous thrombosis; 3 antiplatelets (AP), 2 oral anticoagulants (OAC), 1 AP+OAC and 1 subcutaneous heparin (SH). Twelve patients presented with ischemic stroke, 4 patients with transient ischemic attack (TIA) and 1 patient with cerebral venous thrombosis (CVT). Triple antiphospholipid antibodies (aPL) positivity was detected in 5(29%) and lupic anticoagulant (LA) in 12(71%). On discharge most patients (9, 53%) were prescribed vitamin K antagonists (VKA), 1 dabigatran 110mg bid plus AP, 2 VKA+AP and 4 AP. After 4.9±4.5 year's follow-up, 3 recurrences (1 stroke and 1 retinal artery occlusion in 1 patient and 2 TIA) and 5 deaths (4 related to APS or antithrombotic therapy complications) were registered. Nine patients were functionally independent (mRS 0-2) and 3 were functionally dependent (mRS 3-4) at the end of follow-up. Neither triple aPL nor LA positivity were significantly associated with stroke/TIA recurrence or death.
Conclusion: In our experience, APS related cerebrovascular disease had significant morbidity and mortality. Clinical management was heterogeneous. No predictors of poor prognosis were detected, although small sample size may be responsible.
Disclosure: Nothing to disclose

EPO1022

Intracerebral haemorrhage and venous thromboembolism: ten years experience of a therapeutic challenge

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Background and aims: Venous thromboembolism (VTE) constitutes a major complication in patients with an intracerebral haemorrhage (ICH). In addition, patients on anticoagulation due to VTE may be at increased risk of ICH. Limited evidence is available to guide clinical decisions when VTE and ICH concur.
Methods: We conducted a retrospective analysis of the electronic database of our stroke centre university hospital, and included all patients admitted due to ICH from 2007 to 2017 with either previously diagnosed VTE (pVTE) or with acute VTE (aVTE) diagnosed during admission. Treatment with inferior vena cava filter (IVCF) insertion or anticoagulant drugs was individualised depending on ICH, VTE severity and overall prognosis. Clinical and therapeutic variables were registered.
Results: Thirteen patients (7, 54% male, with a mean age of 78±12 years) were included, 8 in pVTE and 5 in aVTE group (4 symptomatic and 1 incidental VTE). Eight patients (62%) were on anticoagulation prior to ICH. ICH was deep in 7 cases (54%), lobar in 4(31%) and mixed in 2(15%). During admission IVCF was placed in 6(46%). Anticoagulant therapy was prescribed in 5(38%) after a median of 30(range 7-180) days: upon discharge in 3 and later reintroduced in 2. No recurrences of ICH were registered. One patient treated with IVCF insertion developed deep vein thrombosis (DVT). After a follow-up of 25±25 months, 7 patients died (54%), 2 because of VTE related complications and 1 secondary to ICH.
Conclusion: IVCF insertion was associated with DVT recurrence but no other major complications occurred. Concomitant VTE and ICH had significant morbidity and mortality.
Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology

EPO1023

Resistance to eye opening in patients with disorders of consciousness

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Background and aims: Resistance to eye opening (REO) is a commonly encountered phenomenon in clinical practice. We aim to investigate whether REO is a sign of consciousness or a reflex in severely brain-injured patients.
Methods: We recorded REO in chronic patients with disorders of consciousness during a multimodal diagnostic assessment. REO evaluations were performed daily in each patient and clinical diagnosis of unresponsive wakefulness syndrome (UWS), minimally conscious state with (MCS+) or without (MCS-) preserved language processing was made using the Coma Recovery Scale-Revised (CRS-R).
Results: Out of 150 consecutive patients, 79 patients fit inclusion criteria. REO was seen in 19 patients (24.1%). At the group level, there was a significant relationship between the presence of REO and the level of consciousness. We also observed a difference in the repeatability of REO in patients in MCS+ compared to UWS and MCS-. Out of 23 patients in UWS, six showed REO, in whom five showed atypical brain patterns activation.
Conclusion: Our findings suggest a voluntary basis for REO and stress the need for multiple serial assessments of REO in these patients, especially since most patients show fluctuating levels of consciousness.
Disclosure: Nothing to disclose

EPO1024

Neuropsychological and brain gray matter volume (GMV) changes after a computer-assisted cognitive treatment (CACT) in patients with multiple sclerosis (MS)

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Background and aims: MS negatively affects cognitive functions, causing an important impact on quality of life. The aim of this work is to study the effectiveness of a CACT in MS patients and to determine the changes in structural and functional magnetic resonance imaging (MRI) studies.
Methods: Twelve relapsing-remitting MS patients with mild-moderate cognitive impairment (9 women; average age 38.83) and clinically stable disease received 24 sessions (3/week) of CACT focused on information processing, attention, memory and executive function through the neurorehabilitation web platform Neuronup®.
Alternative forms of the Repeatable Battery of Neuropsychological Test, Multiple Sclerosis Neuropsyhcological Questionnaire and the Multiple Sclerosis Impact Scale were used to evaluate patients before and after the intervention. Additionally, a structural and functional (resting-state) MRI studies were performed pre-post treatment.
Results: After intervention, cognitive evaluation showed improvements in verbal memory (p=.04) delayed visual memory (p=.03), working memory (p=.004) and semantic fluency (p=.04). No changes were found in subjective cognitive impairment or in the impact of the disease. Structural MRI analysis (Voxel Based Morphometry) showed an increase of the global GMV (average increase of 0.7%; p=.03) in the majority of patients. Furthermore, resting-state fMRI studies showed a decrease of fALFF (fractional amplitude of low-frequency fluctuations) in the cingulate cortex after the treatment.
Conclusion: The CACT improves cognitive performance and may induce structural and functional changes in the brain of MS patients. These findings suggest that CACT may favor neuroplasticity inducing changes in the cortical reorganization and helping to improve either cognitive or brain reserve.
Disclosure: Nothing to disclose

EPO1025

Nonverbal impairment in the posterior forms of aphasia

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Background and aims: The posterior parts of the brain hemispheres are responsible for receiving, perception processing, and storage of the exteroceptive information. A local lesion leads to impairment of human verbal thinking–aphasia. The difficulty of their rehabilitation because these patients have disrupted cortical control of auditory perception and processing of speech information.
Methods: From 2006-2017 we observed 348 patients, 183 men, 165 women, aged 18-92 years, with 37% of acoustic-gnostic aphasia, 27% acoustic-mnestic aphasia, 29% semantic aphasia. In the process of rehabilitation treatment, the patients received speech therapy. At the same time, we studied impairment of non-verbal thinking and performed the cognitive rehabilitation.
Results: In the examination of patients with severe aphasia, in contrast to the moderate and mild forms, there was domination of non-verbal cognitive functions, namely: 1) neurodynamic disorders in patients with acoustic-gnostic aphasia; 2) considerable changes in the visual gnosis in patients with acoustic-mnestic aphasia; 3) disorders of visual and visual-spatial perception in patients with semantic aphasia. Based on the results of clinical studies were adjusted to a rehabilitation program: in addition to the standard voice rehabilitation of the proposed directional reconstruction of non-verbal cognitive functions.
Conclusion: As a result of complex rehabilitation, it has been a significant regression of speech disorders in more than 2/3 of patients. Thus, the use of simultaneous training of verbal and nonverbal functions, has allowed to increase almost twice the efficiency of the neurorehabilitation.
Disclosure: Nothing to disclose

EPO1026

Attention and working memory throughout the lifespan

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Introduction: Aging determines changes in cognitive performance, with an emphasis on working memory, episodic memory and processing speed. Regarding working memory, age seems to have a particularly negative effect when task requirements increase, demanding higher concentration levels, division of attention and more elaborated strategies of stimulus control.
Aims: To assess the effect of age (from adolescence to late-adulthood) on measures of attention, psychomotor control, and processing speed, namely the Toulouse-Pièron (TP), Trail Making Test A/B (TMT) and Stroop Color Test C/CW.
Methods: Cross-sectional study with 279 community-dwelling subjects without neurological or psychiatric pathology, aged between 15 and 83 years. The sample was divided according to ten years' intervals (age) and into three education groups: 1-4, 5-10 and 11 years or more.
Results: There was a significant interaction between TP, TMT and Stroop Color Test results in all groups. Multiple linear regression analysis showed that age was the most significant predictor of test performance in all measures; particularly in TP, together with education, this model explained 52% of the variance of results. The negative effect of age was only significant above the group of 45-54 years.
Conclusion: Our results demonstrated that both attention and working memory suffer a negative impact across ageing, with a most significant effect in time-dependent tasks, particularly after the age of 45.
Disclosure: Nothing to disclose

EPO1027

Worse task switching in middle-aged patients with uncomplicated grade 1-2 essential arterial hypertension: impact of vascular age

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Background and aims: Executive dysfunction is common in patients with essential arterial hypertension (EAH). Vascular age (VA) is an important factor of target organ brain damage in EAH. Our objectives were to compare vascular age using SCORE and Framingham scales and to find possible correlations with executive functions in untreated grade 1-2 middle-aged patients with EAH compared to controls.
Methods: 50 healthy volunteers (mean age 47.3±5.5 years) and 103 hypertensive patients (mean age 51.2±5.2 years) were recruited. Neuropsychological assessment included Montreal Cognitive Assessment (MoCA), Trail Making test (part A and part B), Stroop Color and Word Test, verbal fluency test, 10-item word list learning task. VA was calculated using SCORE project scales and Framingham Heart Study risk tables.
Results: Hypertensive patients had lower MoCA score (28.4±1.4 points vs 28.9±1,3 points, p=0.02), worse performance in TMT B (119.4±42.5 vs 105.5±31.4; p=0.03) and higher TMT difference score (80.7±42.5 vs 62.9±27.9; p=0.002) compared to controls. In hypertensive patients SCORE and Framingham VA (57.7±7.4 and 64.6±11.0 years) was higher than chronological one (p<0.001) and higher than the same corresponding values in the control group (p<0.001). Significant negative correlations were found between VA and mean MoCA score (SCORE: r=-0.207; Framingham: r=-0.276, p<0.05), and TMT difference score (SCORE: r=-0.128; Framingham: r=-0.254, p<0.05).
Conclusion: Patients with EAH compared to controls have worse task switching which correlates with VA, especially with VA calculated by Framingham Heart Study risk tables. Early vascular ageing is an important factor in brain damage in EAH even in middle-aged patients with early stages of the disease.
Disclosure: Nothing to disclose

EPO1028

Linguistic and Functional Mechanisms of Post-Stroke Dynamic Aphasia: Benefits of Combined Therapy with Donepezil and Memantine.

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Background and aims: Dynamic Aphasia (DA) is a rare form of language disorder characterized by considerably reduced but relatively normal spontaneous speech, with preservation of other verbal language functions. Two types of DA have been described: (I) language-specific type and (II) domain-general type. Research in physiopathology provides evidence to treat specific DA patients with cholinergic modulators. However, strategies combining two drugs have never been reported so far.
Methods: We report an open-label single case study (n=1) in a patient with a chronic type I/II DA secondary to an ischemic infarction in the left fronto-insular and supplementary motor areas (high resolution 3-T MRI). After baseline evaluation, the patient received donepezil 5 mg (2 months), donepezil 10 mg (2 months), donepezil 10 mg/memantine 20 mg (4½ months) and washout (1½ months). No speech-language therapy was used. A comprehensive cognitive and language evaluation was carried out at baseline and at different endpoints, performing four 18FDG-PET along pharmacotherapy.
Results: Donepezil 5 mg significantly improved type I DA features (normalization of verbs generation, p=0.01), whereas donepezil 10 mg did the same with type II traits (normalizing spontaneous speech, verbal fluency and improving generation of novel thoughts, p=0.004), along with improvement of executive-attentional functioning. Combined therapy further enhanced cognitive function, but did not additionally improved DA. No adverse effects were registered and the patient reported a considerable improvement in quality of life after treatment.
Conclusion: In our experience, pharmacological treatment improved language deficits in a chronic type I/II DA and was well-tolerated.
Disclosure: Nothing to disclose

EPO1029

Cognitive impairment in patients with progressive supranuclear palsy and multiple system atrophy

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Background and aims: In most recent neuropsychological studies, only the screening methods were applied to assess global cognition and executive functions in PSP and MSA, e.g. the Frontal Assessment Battery and the Dementia Rating Scale. Our aims were assessment, description and mutual comparison of cognitive impairment in patients with progressive supranuclear palsy (PSP) and multiple system atrophy (MSA).
Methods: In our detailed neuropsychological battery, executive functions, attention, verbal fluency and visual perception were examined; tests such as TMT, Stroop test, ROCF, Verbal fluency, Block design, FAB, MMSE and Clock drawing test were used to explore cognitive domains.
Results: Pilot results show that patients clinically diagnosed with probable MSA (17) had no cognitive impairment in 11 cases, 5 patients had mild cognitive impairment and 1 patient had dementia. Out of patients clinically diagnosed with probable PSP (35), 17 patients meet the criteria for dementia, 15 patients for mild cognitive impairment; in these 32 PSP patients dysexecutive syndrome was present. In other 3 PSP patients only attention deficit was seen.
Conclusion: In both groups of patients cognitive impairment was present. Patients with probable PSP had cognitive impairment more often and was evident already in screening methods in comparison with patients with probable MSA. If patient with probable MSA or probable PSP had at least mild cognitive impairment, deficits in executive functions were present. Nevertheless, the research in larger cohorts is planned to involve more PSP and MSA patients with different phenotypes.
Disclosure: Study supported by: Grant IGA_LF_2017_040, Institutional support MZ CZ–RVO FNOL 2017

EPO1030

Dressing apraxia – not only while dressing

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Background and aims: Apraxia usually occurs after dominant hemisphere lesions. Dressing apraxia, involving a visuospatial dysfunction, is the exception, being associated with right hemisphere lesions. We present a case of dressing apraxia with associated apraxia for other bimanual tasks after ischemic stroke.
Results: A 48-year-old right-handed female, previously healthy, presented with acute left upper limb paresis. She also complained of inability to perform some daily tasks, such as tying a garbage bag. On examination, we observed distal left upper limb paresis and hypoesthesia, with errors in position testing, optic ataxia with the left hand, and topographical disorientation. On praxis evaluation, dressing apraxia was noted. Additionally, she could fold a shirt and tie a garbage bag without mistakes using the right hand. However, with either the left or while using both hands, she was unable to perform the same tasks. There was no neglect. Brain MRI showed a right parieto-occipital ischemic stroke, involving the superior parietal lobule. Brain images were normalized to the MNI152 and the probability of interruption of each neuronal tract was calculated using the Brain Connectivity and Behaviour Toolkit software package. Tracts with >95% lesion probability were the corpus callosum, superior longitudinal fasciculus, cortico-spinal tract, and anterior segment of the arcuate fasciculus. No aetiology for the stroke was found.
Conclusion: Dressing apraxia, topographical disorientation and optic ataxia, while infrequent, occur after right superior parietal lesions. Inter-hemispheric disconnection with lesion of corpus callosum fibers could explain apraxia of the non-dominant limb, by isolating the right motor cortex from left hemisphere motor representations.
Disclosure: Nothing to disclose

EPO1031

Translation, cultural adaptation and assessment of psychometric properties of the Greek version of Parkinson's disease Cognitive Rating scale

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Background and aims: The Parkinson's Disease Cognitive Rating Scale (PD-CRS) was designed for the assessement of cognitive functions especially affected in Parkinson's disease (PD). The purpose of the present study was to translate and culturally adapt PD-CRS in the Greek language as well as to evaluate its ability to distinguish the cognitive performance of PD-patients and healthy controls.
Methods: The PD-CRS scale was translated into Greek and was initially administered to a group of 15 healthy and relatively highly educated individuals in order to identify and adequately replace culturally specific items. Four such items (included in the confrontation naming task) were found. The items were replaced with new ones, preserving the semantic heterogeneity and difficulty level of the original scale. The revised scale was then administred to a group of 118 healthy adults (selected to represent different ages and levels of education) and 59 PD-patients. Next, discriminant function analysis was performed on each scale subcore and total PD-CRS score.
Results: Healthy adults performed better than PD-patients in all PD-CRS tasks. The total cortical score and the total subcortical score contributed to optimal discrimination accuracy of the two groups (total separation accuracy 97%). The final model categorized successfully 98% of the patients and 96% of healthy participants (Wilks' λ=0.244; $x2(2)=249.68$, $p<0.01$).
Conclusion: The Greek version of PD-CRS scale exhibited an excellent discrimination accuracy of PD-patients and healthy subjects. The study is still in process.
Disclosure: Nothing to disclose

EPO1032

Acute ischemic strokes presenting as transient global amnesia

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Background and aims: Transient global amnesia (TGA) is a clinical syndrome characterized by a sudden onset of anterograde amnesia accompanied by various degrees of retrograde amnesia, lasting within 24 hours, without compromise of other neurologic functions. We want to describe 3 cases with acute ischemic stroke of extra-hippocampal location, which presented as TGA.
Methods: We retrospectively reviewed and analyzed the medical records and brain MRIs of all TGA patients, who visited our Neurology department and checked diffusion-weighted MRI from October, 2010 to June, 2017.
Results: Among 67 TGA patients, acute ischemic infarction of extra-hippocampal location was observed in 3 patients. The locations of infracted lesions were left orbitofrontal, left prefrontal, and right frontal plus left parietal cortex in each of 3 patients. Except for the presence of acute infarction, other diagnostic characteristics of TGA were well applied in all patients.
Conclusion: Transient amnesia as the main manifestation of acute ischemic stroke is rare. Our cases showed acute ischemic infarction of extra-hippocampal location (orbitofrontal, prefrontal, and parietal cortices of dominant hemisphere) can present as transient amnesia mimicking TGA.
Disclosure: Nothing to disclose

EPO1033

Executive dysfunction and mood disorders: how Chronic Obstructive Pulmonary Disease may complicate Alzheimer's Disease

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Background and aims: Chronic Obstructive Pulmonary Disease (COPD) is a common lung illness associated with cognitive and psychological impairment, which entails a clear deterioration in the quality of life. By means of a retrospective study on patients with Alzheimer's Disease (AD) with and without COPD, we analyzed clinical and neuropsychological variables to verify if COPD plays a pejorative role on neuropsychological profile in patients with dementia.
Methods: We collected data of 23 adult patients with probable AD and COPD (AD-COPD) and 23 with AD only (AD), matched for sex, age, educational level and Mini Mental State Examination (MMSE) at the disease onset. We compared cognitive and behavioral aspects assessed within two years of the disease onset: memory, executive function and constructional apraxia, language, the presence of anxiety and depression were the variables analyzed. Disease progression was evaluated comparing MMSE two years after the first evaluation.
Results: AD-COPD had worse performances in executive functions tests than AD, and also showed a higher presence of depression. No significant difference there was between the two groups considering the decrease in MMSE score.
Conclusion: COPD is known to be associated with the development of cognitive deficits and mood disorders. Our study shows a higher frequency of executive dysfunction and depression in patients with AD and COPD in comparison with patients with AD only, even in the early stages of the disease. Comorbidity with COPD may complicate the management of AD patients, that could benefit from a closer and multidisciplinary monitoring.
Disclosure: Nothing to disclose

Epilepsy 1

EPO1035

Trazodone: a new antiepileptic drug for Dravet syndrome?

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Background and aims: Dravet syndrome is an epileptic encephalopathy associated with SCN1A mutationstypically refractory to antiepileptic drugs (AED).
Methods: Woman, 25 years old, with refractory epilepsy and developmental delay since 5 months of age, had a genetic test in 2016 that confirmed a SCN1A gene mutation. Her usual pattern of seizures under triple AED was an average of 1-2 tonic-clonic seizures per night.
Results: Electroencephalographic and polysomnographic studies documented bilateral frontal spikes and polyspikes during sleep (averaging 170/h of sleep), frequently associated with subtle eye and eyelid involuntary movements (averaging 90/h of sleep). In June 2017, the patient's mother mentioned worsening of sleep pattern with significant insomnia, which led to the introduction of trazodone (225 mg/day). Since then, a remarkable improvement of both sleep pattern and seizure frequency was registered, with four nocturnal seizures in 4 months. A new polysomnographic study was conducted, that showed a substantial improvement of intercritical activity (averaging 30/h), no documentation of tonic-clonic seizures, and only rare subtle eyelid myoclonic seizures (averaging 0.7/h of sleep). Sleep structure, despite slight increase in N3, was similar.
Conclusion: Recent data from animal studies suggest that serotonergic pathway modulation may function as a therapeutic target for Dravet Syndrome. The beneficial effect of lorcaserin (serotonin receptor agonist) and fenfluramine (serotonin release agent) has been documented in a few human cases. Our case suggests a direct antiepileptic role (as opposed indirect improvement in sleep structure) of trazodone in Dravet syndrome, reinforcing the possible advantageous effect of serotonergic modulation in these patients.
Disclosure: Nothing to disclose

EPO1038

Prediction of motor function for surgical indication of hemispherectomy in epilepsy patients

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Background and aims: Prediction of motor function before hemispherectomy in patients with epilepsy is important to determine surgical approach, information about the most effective test is still restricted.
In this study we evaluated feasibility of tests for prediction of postoperative motor function (MF) in order to determine the indication of hemispherectomy for adults.
Methods: Examinations to determine surgical indication for hemispherectomy were performed in 5 patients since 2004. We examined retrospectively the following evaluations and MF after surgery.
Preoperative motor weakness
- TMS-MEP (Transcranial Magnetic Stimulation-Motor Evoked Potential)
- Wada test (WT)
- DTI–tractography (DTT) (Diffusion tensor imaging)

Results:
- 5/5 patients presented hand weakness after the injection on the affected side in WT
- DTT was detected preoperatively in all patients, not consistent for prediction. Only one patient deteriorated
- Preoperative motor weakness TMS-MEP might be useful to determine the indication for hemispherectomy.
- 2/5 patients had finger movement preoperatively, and 2/5 patients in whom MEP was provoked by TMS. One partially deteriorated the other did not undergo surgery.
- 3/5 patients who were not provoked MEP not suffered deterioration.

Conclusion:
- TMS-MEP has limitation for prediction of MF.
- Selective WT is good
- Quantitative evaluation of piramydal tract (FA value)
- WT and DTT could not be reliable for determining surgical indication
- It is so difficult to predict postoperative MF that we need to perform presurgical multi-modality examinations as TMS-MEP, DTI, WT, according to individual clinical conditon.
- Preoperative MF and TMS-MEP might be useful to predict motor deterioration after hemispherectomy.

Disclosure: Nothing to disclose

EPO1039

Emergency department management of epileptic seizures in known epileptic patients: a descriptive study.

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Background and aims: Seizure is a frequent reason of admission in emergency department (ED). Our aim is to analyse the characteristics of known epileptic patients (KEPs) admitted to ED for seizures. We focus on the seizure precipitating factors (SPFs).
Methods: We retrospectively review of patients older than 14 years admitted for seizure to a tertiary hospital ED during a 23-month period. For KEPs, we collected clinical epilepsy features and characteristics of their management in ED.
Results: 152 (42.69%) out of 356 patients admitted for seizure were KEPs (96 males; median age: 51). Focal seizures were the most frequent clinical presentation (49.3%); 120 (78.9%) of the KEPs admissions concerned single seizure and 6 (3.9%) status epilepticus. There were secondary complications in 14 (9.2%) patients. Epilepsy was structural in 75 (49.3%) patients; 88 (57.9%) KEPs were under a single antiepileptic drug and 28 (18.4%) patients were pharmacoresistant. In the 53.3% of the admissions, SPFs were found. Missing medication was the most frequent SPF (30.9%). In 85 (55.9%) patients the treatment was adjusted and levetiracetam was the antiepileptic drug most employed (35.3%); Of the 152 KEPs admissions, 130 (85.5%) were discharged without hospitalization.
Conclusion: KEPs mean almost the half of ED admissions for seizure. A SPF is found in a high percentage of KEPs seizures, being missing medication the most common factor. We consider important to improve KEPs education about seizure triggers in order to reduce ED admission and secondary complications in this group of patients.
Disclosure: Nothing to disclose

EPO1040

Prevalence and Risk Factors for Posttraumatic Epilepsy

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Background and aims: Posttraumatic epilepsy (PTE) is defined by the presence of two unprovoked seizures at least 1 week after a traumatic brain injury (TBI). It causes 5-20% of structural epilepsies. Underlaying mechanisms are unknown. Risk factors such as age, TBI mechanism and severity, presence of early seizures, skull fracture, subdural haematoma, and age above 35 years have been described.
The aim of our study was to evaluate the prevalence and risk factors associated with PTE in patients with TBI admitted to the Intensive Care Unit (ICU) of our Hospital.
Methods: We retrospectively reviewed 220 medical records from patients admitted into ICU between 2010-2017. We excluded those with incomplete medical records and previous diagnosis of epilepsy. All had a previous normal electroencephalogram. Statistical analyses of demogaphics, TBI mechanism, glasgow, focal neurological deficits, skull fracture, posterior amnesia, brain CT abnormalities, decompressive craniotomy and surgical evacuation was performed with SPSS.
Results: 93 patients were included, 24% developed PTE, 77% were men, the mean age was 37.3. The most frequent mechanism was polytrauma, no statistical significance between the different mechanisms was found. Amnesia and age had statistical significance (p:0.013; p:0.013) as risk factors for PTE. Epidural haematoma doesn't increase the risk for PTE (p: 0.05). Patients who underwent craniectomy or surgical evacuation didn't develop PTE (p:0.035- 0.005 respectively).
Conclusion: The prevalence of PTE was higher in our population compared to the described in literature. We only found association regarding the development of PTE with age, amnesia, epidural haematoma, craniectomy and surgical evacuation.
Disclosure: Nothing to disclose

EPO1041

Efficacy and safety of the AspireSR® VNS at Ghent University Hospital, Belgium

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Background and aims: The AspireSR® VNS system is the first VNS device with an automated seizure detection feature providing stimulation in response to a preprogrammed ictal heart rate change. This study evaluates the efficacy and safety of the AspireSR® VNS in a cohort of 10 refractory epilepsy patients with a minimum follow up of 6 months.
Methods: We investigated the change in mean monthly seizure frequency (MMSF), responder rate (RR) and adverse events (AE) at maximum follow up (FU).
Results: One patient with a 12-month FU had a reduction in MMSF from 30 to 5. Five patients with a 9-month FU had a MMSF reduction from 6 to 4. Four patients with a 6-month FU had an increase in MMSF from 35 to 48. One patient was seizure-free during more than 3 months, but had a significant increase in anti-epileptic drugs. There was a responder rate of 30%. Five patients reported less severe seizures. The most frequently reported AE was hoarseness, experienced by 6 patients. Other AEs were rare. In 5 patients, the stimulation parameters had to be adjusted due to AEs
Conclusion: The first clinical results of the patients implanted with the AspireSR® VNS system in Ghent University Hospital show a RR comparable with previous short-term VNS studies. There appears to be an increase in MMSF at 6 months of treatment, probably due to the small sample size, inclusion of severe childhood epilepsy and short-term follow-up. The safety profile appeared to be comparable to the non-cardiac based VNS devices.
Disclosure: Ann Mertens is supported by a PhD grant from 'Fonds voor Wetenschappelijk Onderzoek' (FWO) Flanders.

EPO1042

Status epilepticus: a retrospective observational study.

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Background and aims: Status epilepticus is a neurological emergency that generates a significant morbidity and mortality. We analize the characteristics in our population.
Methods: Retrospective observational study based on the review of digitalized clinical records at the Hospital Reina Sofía, Murcia, from January 2011 to December 2016.
Results: There were 35 patients, with a mean age of 64 years, of whom 34.3% were diagnosed with epilepsy. The 68% of cases presented convulsive status and 43% required intensive care (37% sedation and 31.4% intubation); 30% finally did not have diagnostic confirmation with electroencephalogram. The most frequent causes were changes in their antiepileptic treatment and cerebrovascular diseases, being also significant the cases of unknown ethiology. Approximately 70% of the patients needed three or more drugs, being the most used Phenitoine, Levetiracetam, Valproate and Diazepam; 23% of status reappeared when the medications were withdrawn. Finally, 28.6% of patients died, 40% had neurological sequelae and 74% presented complications during hospitalization, especially of an infectious cause.
Conclusion: Status epilepticus is a major neurological condition. In our sample, half of patients were controlled with the third anticonvulsant, but there were cases where even nine drugs were needed. In addition, the mortality rate was notorious, as well as the percentage of sequelae, being important to use the adecuate treatment in order to eliminate seizures as soon as possible.
Disclosure: Nothing to disclose

EPO1043

The prevalence of different types of epilepsy in childhood and adolescence in the Siberian region

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Background: The prevalence of epilepsy in developed countries ranges from 1.5 to 18 people, and in some developing countries exceeds 30 per 1000 of the population. In 70-75% cases of epilepsy occur in childhood and adolescence. Long-term observations are shown that the frequency of occurrence of a particular type of epilepsy depends on the age.
Objective: to study the prevalence of different types of epilepsy in childhood and adolescence in the Siberian region.
Methods: The study and dynamic observation involved 882 patients (463 boys and 419 girls) with epilepsy and epileptic syndromes. Children from 0 to 14 years–740 people, adolescents 15-17 years–142. Among children under 14 years of age number of children 0 to 3 years amounted to 199 people, 66 children in the first year of life. Forms of epilepsy were diagnosed by neuroimaging (magnetic resonance tomography of the brain) and functional methods of investigation (EEG with standard functional tests, video monitoring).
Results: The average prevalence of epilepsy and epileptic syndromes among children and adolescents in the Siberian region in 2012-2017 was 3.54 per 1000 population (under 14 years–3.34 ; 14-17 years–4.24). Prevalence of symptomatic focal (structural) epilepsy was a statistically significant superiority (p=0.0001)-45.58% (incidence of 2.11 per 1000 population),second place is occupied by cryptogenic (unspecified) forms -17.35% (prevalence 0.80); idiopathic focal epilepsy-14.74% (prevalence of 0.68), idiopathic generalized-13.49% (prevalence 0.62). Progressive myoclonic epilepsy were rare-0.23% (prevalence 0.01).
Conclusion: Among the forms of epilepsy in childhood and adolescence in the Siberian region dominated by symptomatic focal epilepsy.
Disclosure: Nothing to disclose

Headache and pain 1

EPO1044

Predicting treatment response to candesartan in migraine patients

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Background and aims: Randomised placebo-controlled studies have reported a positive effect of candesartan, an angiotensin II receptor antagonist, in migraine prevention. The aim of our study was to identify response predictors to candesartan in a sample of migraine patients.
Methods: We audited the clinical records of patients who attended the King's Headache Clinic from February 2015 to December 2017, examining their response to candesartan. Univariate and multivariate logistic regression models were used to assess for predictors of outcome. Odds ratios (OR) with confidence intervals (CI) 95% were also calculated.
Results: The clinical history of 236 migraine patients was reviewed. A total of 100 patients (78 females) who had candesartan were included in the final analysis. One hundred and thirty-six patients were excluded cause to missing data. Forty-four patients reported a positive response to candesartan, while 56 did not have a significant therapeutic effect. The median dose of candesartan was 8mg (range: 2−32) and the average treatment period was 7 months (range: 1.5−31). In the univariate logistic regression analysis, no one of the predictors was associated with the outcome. A diagnosis of chronic migraine was associated with higher odds of a positive response to candesartan (OR 9.98, 95% CI 1.3–79.9, p=0.03) in a model adjusting for age, sex, medication overuse, disease duration, number of headache days per month, presence of aura and the total number of preventive therapies tried by patients.
Conclusion: Candesartan is effective for migraine prevention in chronic migraine patients, irrespective of previous failed preventives.
Disclosure: Nothing to disclose

EPO1045

Aura and important prodrome symptoms of migraine: A research in Greek population

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Background and aims: In some cases of migraine, the initial phase of the attack is characterized by the presence of "prodrome" or "premonitory" symptoms. These may not be recognized by the patient as part of the attack and are probably the most neglected aspect of migraine. They include a heterogeneous range of cognitive, psychological and physical changes. Prevalence rates of migraine patients reporting one or more premonitory symptoms vary.
Methods: By using a semi-structured interview, we studied the prevalence of major premonitory symptoms and aura in a population of migraine patients in a Tertiary Neurology Department of Athens University.
Results: Of 206 migraine patients who participated in the study, 176 were women and the mean age was 48.5 y.o, with a range between 18y.o. and 80 y.o. Fifty-four patients (26%) reported aura: visual (72%); sensory (27%); monitory (9%), and; language disturbances (15%). Fifty-six (27%) patients reported various prodrome symptoms. The most frequently reported premonitory symptoms were yawning (36%); mood changes (39%), and; both of them (11%). Of the 206 patients, 19 reported both prodrome symptoms and aura: most frequently yawning and language disturbances (26%).
Conclusion: The presence of premonitory symptoms is important for the diagnosis of migraine. Accurate recording of them may predict the headache phase of migraine and provide an opportunity for early treatment in order to prevent disability of the headache phase.
Disclosure: Nothing to disclose

EPO1046

Microstructural abnormalities on migraine

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Background and aims: Until now among scientists scientific discussions are conducted: whether a migraine is the disease of cerebrum. The aim of our study is to investigate the white matter microstructural differences in the brains of patients suffering from migraine without aura.
Methods: We investigated 29 patients with DT MRI (Diffusion tensor magnetic resonance imaging) and tractography. DT MRI was calculated for each voxel resulting in getting images (map) of fractional anisotropy (FA) and mean diffusibility (MD). 23 normal volunteers were a control for conducting DT MRI.
Results: FA in the control group amounted to 0.560 (0.54÷0.58) for the front quadrants and 0.565 (of 0.56÷0.57 in) for the rear quadrants. We surveyed patients with migraine without aura had lower FA values: for anterior brain–0.52 (0.5÷0.54), for the rear–0.53 (0.52÷0.54), $p>0.05$. In the group of healthy volunteers the values of SDS made up 0.83 (0.80÷0.86) for the front quadrants and 0.85 (0.82÷0.88) for the rear quadrants ($p>0.05$).
The obtained results revealed significant difference of the values of SDS for the rear quadrant on the side of the headache and in the opposite hemisphere in patients with migraine is 0.91 (0.89÷0.93) and 0.87 (0.86÷0.88), respectively ($p<0.05$). While in the occipital lobes of the brain depleted traktorista picture and not visualized posterior commissure. Along with this there has been some relationship between fractional anisotropy in the hemisphere and increased severity of seizures ($r=0.36$, $p<0.05$).
Conclusion: All patients have microstructural changes in the brain.DTI and tractography are integral part methods in migraine diagnostic.
Disclosure: Nothing to disclose

EPO1047

Do The Inflammatory Factors Contribute to The Pathogenesis of Vestibular Migraine?

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Background and aims: Vestibular migraine (VM) is an under-recognized entity with substantial burden for the individual and society. The underlying mechanism of VM and its distinction from other migraine mechanisms still remained unclear. A handful of studies revealed that inflammatory pathways contribute to migraine. We aimed to investigate the possible role of inflammation in the pathophysiology of VM compared to migraneurs and healthy controls.
Methods: We recruited 25 patients with episodic migraine and 32 with VM, diagnosed according to ICHD-3beta criteria and 26 sex- and age-matched healthy controls after their consent and ethical approval. Blood samples could be obtained only from 12 patients during the attack, whereas the remaining samples were taken in headache-free periods. Plasma levels of CGRP, NKA, Substance P (SP), NLPR-1, NLPR-2,CASP-1, IL-1b, IL-6, IL-8, IL-10, TNF-α, IF-γ, NFκB were measured with the commercial kits by following the manufacture's instructions.
Results: Inflammatory cytokines were found positively correlated with inflammasome pathway in both VM and migraine groups. TNF-α and IL-6 were both suppressed in VM and migraine groups while SP was reduced only in the migraine group when compared to the controls. Furthermore, inflammasome pathway factors were correlated with allodynia in patients with VM. Prophylactic treatment had no effect on cytokine levels.
Conclusion: Suppression of the inflammatory cytokines both in migraine and VM patients might be associated with a compensatory anti-inflammatory mechanism. However, VM patients had higher SP concentration while it seems to be suppressed in migraineurs. This finding may suggest that different pathophysiological inflammatory processes are in charge for these two entities.
Disclosure: This study was supported by Istanbul University Research Fund (project number BAP-22652).

EPO1048

Familial trigeminal neuralgia: a case report

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Background and aims: Trigeminal neuralgia is a recurrent paroxistic pain affecting one or more divisions of the trigeminal nerve. Although it is clasically considered a sporadic disease, there are several reports of familial cases.
Methods: Retrospective study of a patient diagnosed of trigeminal neuralgia with several close relatives throughout three generations also diagnosed of trigeminal neuralgia. It includes clinical description, response to treatment and MRI findings.
Results: A 52-year-old woman is diagnosed of trigeminal neuralgia affecting right V3 division of trigeminal nerve. Pain does not respond to medical treatment with carbamazepine and is treated with percutaneous trigeminal thermocoagulation, becoming assimptomatic for 19 years. Then she is diagnosed of trigeminal neuralgia affecting left V2 division of trigeminal nerve. Cranial MRI shows mild neuritis in V2 division and pain is completely relieved by carbamazepine and pregabalin. Control MRI has not specific findings. Five years later, left V2 trigeminal neuralgia reappears and does not respond to medical treatment so she is again treated with percutaneous trigeminal thermocoagulation. She has a family history of trigeminal neuralgia: granddfather, father, two aunts and two sisters.
Conclusion: This is one of the few families with familial trigeminal neuralgia described in Spain and the only one in which three generations are affected. The fact that two men and several women have the disease means that inheritance could be autosomal dominant. The finding of neuritis on one MRI suggests that the mechanism of trigeminal neuralgia in familial cases might be somehow different from microvascular compresion.
Disclosure: Nothing to disclose

EPO1049

Spontaneus pneumocephalus: an uncomommon cause of headache

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Background and aims: Spontaneous pneumocephalus, an intracranial air collection without known etiology, is a rare condition. We describe two cases.
Methods: Case report
Results: Case 1–A 61-year-old male, was admitted with headache and vomiting for five days. Headache was sudden, frontally located, severe and reached the maximum intensity within firts minute, accompanied by nausea and vomiting. An uncolored nose discharge was noticed on the upright position. There was no trauma history, recent infection or previous headache. Physical examination was unremarkable except for a clear discharge from left nostril. Brain CT scan showed a probable fistula in the left cribiform plate and extensive subarachnoid air densities within several cisterns and bilateral. Cisternography confirmed the presence of a CSF leak. Transphenoidal repair of the leak was performed and CSF rhinorrhea stopped. Headache and pneumocephalus completely resolved.
Case 2–A 39-year-old pregnant woman, with no past history of headache, suddenly developed a severe generalized throbbing headache during labour. Neurological examination showed nuchal rigidity. The brain CT scan revealed extra-axial, retroclival and retrosellar hipodensity, without mass effect. Symptomatic treatment was prescribed and headache and meningeal signs remitted in 12 hours. Brain MRI at 1 month follow-up showed air reabsorption.
Conclusion: Headache can be the sole presentation of both massive and localized non-thraumatic pneumocephalus. CT scan was not only diagnostic but also oriented management. In most reported cases treatment is not consensual. In our cases, the distinct radiological severity and the identification of a CSF fistula determined different approaches (surgical versus expectant), with complete clinical and radiological resolution.
Disclosure: Nothing to disclose

EPO1050

Socio-economic impact of severe migraine in France: study in patients with at least 8 days of headaches per month

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Background and aims: Migraine is a common and disabling pathology that notably affects active and young adults. The objective of this study was to estimate the socio-economic impact of severe migraine in French patients with at least 8 days of headaches per month.

Methods: A representative panel of French adult population (15,000 people) was surveyed using an online questionnaire in July 2017 by Kantar Health. The questionnaire's different parts were: socio-demographic data, migraine diagnosis with an extended French version of IDTM Migraine screener and socio-economic impact of the disease.

Results: On the 7,720 survey participants, migraine prevalence with at least 8 days of headaches per month in patients was 3.8% (average age: 41.1, 68% of women). 63% of workers reported an impact of the pathology on their work and especially on their efficiency. Absenteeism at work was estimated at 33 days a year on average with an annual loss of 3.8 billion euros for all actors in society. More than three-quarters of patients had sleep disorders and benefited less from their free time. For 14% of patients, a relative had to adjust his working time during migraine headaches. 58% of patients needed to purchase non-reimbursed medicines for migraine (average monthly cost of 31.9 euros) and 43% others therapies (average monthly cost of 51.7 euros).

Conclusion: Severe migraine patients are affected in their professional lives but also in their social lives and personal budgets. Migraine generates a significant burden for patients and an economic loss for society.

Disclosure: This study was supported by Novartis Pharma France.

EPO1051

Effect of OnabotulinumtoxinA Prevention on Comorbidities of Depression and Anxiety in Chronic Migraine: Analysis in Headache Day Frequency Responders vs Headache Day Frequency Non-Responders

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Background and aims: This analysis of COMPEL Study data assessed onabotulinumtoxinA on comorbid depression and anxiety in people with chronic migraine (CM) who also had a ≥50% reduction in headache day frequency at week 24.

Methods: The 108-week, multicentre, open-label COMPEL Study enrolled adults with CM receiving onabotulinumtoxinA 155U. The effect of onabotulinumtoxinA on Patient Health Questionnaire (PHQ-9) and Generalised Anxiety Disorder Assessment (GAD-7) sum scores in those with clinically significant depression (PHQ-9 ≥5) and anxiety (GAD-7 ≥10) at baseline was analysed in those who had a ≥50% reduction in headache day frequency at week 24 (headache-frequency responders) vs those who did not (non-responders). A ≥1 severity category improvement in PHQ-9 or GAD-7 was considered clinically meaningful.

Results: Patients (N=715) had a mean (range) age of 43 (18–73) years, were primarily women (84.8%, 606/715), and had depression (PHQ-9≥5: 74.5%, 529/710) or anxiety 24.6% (GAD-7≥10: 175/711). Mean (SD) headache day frequency at week 108 significantly decreased from baseline: 22 (±4.8) to 11.3 (±7.4) days ($P<0.0001$). Depressive and anxiety symptoms significantly ($P<0.001$) improved in people with depression regardless of headache day response (Figure 1A, 2A). 83.7% of headache-frequency responders and 60.3% of non-responders experienced a reduction of ≥1 Severity Category in PHQ-9. 86.0% and 71.4%, respectively, experienced a reduction of ≥1 Severity Category in GAD-7.

Conclusion: COMPEL Study results demonstrate that onabotulinumtoxinA improves symptoms of depression and anxiety among people with CM, regardless of whether onabotulinumtoxinA treatment resulted in a ≥50% reduction in headache day frequency.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

EPO1052

Precipitating factors of chronic migraine: description in a series of 725 patients

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Background and aims: Among patients with Episodic Migraine (EM), 2.5% progress to Chronic Migraine (CM) over the course of one year. We herein aimed to analyze precipitating factors for CM evolution in a prospective registry of CM patients.
Methods: Patients firstly attended in an outpatient headache unit in a tertiary hospital (January 2013-January 2018). They were referred from primary care or general neurology offices. CM was diagnosed accordingly to ICHD-2R and ICHD-3 criteria. We assessed demographic and clinical data, comorbidities, and risk factors. We considered in each patient latency from onset of CM to diagnosis, and if they identified any precipitating factor for CM appearance
Results: We included 725 cases (105 males, 620 females), with mean age at inclusion of 40.1±13.7 years (12-80), age at onset of migraine of 19.3±9.7 years (3-65) and latency from onset of MC to diagnosis of 38.4±64.2 months (3-600). Among risk factors, we gathered other chronic pain conditions in 77 patients (10.6%), symptomatic medication overuse in 498 (68.7%), and mood disorders in 95 (13.1%). In 280 cases (38.6%), at least one precipitating factor was remembered. Stressful life events were described in 238 (32.8%). Other precipitants were weight gain (22, 3%), new-onset pain disorders (5, 0.6%), menopause, (4, 0.5%) labour (4, 0.5%) pregnancy (3, 0.4%), or sleep disturbances (3, 0.4%). New prescription medications were observed by 8 patients (1.1%), hormonal contraceptives in 4 cases
Conclusion: In our MC population the identification of a precipitating factor, mainly stressful life events and weight gain, is not uncommon.
Disclosure: Nothing to disclose

Miscellaneous 1

EPO1054

The effect of food intake on haemodynamic parameters during tilt-up test in patients with postural orthostatic tachycardia syndrome (POTS)

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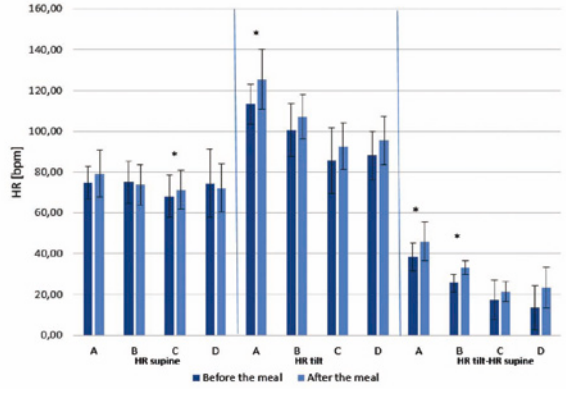
Background and aims: To determine the effect of food intake on heart rate (HR) in POTS.
Methods: In forty-one with suspected POTS on an initial tilt-table test the following protocol was performed: 10-minute supine phase, 10-minute 70° tilted phase, ingestion of 400 ml of Nutridrink Multi Fibre®, 45-minute supine phase and 10-minute 70° tilted phase. Subjects were divided into three groups: A) difference (Δ) in HR (standing vs. supine) before the meal≥30 (N=13); B) ΔHR before the meal <30, but after the meal≥30 (N=12); C) ΔHR before and after the meal <30 (N=16). Group D consisted of 10 healthy subjects.
Results: Before the meal, ΔHR was significantly higher in group A compared to all other groups, and in group B compared to group D ($p<0.00000001$). After the meal, ΔHR was significantly higher in group A compared to all other groups, and in group B compared to groups C and D ($p<0.0000000001$) (Figure 1). Patients from group A and B were pooled into a POTS, and from group C and D into a non-POTS group. According to ROC analysis before the meal, a cut-off value of 30 bpm had the sensitivity of 52.0% and specificity of 96.2%, while a cut-off value of 25 bpm had sensitivity of 92.0% and specificity of 80.8%. After the meal, a cut-off value of 30 bpm had the sensitivity 100.0% and specificity of 92.3%.



Differences in supine HR, tilted HR and the increase in HR after the tilt depending on the meal. Dark blue represents the value before the meal and light blue after the meal. Note that only in group A and B the increase in HR was significantly higher after the meal ($p<0.001$ and $p<0.0001$, respectively).
Conclusion: Food intake can significantly alter results of the tilt-table test and should be taken into account during the diagnosis of POTS.
Disclosure: Nothing to disclose

EPO1055

Evolution and predictors of symptomatic dysautonomia in people with clinically isolated syndrome

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Background and aims: One of the characteristics of structural disorders of the autonomic nervous system (ANS) is that in many patients it can be asymptomatic. Similar observations were seen in people with clinically isolated syndrome (pwCIS), where a significant discrepancy between ANS symptoms and objective assessments of ANS dysfunction was found. Therefore, we aimed to investigate the evolution and predictors of symptomatic dysautonomia in pwCIS.
Methods: In 59 pwCIS (45 females, mean age 31.88±9.12), Composite Autonomic Symptom Score (COMPASS 31) and Composite Autonomic Scoring Scale (CASS) were performed during the CIS diagnosis and 24 months later. Age, baseline Expanded Disability Status Scale (EDSS), total number of supratentorial T2 lesions and presence of brainstem lesions MRI were considered as possible predictors.
Results: Based on distribution of COMPASS 31 and CASS among the pwCIS, cut-off value of >9 and >1 were considered as significant, respectively. On M24, 8 pwCIS had both COMPASS 31 and CASS with values fulfilling pre-specified criteria. According to binary logistic regression model, total number of baseline T2 lesions and age were statistically significant predictors for symptomatic dysautonomia (Exp(B)=1.086, p=0.028 and Exp(B)=1.116, p=0.035, respectively).
Conclusion: Substantial proportion of pwCIS develops symptomatic dysautonomia over 24 months of follow-up. Total number of baseline T2 lesions and age of the patient seems to predict development of symptomatic dysautonomia over the long term.
Disclosure: Funded by the Installation Research project HRZZ UIP-11-2013-2622 of the Croatian Science Foundation.

EPO1056

Cardiovascular autonomic reflexes in syncopal migraine patients

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Background and aims: Migraine and syncope can occur in the same patient. Both conditions are known to present an impairment of autonomic regulation.
Aim: to evaluate cardiovascular reflexes in syncopal migraine patients and compare with healthy controls.
Methods: The study sample consists of 92 persons divided in four groups: Gr I (n=51)-syncopal migraine, Gr. II (n=14)-migraine without syncope, Gr III (n=15)-syncope without migraine and Gr. IV (n=12)-healthy controls. Was performed autonomic cardiovascular tests (Valsalva maneuver, orthostatic testing, deep breathing and isometric exercise). The result was classified as: normal, slight, prominent and severe modification.
Results: Abnormal cardiovascular autonomic reflexes presented 88.23% in Gr.I, 92.8% in Gr.II, 100% in Gr.III and 16.7% in Gr.IV (I vs III<0.05, t=2.6; I vs IV< 0.001, t=5.9; II vs IV< 0.001, t=12.9). Slight modification-13.7% in Gr.I, 7.1% in Gr.II, 13.3% in Gr.III and 16.7% in Gr.IV. Prominent modification: 43.1%–Gr.I, 50%–Gr.II, 60%–Gr.III and 0% in Gr.IV (I vs IV<0.001, t=6.2; II vs IV<0.01, t=3.9; III vs IV< 0.001, t=4.5). Severe modification: 31.4%–Gr. I, 35.7%–Gr. II, 26.7%–Gr.III and 0% in Gr.IV (I vs IV< 0.001, t=4.83).
Conclusion: All groups present modification of the cardiovascular autonomic reflexes more expressed than in the healthy controls, but syncopal migraine group was severely affected, which could reflect the impairment of the autonomic regulation.
Disclosure: Nothing to disclose

EPO1057

Clinical characteristics of intracranial hemorrhages in patients treated with direct oral anticoagulants in secondary stroke prevention

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Background and aims: Risk of hemorrhagic complications in patients anticoagulated after a cardioembolic stroke is double than in primary prevention. Direct oral anticoagulants (DOACs) reduce the risk of intracranial hemorrhage (ICH) by 50% compared to warfarin. We present our clinical experience of ICH secondary to DOACs in secondary prevention.
Methods: We performed an observational, retrospective study of anticoagulated patients with DOACs in secondary prevention of stroke from October 2010 to June 2015 at our tertiary university hospital. Clinical, radiological and ICH variables were collected.
Results: We included 425 patients (57.7% dabigatran, 24.7% rivaroxaban and 17.6% apixaban). 53.4% were women, mean age 77.1±10.2 years. The mean follow-up was 20±18.1 months. Median CHA2DS2-VASc was 5 (2-8) and HAS-BLED was 2 (1-4). During follow-up there were 10 (2.3%) ICH, median of 36 months (7-78) from the beginning of treatment, incidence rate: 0.015 cases / person-year. Patients were receiving treatment with Dabigatran (8), Apixaban (1) and Rivaroxaban (1). There were 5 spontaneous intraparenchymal hematomas, 3 post-traumatic subarachnoid hemorrhage, an intraventricular hemorrhage and a subdural hematoma. Anticoagulation was reversed in 3 cases. There were 2 deaths related to ICH. At 3 months 70% presented mRS≤2. Anticoagulation was discontinued in 4 patients (intraparenchymal hemorrhages). Same DOAC was reinitiated in 3 patients, in one DOAC was changed, and one percutaneous left atrial appendage closure was performed.
Conclusion: The rate of ICH in patients with DOACs in secondary stroke prevention was similar to that of the pivotal studies and patients presented low disability.
Disclosure: Nothing to disclose

EPO1058

Prognostic value of EEG in post-cardiac arrest patients

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Background and aims: In patients of post-cardiac arrest, EEG is a very useful tool to evaluate the severity of the brain damage and to determine the long-term prognosis. So we wanted to evaluate the prognostic values of various early EEG patterns of cardiac arrest patients.
Methods: We reviewed medical records and early EEG findings (within 48hours after cardiac arrest) of all postcardiac arrest patients, who were admitted to our hospital between 2013-2016. Forty-two patients were identified.
Results: Diffuse background suppression (nearly flat or flat EEG) was observed in 31 of 42 patients and was strongly associated with grave outcomes. Burst-suppressive patterns (3 patients), bilateral periodic lateralized epileptiform discharges (BiPLEDs, 3 patients), and alpha coma (2 patients) were also associated with poor outcomes. EEG findings of 4 patients who had recovered without significant cognitive sequelae were theta slowings (3 patients) and generalized beta waves (1 patient).
Conclusion: Early EEG findings have excellent prognostic values in patients of post-cardiac arrest. So called 'malignant' EEG patterns including diffuse background suppression (nearly flat or flat EEG), burst-suppression, BiPLEDs, and alpha coma were strongly associated with poor clinical outcomes.
Disclosure: Nothing to disclose

EPO1059

2-year experience of a "Store-And-Forward" e-Consultations program in a rural area in Central Spain

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Background and aims: Population aging and depopulation of the rural world are major problems in Western Europe what condition an imbalance between the volume of neurological pathologies and the endowment of neurologists. Teleneurology (TN) is an effective tool with proven efficacy in acute stroke, but there are opportunities beyond it such as chronic neurological diseases. TN can easily increase access of eldery patients to specialized care avoiding unnecessary transfers or referrals specially in rural areas.
Methods: In January 2015 a "Store-And-Forward" e-Consultation program (SAFC) was launched in the Tomelloso Hospital area. Five Health-care centers were selected and a non-face-to-face management of patients with reduced mobility was offered, as well as the management of administrative procedures and the doubts of the management of general practitioners through the SAFC program. We conducted a retrospective analysis after 2 years of experience.
Results: There were 302 e-Consultations between January 2015 and December 2017 (12.6 per month, increase of 27% in 2017). The average-resolution time was 2.66 days (50% reduction in 2017) and 51% of e-Consultations were resolved on the same day. Dementia was the main diagnostic group with administrative procedures and behavioral problems as the most frequent topics. In a conservative estimate, at least 150 face-to-face visits were avoided.
Conclusion: A SAFC program is a viable method to cope with the increased burden of neurological diseases in our aging population and can save money by avoiding unnecessary visits.
Disclosure: Nothing to disclose

EPO1062

Clinical Features in Familial Multiple Sclerosis Cases in Kütahya, Turkey

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Background and aims: Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by demyelination and axonal degeneration of the central nervous system, particularly affecting young adults. MS etiology is complex and results from the interaction of multiple environmental and genetic factors.
Methods: We reviewed retrospectively 614 MS patients' records between September 2011 and January 2017.
Results: Familial MS was detected in 42 of 614 MS patients followed in our clinic(6.8%). Of these patients 34 were woman(80.95%) and 8 were male(19.04%). The disease was defined as 71.42% relapsing remitting, 11.9% primer progressive, 11.9% secondary progressive and 4.7% radiologically isolated syndrome. The mean age at onset was 29.65(except RIS). The initial symptoms of the patients were defined as 35% motor, 30% sensory, 15% diğer(sphincter disorder, hearing loss, dizziness vs.), 12.5% brainstem, 5% optic neuritis, 2.5% cerebellar findings). Distribution of MS patients according to EDSS scores at the last visit were found in 27 patients(67.5%) in EDSS 0-3, EDSS 4-5 in 2 patient(5%), EDSS 6-9 in 10 patients(25%) and EDSS 10 in 1 patient(2.5%). Of the patients 61.9% had MS in first degree relatives.
Conclusion: Familial MS frequency was investigated in various series and values ranging from 3-22% were reported. The familial MS frequency was 6.8% in our patient series in Kütahya, Turkey. We present demographic features, clinical course of our patients with MS in our familial cases.
Disclosure: Nothing to disclose

EPO1063

Spinal cord infarction: Clinical and imaging patterns, pathogenesis, and outcomes in 27 patients.

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Background and aims: Spinal cord infarction is a rare condition compared to cerebral infarction, and its clinical presentation has been poorly understood.
Methods: We prospectively investigated patients diagnosed clinically as having spinal cord infarction in our hospital.
Results: A total of 27 cases of spinal cord infarction (17 men; 10 women; aged 38–90 years; average, 64.8 years) were included in the study. Sixteen cases had risk factors of arteriosclerosis, such as hypertension and a smoking history. Many cases suddenly developed paraplegia, sensory disturbance of the lower limb, and bladder and rectal disturbances. Fifteen cases involved complains of lower back pain at onset. In 9 cases, minor exercise or trauma preceded the onset of spinal cord infarction, which tended to be more frequent in younger patients. Magnetic resonance imaging revealed that the infarction was in the anterior and posterior spinal arterial territories in 5 and 4 cases, respectively. Five cases had transverse spinal cord injuries. Seventeen and 15 cases were treated with antiplatelet drugs and corticosteroids, respectively. The average of mRS at discharge was not significantly different with or without corticosteroid treatment.
Conclusion: Relatively many cases have a history of minor exercise or trauma before onset of spinal cord infarction, and this might be associated with juvenile onset spinal cord infarction. Classification of the lesion site suggested that the prognosis of the posterior spinal artery syndrome was more favorable than that of the anterior spinal artery syndrome and transverse spinal cord injury. Corticosteroid treatment for spinal cord infarction was thought not to improve the prognosis.
Disclosure: Nothing to disclose

EPO1064

Neurolymphomatosis mimicking acute polyradiculoneuritis in a case of small B cell non Hodgkin lymphoma with monoclonal secretion of Ig G kappa, despite haematological remission

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Background and aims: Non-Hodgkin's lymphoma (NHL) can associate several neurological complications related to direct invasion of the central or peripheral nervous system, paraneoplastic involvement or iatrogenic adverse events. Neurolymphomatosis associated polyneuropathy is usually thought to follow a subacute or chronic course. We present a case of rapidly progressing demyelinating polyneuropathy due to neurolymphomatosis in the context of small B cell NHL with stable haematological markers.
Methods: A 72-year-old women diagnosed with MALT NHL with monoclonal secretion of IgG kappa 8 months before, for which she was treated with several chemotherapy drugs, was admitted for severe back pain, ascending paresthesias of the lower limbs and rapidly progressive flaccid paraparesis.
Results: Neurological examination at admission showed tetraparesis (with mild paresis of the upper limbs and severe paraparesis) and loss of deep patellar reflexes. Paraproteinemic polyneuropathy was suspected but the acute onset raised the question of acute demyelinating polyradiculopathy due to chemotherapy-associated immunosuppression. Nerve conduction studies revealed sensorymotor axonal polyneuropathy, with signs of proximal demyelination. Repeated CSF analysis showed no albuminocytological dissociation and CSF flow cytometry revealed high numbers of T-lymphocytes and no atypical cells. MRI scan of the spine displayed meningeal enhancement at cervical and lumbar levels which extended to the corresponding nerve roots. Haematological work-up confirmed the stationary phase of the MALT NHL, with no signs of disease relapse.
Conclusion: Neurolymphomatosis should be considered in patients with symptoms suggestive of acute onset demyelinating polyradiculopathy and haematological diseases. Complete haematological work-up is essential for the correct diagnosis of this disease and further guidance of treatment.
Disclosure: Nothing to disclose

Movement disorders 1

EPO1065

Aging effects of Dynein on autophagic degradation of α-synuclein in mice

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Background and aims: As we all know, aging plays an important role in the pathogenesis of Parkinson's disease, while the effect of aging of dynein is still not completely known.

Methods: The behavioral assessment was performed respectively (the rod endurance test, the climbing rod time test). We used Western blot to test the changes of expression of dynein, α-synuclein, TcTex-1, LC3 in substantia nigra of the mice, and the quantitative real time reverse transcription PCR to detect the mRNA levels of dynein, α-synuclein, LC3-Ⅱand tctex1. The changes of expression strength of dynein and α-synuclein were detected by Immunofluorescence.

Results: Compared with the normal mice in the age of 12 months and 20 months, the motor functions of PD mice decreased more significantly($p<0.05$). Western blot showed the expression of dynein, LC3-Ⅱand tctex1 protein in the substantia nigra of the two groups were decreased with age, while the expression of α-synuclein protein increased gradually, and the expression of α-synuclein protein in PD group was significantly higher than normal mice group at the same age($p<0.05$). These trends were found the same in immunofluorescence, which revealed that the fluorescence intensity of dynein, LC3-Ⅱand tctex1 gradually decreased with age, whereas α-synuclein increased gradually especially in PD group.

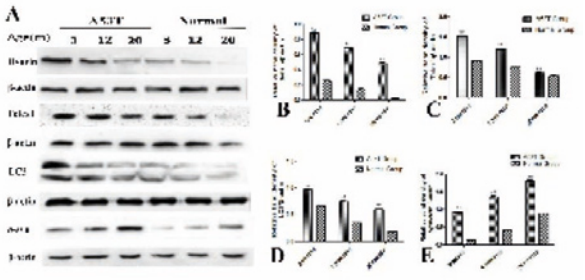

Fig. 1 The changes of protein expression in different month groups

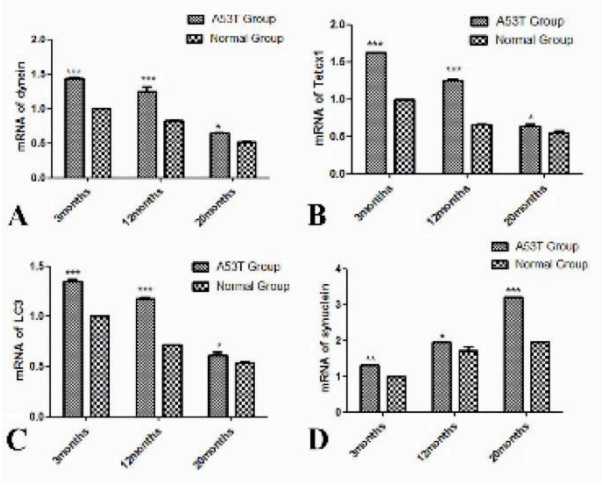

Fig. 2 The changes of mRNA expression levels of mice in different month groups

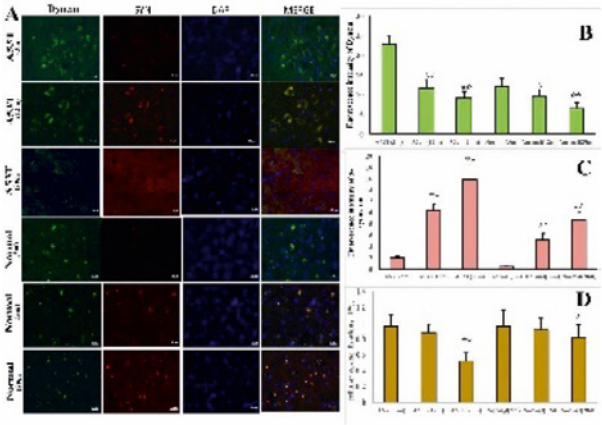

Fig.3 Colocalization of dynein and α-synuclein in cells of substantia nigra

Conclusion: Aging had important effects on the dynein functions changes of both normal group mice and PD mice, especially PD group. Therefore, the development of related drugs to reduce the aging of dynein function may provide a new treatment for Parkinson's disease.

Disclosure: Nothing to disclose

EPO1066

Cognitive Decline in Essential Tremor

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Background: Essential tremor (ET) is no longer considered as a tremorgenic monosymptomatic movement disorder but it has several non-motor manifestations including cognitive dysfunctions.
Objectives: to study the pattern of cognitive decline in ET patients and its relation to the tremor severity.
Methods: This study was performed on 30 ET patients and 15 healthy controls subjected to history taking, neurological examinations with tremor severity assessment using The Essential Tremor Rating Assessment Scale (TETRAS). They were also submitted to the Montreal Cognitive Assessment Scale (MoCA), Stroop Color Word Test, subtest of Wechsler Adult Intelligence Scale IV (WAIS-IV), Wisconsin Card Sorting Test (WCST), brain MRI volumetry and event related potential mismatch negativity (MMN).
Results: the neuropsychological tests revealed significant impairment in the global cognitive functions, attention, working memory and executive functions in ET patients. Brain MRI volumetry showed significant reduction in cerebellar cortical and white matter volumes, thalamic volume and total white matter volume. Patients also had either absent or diminished amplitude and delayed MMN.
Conclusion: Cognitive decline is a common ET manifestation despite its underdiagnoses bad impact on patients' socio–occupational activities. So, it is recommended to consider this cognitive impairment in ET management plan.
Disclosure: Nothing to disclose

EPO1067

Levodopa-induced motor complications on quality of life in Parkinson's Disease patients in Singapore

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Background and aims: The aim of this study was to evaluate the impact of levodopa-induced complications on the quality of life (QoL) of Parkinson's disease (PD) patients in Singapore.
Methods: PD patients were prospectively recruited from a tertiary care centre in Singapore. The motor disabilities were assessed with the Part III (motor) Unified Parkinson's Disease Rating Scale and the modified Hoehn and Yahr staging scale. Levodopa-induced complications were assessed with the UPDRS Part IV questionnaires and quality of life were assessed by the Parkinson's disease Questionnaire-39 items.
Results: The main levodopa-induced complications experienced by patients were wearing OFF (where 40.83% had OFF periods no more than 25% of their waking day, while 14.17% and 2.92% reported experiencing them for 26-50% and 51-75% of their waking day, respectively). The OFF periods were predominantly predictable (98.33%). A small percentage of patients (12.92%) reported having dyskinesia (a majority had either
non-disabling or mildly disabling symptoms). Only a small percentage of the patients (5.42%) had presence of early morning dystonia. In the multivariable analysis motor scores (UPDRSm) were found to be significantly associated with poorer QoL (estimate 0.06, $p<0.001$). However, the total score of levodopa-induced complications had much greater impact on QoL (estimate 0.58, $p<0.001$). Early morning dystonia was the most impact complication on QoL (estimate 2.45, $p<0.001$).
Conclusion: Levodopa-induced complications may significantly worsen the QoL of patients with PD and physicians should take this into account throughout PD patient care.
Disclosure: Nothing to disclose

EPO1068

Experience with Incobotulinumtoxin A in the treatment of shialorrea

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Background and aims: Sialorrhea is an important comorbidity in patients with neurological disorders. Incobotulinumtoxin A (IncoA) may be useful on its treatment, although evidence is limited so far.
Methods: We performed a retrospective analysis of demographic and clinical variables of patients treated with IncoA for sialorrhea in the Movement Disorders Unit of our tertiary hospital during 2017. The severity of the sialorrhea was measured by the Drooling Frequency and Severity Scale (DSFS) scales and the clinical benefit perceived by the patient using the Patient Global Impression of Improvement scale (PGI).
Results: 36 patients with sialorrhea treated with IncoA were included (64% male; age 71.1±17 years). The most frequent diagnoses were Parkinson Disease (58.3%) and Atypical Parkinsonism (16.7%). Patients received 2.6±1.7 infiltrations with IncoA in both parotid glands (42.9±8.2 IU). Basal severity in DSS scale was 4.0±0.5 and 3.4±0.6 in DFS. After infiltrations DSS was reduced to 2.2±1.2 and DFS to 2.1±1. Clinical benefit was perceived by 90% with a mean PGI of 2.1±1.0 (moderate improvement). The average duration of the effect of the toxin was 4.8±3 months. There were no significant adverse effects related to the treatment.
Conclusion: In our experience, Incobotulinotoxin A was safe and effective in the treatment of sialorrhea.
Disclosure: Nothing to disclose

EPO1069

Safinamide improves activities of daily living in Parkinson's Disease patients with motor and non-motor fluctuations.

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Background and aims: Parkinson's Disease (PD) is characterized by a wide range of motor and non-motor symptoms with a significant impact on patients' quality of life (QoL). Safinamide (Xadago®, Zambon SpA Italy) combines dopaminergic and non-dopaminergic mode of action and has shown, in pivotal trials, to improve motor functions and control motor complications without deteriorating dyskinesia.
Methods: The effects of safinamide on the activities of daily living were investigated using the EuroQol-5D (EQ-5D) data from the Phase III, double-blind, placebo-controlled study SETTLE.
Results: Safinamide, compared to placebo, significantly improved the EQ-5D Index score in all PD patients and the EQ-5D change from baseline in patients' subgroups stratified for depression and pain.
Conclusion: When used as add-on to optimized PD therapy, safinamide 100 mg/day significantly improved QoL and activities of daily living, especially in patients with chronic pain and depression. These results were also associated with significant improvements in motor fucntions suggesting that safinamide may have a positive effect on motor and non-motor fluctuations.
Disclosure: Carlo Cattaneo, Viviana Tubazio and Paola Castellani are Zambon's employees. Erminio Bonizzoni was the statiscal consultant for this analyses.

EPO1070

Clinical effect of Safinamide in patients with Parkinson's Disease with motor fluctuations and freezing of gait

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Background and aims: Parkinson´s Disease (PD) is classically defined as dopaminergic disease although it´s clear that other neurotransmitters are also affected. Dopaminergic treatment has been useful, but a ceiling effect has been reached as there are symptoms poorly responsive, including axial problems such as freezing of gait (FOG). It seems necessary to count on new non-dopaminergic drugs. Safinamide has multiple mechanisms of action, representing a valuable therapeutic drug with disease-modifying potential.
Methods: We prospectively analyzed PD patients with motor fluctuations (MF) and FOG treated with safinamide. All of them have been studied on baseline conditions (before safinamide) and after 1 month of treatment.
Results: We studied 52 patients (35men/17women, mean aged 69 years old, mean evolution of PD was 11 years). All patients could be defined as advanced PD with MF (47/52), FOG (41/52) or both and 18 had been already treated with advanced techniques including DBS. Clinical response to safinamide was clear and sustained in 12/52 patients and mild or moderate in 13/52. FOG improved in 18 patients. Eighteen patients had dubious or no response. Nine patients had secondary side effects and safinamide treatment was interrupted.
Conclusion: Besides the already known clinical indications, safinamide can exhibit peculiar effect on axial symptoms even in advanced patients. This unexpected benefit seems to occur in a percentage of patients with PD (1/3) and recalls already described cases treated with amantadine and rasagiline. It seems that a genetic component might explain this benefit.
Disclosure: Nothing to disclose

EPO1071

Evaluating the burden of advanced Parkinson's Disease on caregivers: Real-world evidence from an international survey

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Background and aims: Objective: To evaluate the impact of advanced Parkinson's Disease (PD) on caregivers' perceived burden and health.
Background: Advancing stages of PD are debilitating and may increase the dependence on a caregiver. The impact of higher disease severity on caregivers is often not well understood and under-reported.
Methods: Retrospective analyses from a six country real-world observational study were conducted. Data on clinical, humanistic, and economic outcomes were collected based on clinician assessment and patient/caregiver self-reporting. Analytical sample included data from patient-caregiver dyads. Caregiver burden was assessed using Zarit Burden Instrument (ZBI). Caregiver's health was assessed by self-reported medication use due to PD caregiving. Generalized Linear Models (higher ZBI score indicates higher burden) and Logistic Regression Models (medication use indicates health problems) were run adjusting for patient, caregiver and geographic characteristics.
Results: The analytical sample (n=539) included caregivers of PD patients who were classified by clinicians as early, intermediate or advanced PD (21.3%, 55.3% and 23.4% respectively). Mean ZBI score for the sample was 27.1(SD:16.5). Adjusted models estimated that compared to caregivers of early PD patients, the caregivers of intermediate and advanced PD patients: (i) had a higher perceived burden [3.82($p<0.05$) and 12.34 higher($p<0.001$) ZBI scores respectively]; and (ii) were more likely to use additional medication due to PD caregiving [aOR:1.26.95% CI:0.56-2.81 and aOR:2.92,95% CI:1.10-7.70 respectively].
Conclusion: This is the first large-scale international study to quantify the increased burden of intermediate and advanced PD over early PD. Increased likelihood of taking medications due to PD caregiving may result in additional economic burden.
Disclosure: YJJ, PLK, JAP, MS and JZ are employees of AbbVie and may own stocks/shares in the company. DS was an employee of AbbVie at the time of the study. PMM Disclosures: Honorarium: from Editorial Viguera; International Parkinson and Movement Disorder Society; and HM Hospitales de Madrid. License fee payments for the King's Parkinson's Disease Pain scale. Grant: from the International Parkinson and Movement Disorder Society. This study was supported and funded by AbbVie Inc. AbbVie participated in study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO1072

Parkinson's disease as a multisystem disorder: whole transcriptome study in Parkinson's disease patients' skin and blood–finding the pathomechanistic link.

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Background and aims: Next to characteristic motor triad of Parkinson's Disease (PD) due to loss of nigrostriatal neurons, more symptoms associated with non-neuronal tissues are emerging. Little is known about the molecular alterations underlying dermatologic issues or epidemiologic associations like increased incidence of melanoma in PD. The aim is to give an overview of the altered gene expression profiles of PD skin and blood using the novel method of RNA Sequencing. Networks of different genes are analyzed to map affected pathways that contribute to pathomolecular mechanism of PD in the periphery.
Methods: Whole transcriptomic profiling of 12+12 idiopathic PD patients' and matched controls' skin biopsies and venous whole blood was performed with high-throughput RNA-sequencing analysis. Followingly, pathway analysis of differentially changed gene expressions was performed. The results were validated using RT-qPCR.
Results: PD skin RNA-Seq resulted in a large collection of over 1000 differentially expressed genes, among which a clear pattern of global downregulation appeared. In blood, the differential changes were more subtle, blood being a heterogenous tissue. Pathways associated with mitochondrial metabolism and protein degradation by the ubiquitin-proteasome system were dysregulated in both.
Conclusion: The concordance of these results with previous gene expression profiling studies demonstrate that the molecular alterations in PD leading to neurodegeneration in the CNS are systemic and manifest also in peripheral tissues. Major affected pathways include dysfunction in protein metabolism, mitochondrial dysfunction and impaired immune system. Homeostatic imbalance in the skin can lead to increased susceptibility to mutagenic hazards and provide a possible molecular link between melanoma and PD.
Disclosure: Nothing to disclose

EPO1073

Can we use the term Shy-Drager syndrome?

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Background and aims: Shy-Drager syndrome (SDS) was first described in 1960 as a condition characterized by autonomic dysfunction combined with motor symptoms. Later, an umbrella term, multiple system atrophy (MSA), was proposed, MSA is classified as MSA with predominant cerebellar ataxia (MSA-C) or with predominant parkinsonism (MSA-P), and SDS is not included in the disease-type classification. However, we have encountered not a few MSA patients presenting with autonomic dysfunction as the initial symptom. Here we reviewed MSA cases with autonomic dysfunction before the onset of motor symptoms, and discussed the clinical significance of the diagnostic term, SDS.
Methods: The study subjects were 38 patients (17 men, 21 women) diagnosed with probable MSA. Disease types and initial symptoms were retrospectively investigated. Patients presenting with autonomic dysfunction as the initial symptom were selected, and the incidence, symptoms, and between autonomic dysfunction and motor symptoms were examined.
Results: The final diagnosis was MSA-C in 27 patients and MSA-P in 11. There were 9 patients with autonomic dysfunction as the initial symptom. The autonomic symptom was dysuria in all 9 patients. Most of the patients developed motor symptoms within 3 years after autonomic dysfunction while 1 patient developed later than 5 years.
Conclusion: Our study showed one-quarter of the MSA patients presented with autonomic dysfunction as the initial symptom. Motor symptoms are important to diagnose MSA. However, considering the disease modifying therapy, attention should be given to the autonomic symptoms, because early diagnosis and treatment may be possible. Thus, SDS should be considered as a disease concept in clinical practice.
Disclosure: Nothing to disclose

EPO1074

Phenotypic spectrum of movement disorders in 18p deletion syndrome

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Background and aims: Deletion of the short arm of chromosome 18 is a chromosomal abnormality and occurs in approximately 1/50,000 live births. The clinical features of the 18p deletion syndrome (18p-syndrome) include short stature, facial dysmorphism, genito-urinary abnormalities, holoprosencephaly, developmental delay, mental retardation and several types of movement disorders.

Methods: The 18p-syndrome was diagnosed in the presented patient using karyotype analysis in peripheral blood cells. We have conducted a literature review and have included all previously reported patients with 18p-syndrome and movement disorders in publicly available databases.

Results: We report a 41-year-old patient with craniocervical and upper limb dystonia accompanied by a dystonic gait. The cervical dystonia started insidiously in the last 6 years. We noticed a short stature, mild mental retardation and a history of orthognathic surgery. The cervical dystonia responded well to treatment with periodic botulinum toxin injections. Dystonia is the most common movement disorder in patients with 18p-syndrome and can present as focal, segmental, multifocal or generalized dystonia. Chorea, myoclonus, tremor and ataxia have also been reported in 18p-patients. The onset age of the movement disorder in 18p-syndrome is variable and ranges from infancy to adulthood.

Conclusion: We have presented a patient with 18p-syndrome and adult-onset multifocal dystonia. Among other movement disorders, dystonia can commonly be observed in 18p-syndrome. The variable size and location of the deletion on 18p and the different involved genes are probably responsible for the broad phenotypic variability of movement disorders in this syndrome.

Disclosure: Nothing to disclose

EPO1075

Weight loss in Parkinson's disease patients under levodopa/carbidopa intestinal gel infusion treatment

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Background and aims: Weight loss (WL) has been suggested to be a biomarker of disease progression for Parkinson's disease (PD) and other neurodegenerative disorders. WL is reported as a frequent adverse event among PD patients under levodopa/carbidopa intestinal gel (LCIG) treatment. However nor its prevalence neither its causes have been systematically analyzed.

Methods: A retrospective and cross-sectional studies were performed, among all the PD patients who were under LCIG treatment at our Center, for at least six months. Weight/ body max index, MDS-UPDRS/UPDRS, Mini Mental State Examination, Beck Depression Inventory Scale, Hoehn Yahr (HY) Stage, and levodopa equivalent daily dose (LEDD) were evaluated before LCIG inset (T0), by means of a retrospective analysis, and during the last visit (T1). At T1 the Mini Nutritional assessment (MNA) and Schwab and England ADL Scale (SE) were also assessed.

Results: We recruited 44 patients out of the 55 PD patients treated with LCIG. Baseline and follow-up patients' clinical and nutritional characteristics are detailed in Table 1. WL showed positive correlations with UPDRS IV score, dyskinesia duration/disability (UPDRS item 32-33), a history of device complications/granuloma and MNA score, while no correlations were found with disease duration, LEDD/Kg, dysphagia and disease severity (MDS-UPDRS III, HY and SE). At a multiple linear regression analysis, corrected for LCIG therapy duration, the only variable that kept significance was "dyskinesia duration" (p=0.023).

	Baseline (n=44)	Follow-up (n=44)	P - value
Age (yrs)	67 ± 4	71 ± 6	/
Disease duration (yrs)	/	18 ± 6	/
Duodopa therapy duration (months)	/	50 ± 27	/
LEDD/Kg/day	20.6 ± 6.1	24.6 ± 8.6	**0.002**
Clinical Phenotype n (%)	AK= 34 (77%) TD= 10 (23%)	/ /	
HY	3 ± 0.9	3.3 ±1.2	**0.003**
SE	NA	57 ± 20	/
MDS.UPDRS II	17.1 ± 7.2	28.6 ± 10	**<0.001**
MDS.UPDRS III	31±12.4	49.1 ±15.2	**<0.001**
UPDRS IV, Total score (items 32–42)	9.5 ± 3.2	6.1 ± 2.4	**<0.001**
Dyskinesia duration (Item 32)	1.7 ± 1	1.6 ± 0.7	0.7
Dyskinesia disability (Item 33)	1.2 ± 1.2	1.2 ± 0.8	0.9
Off state duration (Item 39)	2 ± 0.6	0.9 ± 0.5	**<0.001**
MMSE	27.2 ± 2.5	24.1 ±4*	**<0.001**
BDI	14.5 ± 7.8	18.5 ±9.5	**0.01**
Mean Weight loss (kg) – n (%) Weight loss > 10kg, n (%)	/ 	7 ± 6 – 33 (75%) 9 (35%)	/
BMI (Kg/m^2)	26.2 ± 4.7	23.1 ± 4.1	**<0.001**
MNA classification	NA	Normal nutrition status: 17 (39%) Undernutrition risk: 18 (41%) Undernutrition state: 9 (20%)	/
Enteral feeding, n (%)	0	6 (14%)	/

Table 1. Patients' clinical and nutritional characteristics. Values are presented as mean (SD) if no otherwise specified. *: two patients were not able to complete the MMSE at follow-up evaluation due to severe cognitive impairment. NA: not available.

Conclusion: WL is a common event among PD patients treated with LCIG with implications on patients' nutritional status. Dyskinesia duration seems to be the most related factor for WL occurrence.

Disclosure: Nothing to disclose

MS and related disorders 1

EPO1076

Cryptococcal meningoencephalitis in sarcoidosis patient associated with positive CSF anti-NMDA receptor antibodies–a therapeutic challenge

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Background and aims: Sarcoidosis patients are at risk for opportunistic infections, namely cryptococcal disease. Post-infectious anti-NMDA receptor (anti-NMDA-r) encephalitis has been described in cases of herpetic encephalitis (herpes simplex and herpes zoster). A 39 years-old male with pulmonary sarcoidosis treated with low-dose steroids presented with headache and vomiting for one month. Suspecting neurosarcoidosis, corticosteroid dosage was increased. However, he developed progressive behavioral changes, visual hallucinations, pronounced insomnia and gait difficulty. Neurologic examination revealed an inattentive patient, with mild language impairment and gait ataxia. Lumbar puncture revealed inflammatory CSF (polymorphonuclear predominance) with hypoglycorrhachia and India ink stain showed Cryptococcus. The patient was HIV-negative but had marked CD4 lymphopenia(66/mm3). Anti-NMDA-r antibodies (included in initial work-up) in CSF were positive. Brain MRI revealed basal ganglia enhancing lesions and subcortical white matter and splenium restricted diffusion areas. Treatment with amphotericin B, flucytosine and repeated lumbar punctures was started. Corticosteroids were reduced. Despite initial improvement, the patient deteriorated further. CSF anti-NMDA-r antibodies remained positive and EEG showed delta brush pattern. Considering a possible immune-mediated process, intravenous immunoglobulin and small increase in steroids were attempted. Thereafter, he improved, although with a fluctuating course. After 6-weeks of anti-fungal treatment, neurological deficits resolved except for mild cognitive slowing.
Conclusion: We report a cryptococcal encephalitis in a non-HIV patient with clinical and EEG features resembling auto-immune encephalitis and positive CSF anti-NMDA-r antibodies. Recent experimental studies have shown significant inflammatory response in cryptococcal CNS disease, driving tissue damage. We suggest a post-infectious immune-mediated mechanism triggering anti-NMDA-r antibodies production contributing to clinical and EEG manifestations.
Disclosure: Nothing to disclose

EPO1077

Link between health-related quality of life, occupational disability and sick leaves in patients with Multiple Sclerosis in Germany

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Background and aims: There is strong evidence that patients with Multiple Sclerosis have lower health-related quality of life (HRQOL) and that this steadily worsening neurologic disease causes enormous indirect costs mainly due to lower workforce participation. Many studies conducted research on the link between HRQOL and workforce participation of patients. However, little is known about the magnitude of the effect of specific HRQOL impairments on workforce participation. The objective of this investigation is to quantify the impact of specific HRQOL impairments on the occupational disability and sick leaves in patients with Multiple Sclerosis.
Methods: PANGAEA is a non-interventional study that assessed in a sub-study (n=559), HRQOL by the UK Neurological Disability Scale (UK-NDS). Logistic regression and negative binomial regression were used to estimate the effect of UK-NDS-dimensions and sociodemographic data on the occupational disability and number of sick leaves.
Results: Cognitive impairment (OR:1.4), mobility impairment (OR:1.6), fatigue (OR:1.2), "others" (OR:1.1), female gender (OR:2.2) and patients living in a single household (OR:1.7) have a significant impact on the occupational disability ($p<5\%$). Mobility impairment, (IRR:1.8), pain (IRR:1.4), "other" (IRR:1.7) as well as number of reluctance (IRR:3.2) have a significant impact on the number of sick leaves ($p<5\%$).
Conclusion: The results highlight the association between HRQOL and workforce participation. Mobility impairment has the greatest impact on occupational disability as well as on the number of sick leaves. Interventions targeting mobility, cognition, fatigue may help obtaining the workforce participation of the patients. Once again, the significance of the dimension "other" shows the great diversity of symptoms in patients with Multiple Sclerosis.
Disclosure: This study was supported by the Novratis Pharma GmbH, Nuremberg, Germany

EPO1079

Alemtuzumab Safety, Efficacy, and Tolerability in Paediatric Patients with Active Relapsing-Remitting Multiple Sclerosis Despite Prior Treatment with Disease-Modifying Therapy: LemKids Study Design

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Background and aims: LemKids (EudraCT 2016-003100-30) is evaluating efficacy, safety and tolerability of alemtuzumab in paediatric patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: LemKids is a 5-year, multicentre, multinational, open-label, single-arm, before-and-after switch study. Inclusion criteria: patients aged 10 to <18 years with ≥2 relapses (≥1 on-treatment relapse in the last year after ≥6 months of disease-modifying therapy [DMT; interferon beta or glatiramer acetate]); and ≥1 new/enlarging T2 hyperintense or gadolinium-enhancing lesion while on DMT, ≥2 relapses in prior year, and/or ≥2 DMTs tried. After enrolment (target N=60), patients will continue prior DMT for 4 months (Period 1) before discontinuing that therapy and switching to alemtuzumab treatment. Alemtuzumab will be administered in 2 annual courses (Course 1: 5 consecutive days; Course 2: 12 months later on 3 consecutive days), at a dosage according to patient weight (≥50 kg, 12 mg/day; <50 kg, 0.24 mg/kg/day). MRI scans will be conducted at screening, at end of Period 1, and Months 4, 8, 12, 24, 36, 48 and 60 after alemtuzumab initiation. Primary endpoint: Number of new/enlarging T2 lesions during Period 1 versus Period 2 (Months 4-8 after alemtuzumab initiation). Secondary endpoints: Number of patients with new/enlarging T2 lesions during Period 1 versus Period 2; annualised relapse rate at Year 2; cognition scores (Brief Visuospatial Memory Test-Revised, Symbol Digit Modality Test); and quality of life (PedsQL and Pediatric NeuroQoL). Safety endpoint: AEs over 5 years.

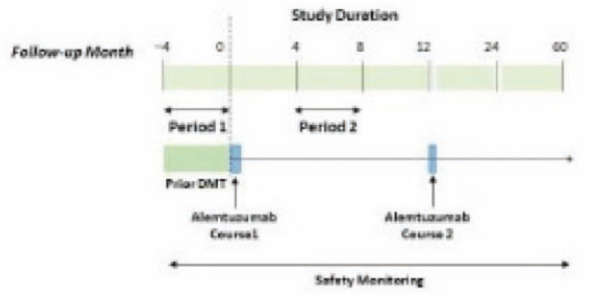

Figure 1: Schematic representation of LemKids study design
Results: Enrolment began in June 2017.
Conclusion: LemKids will provide data to help guide treatment of children with RRMS.
Disclosure: Study supported by Sanofi.

EPO1080

Atrophy of the mid-anterior and central segments of the corpus callosum is associated with impaired performance in selected cognitive tests in patients with relapsing-remitting MS

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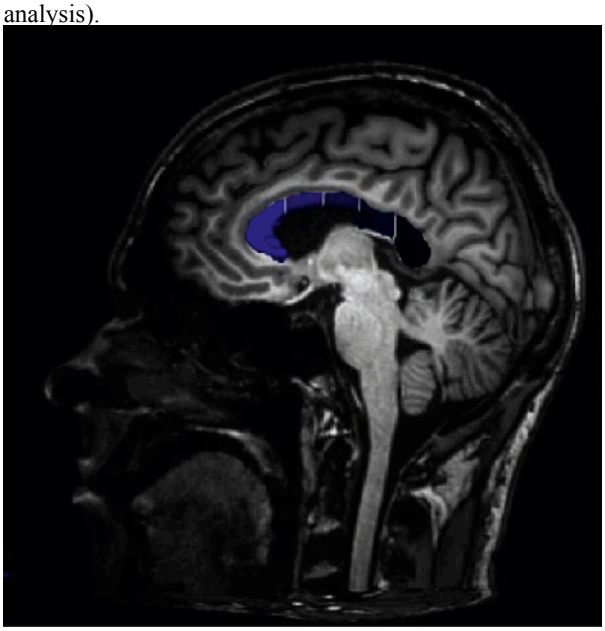
Background and aims: Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease leading to physical disability, chronic fatigue, depression and cognitive impairment. Pathomechanisms of cognitive impairment in MS are only partially understood. We hypothesized that atrophy of the corpus callosum (CC), and especially of some of its segments, occurring in the course of the disease, play an important role in cognitive decline in MS patients.
Methods: We performed neuropsychological examination (including cognitive tests assessing attention, verbal and visual memory, verbal fluency, working memory, executive functions and information processing speed (IPS) and collected MR Imaging data (1.5T scanner with a 20-channel head/neck coil) in 65 Polish-speaking patients with relapsing-remitting MS (RRMS), all receiving IFN-beta. On 3D T1-weighted sequence we calculated volumes of posterior (CC-P), mid-posterior (CC-MP), central (CC-C), mid-anterior (CC-MA) and anterior (CC-A) segments of the CC(Fig_1) using Freesurfer Software, and compared these numbers with the results of the cognitive tests (Spearman analysis).



Segmentation of the corpus callosum-a schematic view

Results: Decline of volume of CC-MA was associated with phonemic and semantic verbal fluency (rho=0.31), CC-C atrophy was related to decreased IPS (rho=0.34) and second part of the Color Trail Test (rho=-0.31), whereas decreased volumes of both (CC-C and CC-MA) were associated with more frequent rotation mistakes in the right side of the visual field in the Benton Visual Retention Test (rho=-0.34).
Conclusion: Atrophy of the mid-anterior and central segments of the CC are associated with impaired phonemic and semantic verbal fluency, IPS, visual memory performance and sequential information processing and divided attention respectively, in patients with RRMS.
Disclosure: Nothing to disclose

EPO1081

Fatal outcome in aspergillosis in the natalizumab-treated multiple sclerosis patient

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Background and aims: Natalizumab is a humanized monoclonal anti-alpha-4 integrin antibody, that prevents immune system cells to cross endothelium in blood-brain barrier. It is approved for treatment of relapsing-remitting multiple sclerosis (MS).
We present a case of central nervous system (CNS) Aspergillus opportunistic infection in natalizumab-treated MS patient.
Methods: Single case retrospective observational study
Results: A 39-year-old male was diagnosed with MS in 2005. In December 2014 he started natalizumab treatment that was uneventful until May 2017. Then the first MS relapse on treatment was diagnosed. He was unable to sit or walk due to severe spasticity. Brain MRI revealed multiple new contrast-enhancing lesions interpreted as active MS plaques (Fig. 1). Intravenous methylprednisolone was started and followed by next dose of natalizumab. One month later he experienced substantial improvement in daily-life activities and was able to walk with one crutch. In July 2017 the patient was readmitted in severe condition: he was somnolent, malnutritioned, afebrile and developed pressure ulcers. MR scans revealed multiple brain abscesses (Fig. 2). Empirical intravenous antibiotic therapy, acyclovir and amphotericin B with adequate premedication were started.
Cerebrospinal fluid qualitative DNA tests were positive for Aspergillus and negative for Candida, bacteria and viruses. Both anti-HIV and anti-JCV antibodies tests were negative. Neurological status gradually deteriorated and severe brain edema developed. He was declared dead due to irreversible brainstem injury.

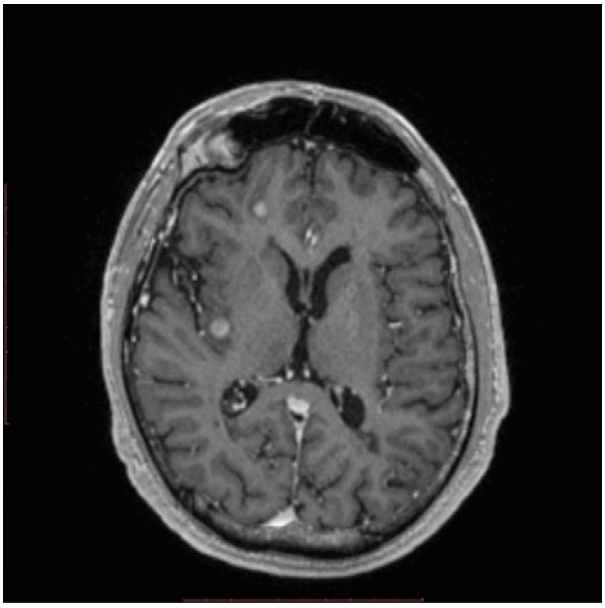

Fig. 1. Multiple contrast-enhancing lesions-ontrast ehnhanced T1 MRI, May 2017

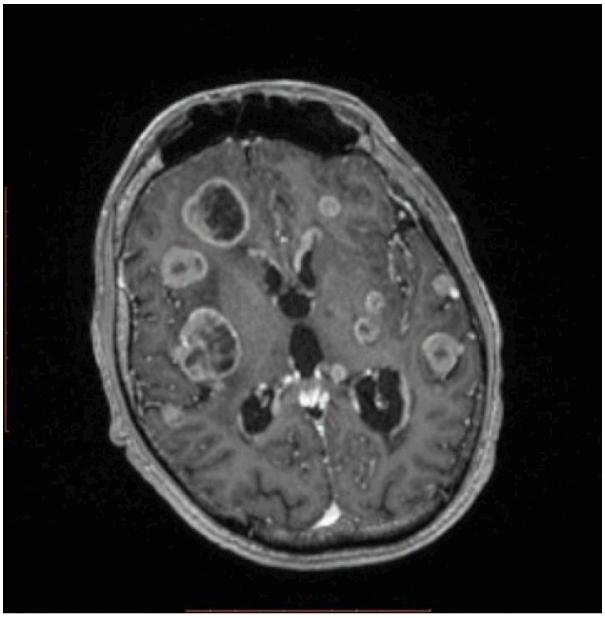

Fig. 2. Multiple brain abscesses with marginal contrast enhancement-contrast enhanced T1 MRI, July 2017

Conclusion: Probable fungal CNS infection should be considered in case of unexpected deterioration of MS patient treated with natalizumab. Our case report might help other practitioners in precise monitoring of natalizumab therapy.
Disclosure: Nothing to disclose

EPO1082

Infections during periods of Grade 3 or 4 lymphopenia in patients taking cladribine tablets 3.5 mg/kg: data from an integrated safety analysis

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Background and aims: In CLARITY, cladribine tablets 3.5 mg/kg (CT3.5) demonstrated efficacy in relapsing MS patients. The most common AE was lymphopenia, reflecting cladribine's mode of action. Integrated safety analysis showed infection incidence was not higher in patients receiving CT3.5 vs. placebo, bar a small increase of herpes zoster (HZV). Post hoc analysis examined the infectious AEs occurring concurrently with Grade 3/4 lymphopenia (with G3/4) in patients treated with CT3.5.

Methods: A CT3.5 monotherapy oral cohort was derived from CLARITY, CLARITY-Extension, ORACLE-MS and PREMIERE, encompassing 923 patients. The AE profile for CT3.5 during periods with G3/4 (defined as the onset of the Grade 3/4 lymphopenia to first Grade 2 or lower plus 2 weeks) was analysed. Adjusted-AE incidences per 100-patient-years (Adj-AE/100PY) were calculated.

Results: Adj-AE/100PY for any infections and infestations during periods with G3/4 was 57.53 vs. 24.50 outside these periods (without G3/4). Types of infectious AEs were similar during periods with and without G3/4 and did not show any specific pattern. >50% of cases occurring with G3/4 were easily-treatable infections of the upper respiratory tract (nasopharyngitis, upper respiratory tract infection, pharyngitis; Table 1). HZV was reported in 4 patients with G3/4, cases were dermatomal and mild-to-moderate in severity. Single occurrences occurred for most infectious AEs. Opportunistic infections were single occurrences, not severe, serious or difficult to treat.

Preferred Term	Cladribine tablets (n=923) with G3/4 lymphopenia			Cladribine tablets (n=923) without G3/4 lymphopenia*		
	n	T	Adj-AE per 100PY	n	T	Adj-AE per 100PY
Any infections and infestations	40	69.5	57.53	468	1910.5	24.50
Nasopharyngitis	11	81.6	13.48	152	2899.7	5.24
Upper respiratory tract infection	8	82.7	9.67	104	3045.8	3.41
Pharyngitis	4	88.6	4.51	24	3269.1	0.73
Herpes zoster	4	88.9	4.50	24	3280.4	0.73
Influenza	3	89.6	3.35	85	3096.4	2.75
Urinary tract infection	3	89.2	3.36	54	3170.9	1.70
Bronchitis	2	89.7	2.23	54	3148.4	1.72
Viral upper respiratory tract infection	2	89.6	2.23	21	3259.7	0.64

*Not necessarily the most common infectious AEs occurring during periods without Grade 3 or 4
n is the number of patients with events. T is the total patients time at risk in years (cumulative periods).
Periods of Grade 3 or 4 lymphopenia were defined as the onset of the Grade 3 or 4 lymphopenia to first Grade 2 or lower plus 2 weeks.
Adj-AE per 100PY, adjusted AE incidences per 100 patient-years; AE, adverse event; CT3.5, cladribine tablets 3.5 mg/kg; SOC, system organ class.

Table 1: Adverse events of the SOC infections and Infestations by preferred term occurring during the exact periods of Grade 3 or 4 lymphopenia occurring in >2 patients receiving CT3.5 and the corresponding incidences during periods without Grade 3 or 4 lymphopenia

Conclusion: G3/4 lymphopenia increased the frequency of infections but did not affect the type of infectious AEs in CT3.5 treated patients. HZV profile was uncomplicated; consistent with the findings of previous analyses.

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).

EPO1083

An analysis of malignancy risk in the clinical development programme of cladribine tablets in patients with relapsing multiple sclerosis

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Background and aims: An independent meta-analysis (Pakpoor et al. Neurol Neuroimmunol Neuroinflamm 2015;2:e158) in Phase III trials (with a 2-year duration) of disease-modifying-drugs (DMDs) in relapsing MS patients found no increased rate of malignancy with cladribine tablets (CT) vs. other DMDs . Here, we assess malignancy risk with CT 3.5mg/kg (CT3.5) monotherapy and placebo using data from 3 Phase III trials and the PREMIERE safety registry (up to 8 years' follow-up), and compare incidence rate with a global database.
Methods: The CT3.5 population comprised 923 patients (3433 patient-years' [PY] total exposure time) and the placebo group comprised 641 patients (2026 PY). Individual case reports of malignancies were reviewed by an independent, blinded adjudication committee. Standardised incidence ratios (SIR) were calculated using the GLOBOCAN reference population (excluding non-melanoma skin cancers [NMSCs]) and a Danish reference population for NMSC rates).
Results: The incidence per 100 PY and risk difference (95%CI) of confirmed malignancy for CT3.5 and placebo are shown in Table 1. CT3.5 malignancy SIR was almost identical (0.97, 95%CI 0.44–1.85) to the GLOBOCAN matched reference population. For placebo, SIR was numerically lower (0.48, 95%CI 0.14–1.53). There were no cases of haematological or lymphoproliferative cancers (Table 2); no clustering of specific tumour types; and incidence of skin cancer was not increased after treatment with CT3.5 vs. placebo. Incidence of malignancies with CT3.5 was constant and did not increase over time.

	Monotherapy oral cohort	
	Placebo (n=641)	CT3.5 (n=923)
Patients with events/Patients years at risk	3/2022.11	10/3414.20
Incidence per 100 PY	0.1486	0.2929
95% CI of incidence*	0.0478–0.4600	0.1576–0.5444
Risk difference per 100 PY		0.1445
95% CI of risk difference per 100 PY†		0.1656–0.4141
Risk Ratio		1.9742
95% CI of Risk Ratio‡		0.5133–7.1733

CI, confidence interval; PY, patient year.
* CI computed with the exact Clopper-Pearson formula.
† CI computed using the Miettinen and Nurminen method.
‡ CI computed with the Wald method for the number of subjects with events using a Poisson regression model with fixed effect for treatment group and log of time at risk as an offset.

Table 1: Incidence rates, risk differences and risk ratio for malignancies in patients treated with CT3.5 or placebo in the monotherapy cohort

SOC: malignancy or unspecified tumours*	Placebo (n=3)	CT3.5 (n=10)
Basal cell carcinoma	1	1
Bile duct adenocarcinoma	0	1
Breast cancer	0	1
Cervix carcinoma stage 0	2	0
Malignant melanoma	0	2
Ovarian cancer	0	1
Pancreatic carcinoma	0	1
Papillary thyroid cancer	0	1
Rectal cancer	0	1
Squamous cell carcinoma of skin	0	1

* Malignant or unspecified tumours determined by external adjudication.
SOC, System organ class.

Table 2: Type of malignancies or unspecified tumours reported in the monotherapy oral cohort

Conclusion: Analysis of malignancy rates in a cohort that includes patients with up to 8 years of follow up confirms the conclusions of the earlier meta-analysis.
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).

EPO1084

Benefit-risk assessment of cladribine tablets using Multi-Criteria Decision Analysis (MCDA) for patients with relapsing multiple sclerosis demonstrating high disease activity

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Background and aims: Relapsing multiple sclerosis (RMS) with frequent relapses is described as high disease activity (HDA). Benefit-risk assessment of disease modifying drugs (DMDs) for HDA patients is important. Increasingly, treatment decisions with multiple criteria employ Multi-Criteria Decision Analysis (MCDA). We apply MCDA to a structured benefit-risk assessment of cladribine tablets (CT) and newer DMDs for HDA patients.
Methods: Decision conferencing with physicians created an MCDA model incorporating available evidence and clinical decisions. Workshops followed the PrOACT-URL (Problem formulation, Objectives, Alternatives, Consequences, Trade-offs, Uncertainties, Risk attitude, and Linked decisions) framework. Benefit-risk assessments were conducted for DMDs in RMS and HDA patients. Experts identified 7 favourable and 11 unfavourable effects and a preference value for DMDs using hypothetical treatment effect data. Preference values were 'swing-weighted' by experts to represent trade-offs between favourable and unfavourable effects. Overall weighted preference values were calculated for each DMD. Benefit-risk profiles of CT and other DMDs were compared.
Results: CT had the highest overall weighted preference value followed by alemtuzumab and natalizumab. Comparisons of risk-benefit profiles favoured CT for severe lymphopenia, autoimmune disease, infections, gastrointestinal effects and ease of use, and favoured alemtuzumab for T1 Gd+ and T2 lesions. Differences favoured CT for progressive multifocal leukoencephalopathy, effect durability and 3-month and 6-month confirmed disability progression. Natalizumab was favoured for relapse rate, T1 Gd+ and T2 lesions.
Conclusion: Using MCDA with decisions from blinded expert physicians, the benefit-risk profile of CT in HDA patients was favourable compared to other DMDs.
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).

EPO1085

Effects of cladribine tablets on CD4+ T-cell subsets in the ORACLE-MS study: Results from an analysis of lymphocyte surface markers

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Background and aims: Lymphocyte subtype evaluation in patients from the cladribine tablets 3.5mg/kg (CT3.5) cohort of ONWARD-MS showed a transient ~82% median reduction in CD19+ B cells by week-13 with reconstitution from weeks-24 to 48. CD4+ and CD8+ T-cells were also reduced between ~40% and ~55%. Because of the durable clinical effects of CT3.5 in MS patients, the effect on regulatory-immune function cells is of interest.
Methods: Peripheral blood T-lymphocytes were immunophenotyped at baseline, and weeks-5, 13, 24, 48 in patients treated with CT3.5 at week-1 and week-5 in ORACLE-MS (n=41). Absolute numbers and proportions of CM (CD4+RO+CCR7+), EM (CD4+RO+CCR7-), Th1-type (CD4+CXCR3+), nTregs (CD4+CD25+CD127-), naïve-like nTregs (CD4+CD25+CD127-RA[HI]+) and memory-like nTregs (CD4+CD25+CD127-RA-) were measured.
Results: Greatest median reductions from baseline in absolute numbers occurred at week-13 for EM (-54%); week-24 for CM (-63%) and Th1-type cells (-51%); with similar/slightly increased levels at week-48. There was ~5% reduction in the proportion of CM, but no change in proportions of EM and Th1-type cells. Absolute numbers of nTregs (-48%), naïve-like (-67%) and memory-like nTregs (-42%) decreased by week-48. The proportions of nTregs and naïve-like nTregs were unchanged; memory-like nTregs proportions slightly increased up to 48-weeks (median 11% increase from baseline at week-48).
Conclusion: The first administration of CT3.5 has a comparable effect on CD4+ T-cell subpopulations, with no dramatic shifts in proportions.
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)

EPO1087

Prevalence of NMOSD in Central Serbia

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Background and aims: Population-based prevalence studies on neuromyelitis optica spectrum disorders (NMOSD) are limited. The aim of our study was to estimate the prevalence of NMOSD in Central Serbia, using the 2015 criteria.

Methods: In this population-based retrospective study, we included all patients from Central Serbia diagnosed with NMOSD according to the 2015 criteria. All those patients are included in the National NMOSD Registry of Central Serbia, established at the Clinic of Neurology, Clinical Center of Serbia in 2014. All tests for antibodies to aquaporin-4 (AQP-4) were performed in a single reference laboratory at the above-mentioned Clinic. Prevalence was calculated after re-evaluation of each patient according to the 2015 criteria on the day December 31, 2017. The projective number of inhabitants in Central Serbia (2016 projections) was 7,058,322 people, 3,437,630 males and 3,620,692 females.

Results: We identified 69 patients. All patients were Caucasian, and female (81%) with a median age at disease onset of 38 years (range, 7-68 years). In total, 60 (87%) patients were positive for AQP4 antibodies. Median Expanded Disability Status Scale score at the last visit was 2.5 (range 0-8.5). The prevalence was 0.98/100,000, for males 0.38/100,000, and for females 1.55/100,000. Lowest values were seen in children and elder people and highest in women and middle-aged people (40-59 years).

Conclusion: Based on the prevalence data, NMOSD remains to be in the group of rare disorders. The differences in age- and gender-specific prevalence highlight the necessity of further investigation of these variables on the disease susceptibility.

Disclosure: Nothing to disclose

EPO1088

Clinical frontal release signs correlate with cognitive impairment in patients with multiple sclerosis

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Background and aims: Cognitive impairment (CI) is frequent in all disease stages and subtypes of multiple sclerosis (MS). Presence of CI is underestimated and the neurologist's accuracy in predicting CI is rarely better than chance. We investigated the presence of frontal release signs with a validated clinical antisaccade test (CAT) and palmomental reflex (PMR) and its correlation to a neuropsychological test for detection of CI in MS patients.

Methods: CI and fatigue were assessed with the Multiple Sclerosis Inventory Cognition (MUSIC). CAT and PMR were performed by neurologists blinded to cognitive test results. The number of errors in 20 antisaccadic tasks was counted for evaluation of CAT. PMR was rated unilateral (1 point) or bilateral (2 points) positive if a reproducible (2 of 3 attempts) contraction of mentalis muscles was observed.

Results: 47 MS patients (29 females, 18 males, 39 RRMS, 5 PPMS, 3 SPMS, mean age 43 years, mean disease duration 8 years, mean EDSS 2.6) were investigated. 16 patients (34%) had CI (9 mild, 4 moderate, 3 severe). Age (Pearson r=-0.35, p=0.015) and EDSS (Spearman r=-0.27, p=0.04) correlated inversely with the MUSIC score. CAT Error rate showed an inverse correlation trend (Spearman r=-0.23; p=0.06). PMR (Spearman r=-0.29, p=0.024) and a sum score of PMR and CAT error rate (SSPC) (Spearman r=-0.3, p=0.02) correlated inversely with the MUSIC score (figure 1). Patients with CI had a significantly higher SSPC compared to those without CI (p=0.01, figure 2).

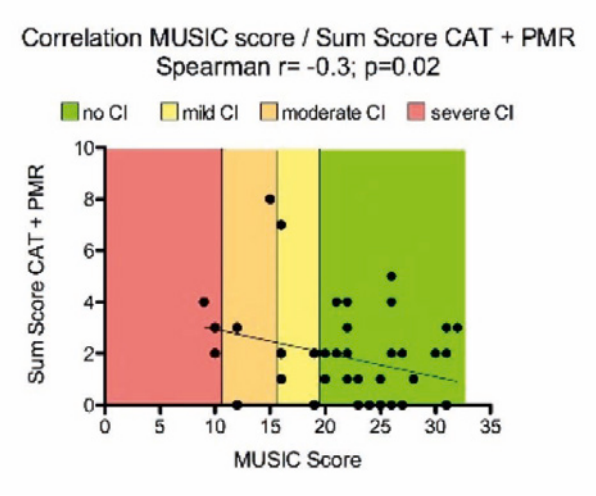

Figure 1

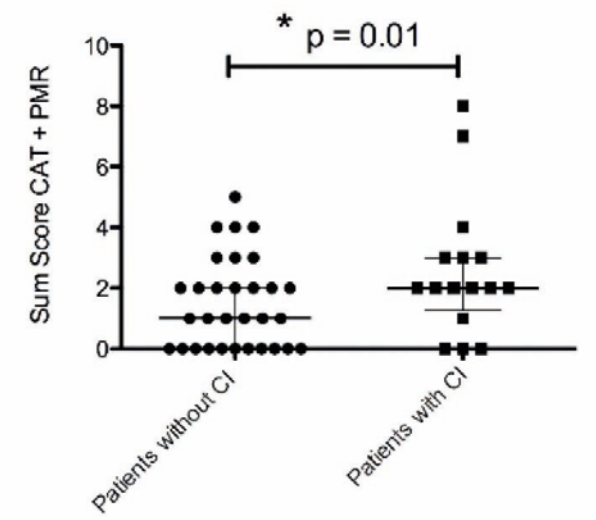

Figure 2

Conclusion: CAT and PMR might be useful clinical screening tests for the detection of CI in MS patients.
Disclosure: Nothing to disclose

EPO1089

Interim analysis of the non-interventional study COPTIVITY assessing the alteration of activity in ambulatory patients with relapsing MS treated with COPAXONE® 40 mg tiw.

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Background and aims: Real-world (RW) data on effectiveness, tolerability and patient-reported outcomes (PRO) of newly approved disease-modifying therapies (DMTs) are missing and gaining increasing importance in the rapidly changing treatment landscape in Multiple Sclerosis (MS). Such data are not available for newer DMTs including Copaxone® 40mg tiw (glatiramer acetate (GA) 40mg tiw) and RW evidence on effectiveness after switching from other DMTs are needed. Here, we describe the efficacy and safety profile of ambulatory MS patients treated with GA 40 mg tiw.
Methods: The ongoing two-year non-interventional study was performed to evaluate traditional clinical endpoints such as annual relapse rate (ARR), Expanded Disability Severity Score (EDSS) and emerging endpoints like Fatigue, Cognition, patient reported neurological disability, work productivity, and treatment satisfaction of patients treated with both formulations of GA. Only patients with documentation of GA dosage were included.
Results: 687 MS (86.9% RRMS and 8.0% CIS) patients (80.6% female), mean age 38.0± 10.8 years with a disease duration 4.6 ±6.6 year. 48.3% of patients were pre-treated with GA 20 mg/ml, 35.4% were de-novo and 15.3% switched from other DMTs. The ARR decreased significantly from 0.76 ±0.0.71 to 0.33 ±1.0, the EDSS score was stable (Baseline 2.00 ±1.4 vs 1.9 ±1.4) and significant improvement of the information processing scores (SDMT) and patient reported disability (UKNDS) was observed. All other parameters were stabilized at data cut-off.
Conclusion: The results provide real-world confirmation on effectiveness, tolerability and safety of Copaxone® 40mg tiw including aspects of cognitive performance and positive outcome on PRO.
Disclosure: Tjalf Ziemssen has received reimbursements for participation in scientific advisory boards from Bayer Healthcare, Biogen Idec, Novartis Pharma AG, Merck Serono, Teva, Genzyme, and Synthon. He has also received speaker honorarium from Bayer Healthcare, Biogen Idec, Genzyme, Merck Sharp & Dohme, GlaxoSmithKline, Novartis Pharma AG, Teva, Sanofi Aventis, and Almirall. U. Schulze-Topphoff and D. Fendji are employees of TEVA GmbH, Germany.

MS and related disorders 2

EPO1078

Measuring burden in informal caregivers of patients with multiple sclerosis: the psychometric properties of the CSI questionnaire

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Background and aims: The Caregiver Strain Index (CSI) is a brief self-assessment tool for measuring the caregivers' perceived level of burden. Limited information is available on the psychometric performance of the CSI in multiple sclerosis (MS). The aim of the study was to assess the factor structure and construct validity of the CSI.
Methods: A multicentre, cross-sectional study in patients with relapsing-remitting and primary progressive MS (McDonald 2010 criteria) was conducted.
Results: A total of 72 caregivers of a sample of 201 patients (86% with relapsing-remitting MS and a median EDSS score: 2.0 [IRQ: 1.0-3.5]) were studied. The prevalence of a high level of strain was 23.6% (n=17). CSI presented good reliability (Cronbach's alpha=0.84, 95% CI=0.79 to 0.89). According to Mokken analysis, CSI represented a unidimensional construct of caregiver burden although 2 of the total 13 items (#1 and #13) could not be assigned to any factor by an automatic item selection procedure. Without these items, the scalability of the CSI moved from a weak (Hi=0.37) to a medium scale (Hi=0.44). However, the item characteristic curve (ICC) of the Rasch model (including both odd items) showed a range of appropriate difficulty and the item and person parameters presented good fit (Andersen LRT=18.40, df=11; p-value=0.07; all item values for the infit).
Conclusion: Understanding strain among informal caregivers of patients with MS may be useful to identify people who would benefit from a more comprehensive support. CSI may constitute a valuable addition to measure caregiver burden in a clinical setting.
Disclosure: This study was funded by the Medical Department of Roche Farma Spain. Daniel Prefasi and Jorge Maurino are employees of Roche Farma Spain.

EPO1090

Impaired glucose tolerance in patients with multiple sclerosis: a pilot study

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Objectives: There are limited data regarding glucose metabolism dysregulation in multiple sclerosis (MS). The aim of this pilot study was to investigate the frequency of impaired glucose tolerance (IGT) using a two-hour oral glucose tolerance test (OGTT) in a cohort of MS patients.
Methods: Methods: Included in the study were 31 MS patients (24 relapsing-remitting and 7 chronic progressive, median Expanded Disability Status Scale-EDSS score 2.5) from Clinical Center of Serbia, Belgrade, diagnosed according to the McDonald criteria and age 18 years and above, and 24 healthy controls (HC) matched for age, gender, and body mass index (BMI). An OGTT (1 g glucose/kg body weight), including determination of blood glucose and serum insulin levels, was performed to investigate glucose tolerance. Glucose and insulin responses were expressed as the total areas under the curve (tAUC).
Results: Plasma glucose concentrations of MS patients were significantly higher at multiple time points during OGTT ($p<0.05$). Two MS patients demonstrated elevated fasting plasma glucose concentrations compared to none of the HC ($p=0.299$). In addition, 16.1% of MS patients and none of HC showed IGT ($p=0.039$). Accordingly, both glucose tAUC and insulin tAUC were significantly higher in MS patients compared to HC ($p<0.05$). The areas under the glucose and insulin curves were similar in patients with different MS phenotypes and levels of disability, measured by EDSS.
Conclusion: The results of our pilot study showed an elevated frequency of IGT in MS patients. Further investigations in the larger cohorts of MS patients are warranted.
Disclosure: Nothing to disclose

EPO1091

INSPIRATION: An approach to brain volume and quantitative lesion load assessments from standardized MRI acquisition in daily clinical routine of MS patients.

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Background and aims: In Multiple Sclerosis, common standards and quantitative analysis of MRI scans has mainly been realized in clinical trials. In addition, common standards in MRI acquisition are largely not applied in routine practice. Tools for quantitative data analysis do exist, but are not widely available. INSPIRATION is a non-interventional study, conducted in Germany, to validate the feasibility and explore the potential benefit of standardized MRI acquisition and quantitative MRI reading in clinical practice.
Methods: INSPIRATION included 253 patients. MRI and clinical data were documented over 3 years. Sites underwent expert training and standardized sequence implementation. A centralized quantitative MRI data analysis was performed. The results were visualized and reported to the neurologist and radiologist.
Results: 99.6% of the data sets obtained from 510 data transfers passed the quality analysis. <0.03% of cases led to site inquiries or data exclusion. The mean number (±SD)/ml volume (±SD) of T2 lesions at baseline was 30.1 (±2.8)/11,033.1 (±1,578.9) and black holes 4.0 (±0.9)/490.3 (±136.6). After 12 months follow-up the mean number and volume of T2 lesions was 32.3(±3.6)/11,479.9(±1927.5) and of black holes 4.1(±1.1)/488.9(±165.2). Whole brain volume at baseline was 1,142,397(±15,988) mm^3. Brain volume reduction after 12 months was 3,231±1,944 mm^3 (0.28±0.1%). Here we present follow up data 36 months after baseline.
Conclusion: A centralized quantitative MRI-analysis is provided in a real-world situation and might improve the comparability of MRI scans in daily clinical routine. The quantification of lesion volumes and visualization of MRI abnormalities may facilitate MRI data integration by the responsible neurologist to support patient management.
Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany

EPO1092

Dimethyl Fumarate demonstrates Cost-effectiveness vs Teriflunomide in Treatment-naïve Patients with Relapsing-remitting Multiple Sclerosis in Sweden

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Background and aims: Dimethyl fumarate (DMF), oral 240mg twice daily, and teriflunomide (TER), oral 14mg once daily, are first-line standard of care oral disease-modifying therapies for relapsing-remitting multiple sclerosis (RRMS) in Sweden. A cost-utility analysis was conducted to assess the health economic impact of DMF versus TER for RRMS from the Swedish societal perspective.
Methods: A cohort-based Markov model simulated treatment-naïve patients' disease progression over 50 years through a series of health states based on the Expanded Disability Status Scale (EDSS). Over time, patients could also experience relapses or progress to secondary-progressive MS (SPMS). Natural history for EDSS progression was obtained from the placebo arms of the CONFIRM and DEFINE studies and extrapolated with data from the British Columbia database. Relapse rates were based on a population-based MS survey. A network meta-analysis provided treatment efficacy inputs for disease progression and relapses. Public databases and literature provided cost data for: direct and indirect disease management, relapses, direct treatment-related attributes, and adverse events. All utility-related inputs were acquired from the literature including: patient and caregiver utilities, for patient EDSS; and relapse and adverse event disutilities. Costs and health outcomes were discounted at 3.0% per year.
Results: DMF yielded greater clinical benefits (0.86 additional quality-adjusted life years [QALYs]) and cost savings (642,573kr; approximately €65,044) over 50 years compared with TER (ie. DMF dominated). Results were robust across a wide range of one-way and probabilistic sensitivity analyses.
Conclusion: DMF is a cost-effective treatment for treatment-naïve patients with RRMS in Sweden, delivering cost savings and improved health outcomes compared with TER.
Disclosure: Study Funding: Biogen

EPO1093

The Rao's Brief Repeatable Battery (BRB): Normative values corrected for age, education and gender in an Italian pediatric population.

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Background and aims: The Brief Repeatable Battery (BRB) is the most used tool to estimate cognitive dysfunction in patients with multiple sclerosis (MS). However, the availability of normative data in pediatric population currently limits its applicability.
Methods: We administered the BRB version A to healthy subjects aged 14 to 17. All the subjects underwent the complete BRB. When a significant relationship between test scores and age, gender and education was found, the regression coefficients were used to adjust raw data. 5°percentile of corrected score for each test was used as cut-off for pathological performances.
Results: We included 76 subjects (45 females) with a mean age at baseline of 15.8±1.6 years, and a mean education of 10.6±1.5 years. Raw scores of neuropsychological tests for the BRB are shown in Table 1. Table 3 shows the mean scores and cut-off values for the BRB tests after correcting for relevant demographic factors.

Table 1.

Test	Meand Score (SD)
SRT-LTS	52,95 (±9,87)
SRT-CLTR	44,84 (±12,41)
SRT-D	9,868 (±1,87)
SPART	24,29 (±4,56)
SPART-D	8,763 (±1,82)
SDMT	59,8 (±11,21)
PASAT 3	43,42 (±10,33)
PASAT 2	35,83 (±10,85)
WLG	21,33 (±4,74)

Table 1

Table 3.

Test	Mean Score (SD)	Percentile 5%
SRT-LTS	50,65(9,54)	35,38
SRT-CLTR	41,13(12,21)	19,93
SRT-D	9,37(1,77)	6,76
SPART	20,90(4,35)	14,36
SPART-D	7,36(1,75)	3,99
SDMT	55,59(10,99)	38,13
PASAT 3	40,35(9,73)	24,27
PASAT 2	30,76(9,68)	15,80
WLG	19,69(4,11)	13,57

Table 3

Conclusion: Compared to adults, in younger subject, education can only predict verbal memory, whereas other functions are mainly predicted by age and gender. This could reflect the lower educational level of juvenile subjects (max 13 years) or the low inter-sample variability due to mandatory school attendance. Moreover, we found that the calculated cut-offs for each BRB test were generally higher than those calculated for adults, as in previous reports, apart from verbal fluency, that we could speculate to be linked to higher education and social stimulation in adults life.
Disclosure: Nothing to disclose

EPO1094

A SCA7 premutation suggested to influence the course of MS. A case report.

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Background and aims: While MS has a polygenic background, mutations pathogenic for monogenic disorders may augment symptoms from specific systems in MS patients, as reported for hereditary spastic paraparesis (HSP), and Leber's mutations. To discuss the notion that mutations which should be unable, in themselves, to produce symptoms may nevertheless influence the manifestations of MS, we here present the case history of an MS patient carrying a premutation for SCA7.
Methods: The diagnosis of primary progressive MS was based on polyfocality, characteristic MRI findings including periventricular right angle lesions, and an intrathecal olicoclonal IgG reaction, in accordance with the 2017 revisions of the McDonald criteria. The CAG trinucleotide expansion was examined using a PCR based diagnostic analysis for SCA7, showing an expansion in his ATXN7 gene with 29 CAG repeats, in the range of mutable normal alleles not expected to influence the phenotype.
Results: The patient's father died from MS dominated by a central paraparesis. With insidious onset at age 15 the patient developed a cerebellar tetraataxia which soon became debilitating, and a severe visual deficit. From age 20 a progressive paraparesis dominated the deficit. At age 45 he has an expanded disability status scale (EDSS) of 9.5. Features indicating MS (rather than SCA) lesions were oscillopia (not slow sackades), optic atrophy (not retinopathy), and the partial remission of ataxia coincident with paraparesis.
Conclusion: We suggest that the SCA7 premutation explains the extremely atypical onset of devastating cerebellar ataxia at age 15, a feature never observed in an MS incidence cohort of 308 patients.
Disclosure: Nothing to disclose

EPO1095

Machine-learning approach identifies a pattern of alterations that can discriminate Relapsing-Remitting Multiple Sclerosis Patients and Healthy Controls using pupillary response characteristics measured by pupillometry

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Background and aims: One of the most common symptoms of MS is optic neuritis, which can cause relative afferent pupillary defect. The objective of this study was to identify major features of pupillary light response by using machine learning technique which enables us to discriminate healthy cases from patients and, thereby, to realize the value of manual quantitative pupillometry for assessing relative afferent pupillary defects (RAPD) in Relapsing-Remitting Multiple Sclerosis (RRMS) patients
Methods: In the cohort of 182 RRMS patients, pupillometry parameters of 100 randomly selected subjects equal to the size of healthy control were included in this study.We have used six base learners including Linear SVM, Poly SVM, Radial SVM, random forest, decision tree and Cart tree. Majority voting on the base learners' decisions has been used to make the final decision about each sample. This ensemble learning method, achieved the sensitivity, specificity, and accuracy of 0.85, 0.78, and 0.77, respectively in a 10*10-fold cross-validation procedure.
Results: Among all pupillary response features Constriction Velocity (CV), Maximum of Constriction Velocity (MCV), Dilation Velocity (DV), Latency and discrepancy between two eyes in neurological pupil index (Npi), DV, and MCV were more discriminative than other features according to the calculated feature importance.
Conclusion: We observed that applying machine learning technique to pupillometry data has potential to yield better discrimination of group differences. In conclusion, with this innovative approach pupillary response features of pupil reflex velocity and initial latency are altered significantly under the course of MS.
Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 1

EPO1096

Collagen VI-Related Myopathy: A mutation of COL6A3 gene

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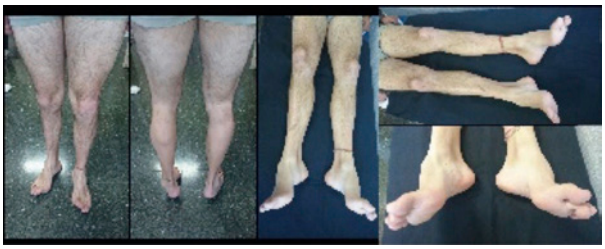
Background and aims: Mutations in collagen VI-related genes cause collagen VI-related myopathies, which cover a broad clinical spectrum. We are exposing a case report of a patient who presents Collagen VI-related myopathy.
Methods: When our patient was nine years old, presented elevation of creatine-kinase levels. When he was thirteen, he was diagnosed facioscapulohumeral dystrophy because he presented muscular atrophy in scapular and peroneal girdles, mild dorsal scoliosis and pes cavus. When he was twenty he experimented muscle fatigue and some difficulty climbing stairs (now incapability for climbing three floors).
Results: In the neurologic examination, we detected bilateral pes cavus, weakness in psoas-iliac(4+/5), knee flexors(4+/5), tibialis anterior(4-/5) and peroneus(3/5); tibialis anterior atrophy; upper limbs and patellar hyporeflexia; walking tiptoes was very difficult and walking on heels was impossible.
The creatine-kinase levels were 1973 IU/L. Lysosomal acid alpha-glucosidase and Emery-Dreifuss and Miyoshi genetic tests were normal.
Electroneurogram was normal. In electromyography, we detected myopathic pattern in quadriceps and neurogenic pattern in tibialis anterior and gastrocnemius.
In genetic tests, we detected c.7447A>G variant in homozygosis in COL6A3 gene. This was present in homozygosis in a diseased brother. In his healthy parents and one brother, we found it in heterozygosis.



Legs photographs of our patient.

Conclusion: The mutations in the COL6A3 gene cause collagen VI-related myopathy with the same neuromuscular clinic that our patient presents.
C.7447A>G variant detected in homozygosis in our patient has been reported in the literature in compound heterozygosity in a patient with attenuated collagen VI-related myopathy. The residue is very conserved and the bioinformatic study suggests it is pathogenic.
Disclosure: Nothing to disclose

EPO1097

Baseline Characteristics and Disease Burden in the Myasthenia Gravis Foundation of America (MGFA) Registry

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Background and aims: The MGFA Registry is a large, US-based, voluntary, patient-driven, online database of persons diagnosed with myasthenia gravis (MG) initiated in 2013. The goal of the Registry is to improve understanding of patient care and disease impact on daily living. Disease burden assessment in this large cohort of patients has not previously been reported.

Methods: Cross-sectional analyses included all available records (n=1140) with data on MG-ADL or MG-QOL15 as of 7/2017, two validated scales assessing health-related quality of life in MG, at baseline entry into the Registry.

Results: Mean age was 54.6 years, 66.2% were female, and 80.4% Caucasian. The majority of patients reported moderate to severe impairment in their activities of daily living and health-related quality of life as indicated by a median MG-ADL score of 6 (range 0-21) [Figure 1] and a median MG-QOL15 score of 21 (range 0-60) [Figure 2]. There was good correlation between these measures (r=0.778, p<0.001).

71% of patients reported currently receiving pyridostigmine; 42% corticosteroids; 24% mycophenolate mofetil; 19% azathioprine; 19% intravenous immunoglobulin (IvIg); and 4% plasma exchange. Prior therapies included corticosteroids (36%); IvIg (28%); and plasma exchange (26%). Few patients (<5-10%) reported ever receiving other treatments, although around 40% were unsure whether they had received any of these rarely used therapies [Figure 3]. 40% had undergone thymectomy.

Conclusion: While a disease registry may attract somewhat sicker patients, these data nevertheless highlight that, contrary to common belief, MG remains a disease that negatively impacts the health-related quality of life of many patients despite symptomatic and immunosuppressive therapies.

Figure 1

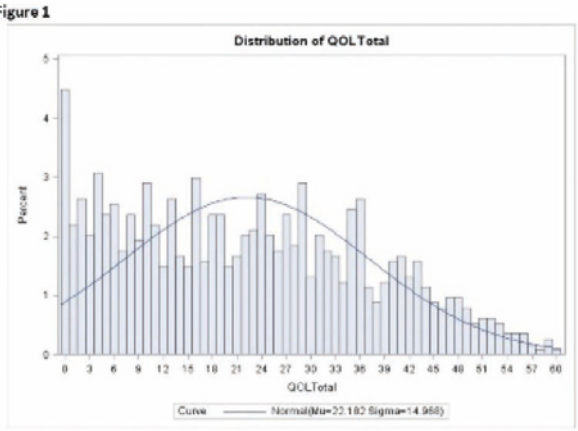


Figure 2

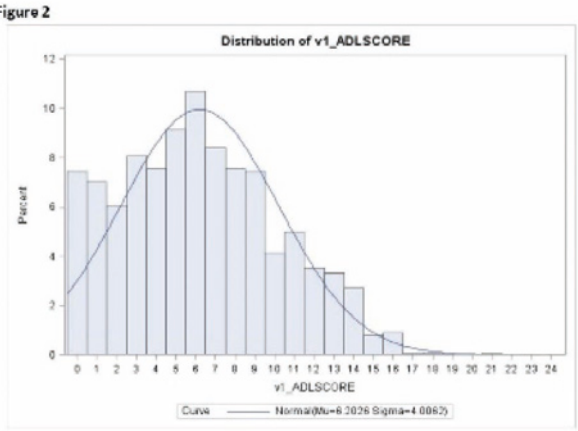
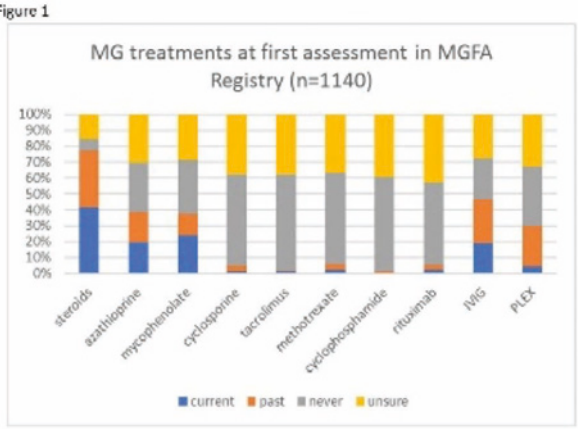


Figure 1



Disclosure: This analysis was supported by a research grant from Ra Pharmaceuticals, Inc.

EPO1098

Effectiveness of treatment based on the simultaneous administration of pyridostigmine, prednisolone, calcineurin inhibitor, and intravenous immunoglobulin (PPCI therapy) in patients with myasthenia gravis

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Background and aims: Intravenous immunoglobulin therapy (IVIG) is recommended in patients with myasthenia gravis (MG) during acute exacerbations. However, according to existing reports, it takes about one week before the full effects of IVIG are achieved. Recently, we preferentially and simultaneously administered pyridostigmine (cholinesterase inhibitor: ChEI), prednisolone (PSL), a calcineurin inhibitor (CNI), and IVIG to patients with MG receiving the initial treatment (PPCI therapy). We evaluated the daily therapeutic effects of PPCI therapy using the quantitative myasthenia gravis (QMG) score.

Methods: Twenty patients in our hospital who were receiving PPCI therapy were evaluated. MG symptoms were reviewed using the daily consecutive QMG scores, starting just before the onset of PPCI therapy and continuing through the 15th day of therapy. We performed a retrospective analysis, assessing MG symptoms via daily QMG scores and the MG-ADL (ADL=activities of daily living) scale.

Results: The mean QMG score in this group of patients was 12.55±4.64 before IVIG, decreased significantly to 10.3±5.14 on the third day of the IVIG therapy (p=0.001), and then decreased further to 8.2±4.35 on the 15th day of therapy.

Conclusion: Patients with MG receiving PPCI therapy may experience therapeutic effects more quickly and more vigorously when compared to currently existing treatments. The addition of IVIG may improve the quality of life in patients with MG.

Disclosure: Nothing to disclose

EPO1099

ANO5 mutations in a Portuguese limb girdle muscular dystrophy population – A case series

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Background and aims: The limb-girdle muscular dystrophies (LGMDs) are a group of disorders with wide genetic and clinical heterogeneity. The LGMD-2L is an autosomal recessive subtype LGMD due to mutations in ANO5 gene. We aim to describe the clinical, pathological and molecular features of patients, diagnosed between 2004 and 2017, at our center with ANO5 mutations.

Methods: We obtained retrospective data from clinical history, neurological examination, blood workup, biopsy and genetic study.

Results: A total of 9 patients were included, all male and Caucasian. Parental consanguinity was documented in just one patient and family history of similar neuromuscular affection was described in 6 patients. Mean age of symptom onset was 59.44(SD=18.86) years. 4 patients (44.4%) presented initially with isolated hyperCKemia, 3(33.3%) with a Miyoshi distal myopathy(MDM), and 2 with LGMD (22.2%) phenotype.

During follow-up, all the patients that initially presented an MDM phenotype progressed to a mixed phenotype. All remaining patients did not change phenotype during follow-up. Gait autonomy loss was described in just one case. Dystrophic changes on muscular biopsy were described in 5 patients. Mean highest CK value was 3198.44(SD=2013.62) mg/dL. The mutation c.191.dupA was the most frequent, present in 7 patients.

Conclusion: These findings are in line with the previously described in the literature, despite the discrepancy regarding the main presenting phenotype. This case series helps to further characterize a rare disorder in our country and reinforces the clinical value of novel molecular diagnostic tools in the face of an overlapping and heterogeneous disorder.

Disclosure: Nothing to disclose

EPO1100

A novel c.2717G>C benign polymorphism of SCN4A gene responsible of severe myotonia in a family with myotonic dystrophy type 2: a precision medicine approach

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Background and aims: Myotonia is mild and inconsistent in myotonic dystrophy type 2 (DM2) and it is related with CLCN1 alternative splicing deregulation. Mutations in CLCN1 and SCN4A can act as modifier genes in these patients leading to an intensification of myotonia. Recently, a 32 years old DM2 patient with an early severe myotonia since he was 12 came to our Neuromuscular Center. Mexiletine treatment resulted ineffective. No mutation was found on CLCN1, but SCN4A gene showed a c.2717G>C base exchange, a variant considered a benign polymorphism. In his mother, affected by DM2 but without the polymorphism, no clinical myotonia was observed.
Methods: The biophysical alterations of the polymorphism was studied in combination with DM2 mutation in muscle cells from the proband and his mother. Patch clamp in voltage and in current clamp mode was used for electrophysiological recordings.
Results: Myoblasts showed no change in the steady state activation properties, but a significant shift in the availability curve (V1/2 -73.9±1.3 mV n=8 and V1/2 -78.8±1,0 mV n=9 proband and mother respectively). No differences were found in the recovery from the fast inactivation. In myotubes, the minimum current necessary to elicit an action potential was lower in the proband than in his mother (352.4±80.7 pA n=59 and 578.6±134.1 pA n=57 respectively).
Conclusion: SCN4A polymorphism induces a more excitable substrate potentially aggravating the effect of the DM2 mutations in our proband. When phenotype is uncommon, additional genes and/or modifying factors need to be explored to account for the phenotype and for the identification of appropriate drug treatment.
Disclosure: Nothing to disclose

EPO1101

Myasthenia Gravis in octogenarians and beyond: What is the difference? A tertiary hospital experience

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Background and aims: Myasthenia gravis (MG) is a treatable autoimmune disorder affecting patients of all ages. It is uncertain whether age affects clinical profile of the disease and/or its management.
Methods: Retrospective analysis of Neurology admissions (2011-2017) with diagnosis of MG. Patients were assigned to MG-elderly (MG-E) group if ≥80 years and to MG-non elderly (MG-NE) if <80.
Results: 87 admissions were included (61% female, 64 ±20 years), 71% of patients in MG-NE and 29% in MG-E group. 48% of MG-NE and 38% of MG-E had a previous MG diagnosis. There were no significant differences between groups on symptoms duration, clinical involvement (15% ocular in both, bulbar in 61% MG-NE vs. 73% in MG-E, respiratory in 28% vs. 31%, generalized in 85% vs. 88%). Myasthenia Crisis occurred in similar proportion (51% vs. 58%) and acute treatment was similar (steroids >96% in both, gammaglobulin in 44% vs. 54%, intensive care in 13% vs. 11%), without fatal cases. Upon discharge, Acetylcholine esterase inhibitors and steroids were scheduled in 96% in both groups, but immunosuppressants were prescribed more in MG-NE (36% vs. 19%, p: 0.03). Thymoma was less frequent in MG-E group (0% vs. 36%, p<0.0003) and anti-striatal muscle (SM) antibodies positivity higher (77% vs 44%, p:0.0051), without differences in other serological markers.
Conclusion: We ascertained differences on thymoma frequency and anti-SM antibodies positivity in elderly patients with MG, which might relate to a different underlying mechanism of disease. MG-E patients benefited from the same acute therapies and shared the same good prognosis as younger ones.
Disclosure: Nothing to disclose

EPO1102

Myopathies acutely admitted to the adult intensive care unit – a single centre case series.

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Background and aims: We present a series of patients acutely admitted to the adult ICU in whom a previously undiagnosed primary muscle disease was found to be the underlying diagnosis, and investigated whether the outcomes justified a decision to provide invasive intensive care.
Outcomes of intensive care myopathy-single centre.
Methods: We studied patients admitted directly to intensive care at our institution in whom a primary myopathy was newly diagnosed and considered to be the underlying cause for admission. The diagnosis was established either through muscle biopsy or genetic analysis. Clinical course and outcomes were analysed retrospectively from case notes or follow up examination.
Results: 14 patients were identified between 2012 through 2017 in whom a specific diagnosis of myopathy was established during their ICU stay. The reason for admission was respiratory (n=9), cardiac (n=4), or renal failure (n=1). The diagnosis was established histologically in 11 patients and genetically in 3. 4 patients stayed in ICU for <7 days, and 4 >50 days. 12 patients required ventilatory support. 2 patients had heart transplants. 11 were discharged home or transferred to a rehabilitation unit. All survivors regained their previous functional status except 1 patient with a tracheostoma for dysphagia.
Conclusion: Chronic, unrecognised myopathies can present with an acute admission to the ICU. Intensive care in these patients is complex, but most return to their baseline function even after a prolonged stay. This study underlines the feasibility of advanced intensive care in patients with severe degenerative muscle disease.
Disclosure: Nothing to disclose

EPO1103

Treatment and follow-up of late onset myasthenia gravis

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Background and aims: An increasing incidence of myasthenia gravis (MG) has been reported in the elderly. Treatment decisions may be especially complicated at this age, because of comorbidities and higher risk of iatrogenicity. We aim to describe our cohort of patients with late onset MG (LOMG) with an emphasis on treatment regimen, its efficacy and complications.
Methods: Retrospective analysis of medical records of a cohort of patients followed in a Portuguese tertiary centre. LOMG is defined herein as disease onset after the age of 50 and no clinical evidence of thymoma.
Results: Of 192 myasthenic patients, we identified 39 cases with LOMG (20.3%). Age at onset ranged from 50 to 81 years (median=70) and 61.5% were man. Nineteen patients (48.7%) had generalized disease and anti-AChR antibodies were positive in 64.1%. Almost all received pyridostigmine (35/39;89.7%). At some time, 28 patients (71.8%) required prednisolone (average maximum daily dose=21mg) and 17 (43.6%) immunosuppressive therapy (AZA, MMF or MTX). Intravenous immunoglobulins were used in 8 patients and only one needed ventilatory support. Treatment complications included diabetes (1), cataract (2), elevated liver enzymes (2), infections (2), tumours (4), cytopenia (3), vertebral fracture (1) and hypertension (2). Nineteen patients had mild (4) or significant (15) improvement, 3 are in complete remission, 13 in pharmacological remission and 4 had no change.
Conclusion: In our series, the prognosis of MG in older people seems to be favorable, with a good rate of improvement and remission, although most patients required corticosteroids/immunosuppressants. Treatment was overall well tolerated, but side effects are still a concern.
Disclosure: Nothing to disclose

EPO1104

Atypical desminopathy with new mutation and autosomal recessive transmission

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Background and aims: Desminapathies may manifest different clinical profiles, ages of presentation and even different types of inheritance. We aim to report a family with desmin myopathy with an atypical phenotype and recesive transmission.
Methods: A 14-year-old male patient was attendeded in our clinic presenting myalgia, exercise intolerance and serum creatinine kinase (CK) levels m around 1000 IU/L; his middle sister has the same symptomatology and an older brother was healthy. Their parents were consaguineous.
Results: A non-invasive hyperCKemias protocol was applied, including Pompe DBS and MLPA DYS that were normal. MRI presentented a pattern of local muscle involvement (soleus, gastronemius and semitendinosus (grade 1) and paravertebral (grade 2)). Cardiac investigation were normal. Muscle biopsy presents a dystrophic profile with vacuoles. In successive years he developed mild palpebral ptosis and minimal facial, scapular and axial weakness (4-). A NGS genetic study with 40 genes detected a not described homozygous DES gene variant (c.1372-1G> A). The mutation segregated with a recessive pattern in the family study. Myofibrillar protein markers were abnormal, highlighting Desmin accumulations. Currently both siblings have similar manifestations at 22 and 28 years of age.
Conclusion: We describe a new pathological variant in the DES gene (c.1372-1G> A) with AR transmission causing a desminopathy that presents as paucisintomatic HCK and evolved with an atypical phenotype of palpebral ptosis and facial scapular weaknesss.
Disclosure: Nothing to disclose

EPO1105

Clinical, pathological and molecular characterization of a Limb-girdle muscular dystrophy type 2I (LGMD-2I) cohort

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Background and aims: LGMDs are rare hereditary muscular diseases with a wide clinical and genetic variability. The autosomal recessive account for 90% of cases and the subtype LGMD-2I (FKRP gene) is the third most common. Studies regarding clinical and molecular characterization of this subpopulation are sparse.
Methods: Retrospective analysis of the clinical, pathological and molecular findings of patients with LGMD-2I diagnosed at our center in CHUC between 2004-2017.
Results: We report 8 patients (mean age 45.9yo, 37% female) with a mean follow-up time of 18.9y. Parental consanguinity was identified in 75% of cases. The mean age at onset of symptoms was 15.1yo. Seven patients underwent muscle biopsy, with a mean interval between it and the first symptoms of 8.3y. The biopsy revealed a dystrophic pattern in 57% of the cases and immunohistochemistry was normal in all. The mean time between molecular diagnosis and symptom onset was 16y. The most frequent mutation identified was g.826C> A (87.5% of cases). At the first assessment, 75% of patients presented with LGMD phenotype and the remaining with an isolated hyperckemia. During follow-up, 62.5% of the patients presented a restrictive respiratory pattern and 37.5% developed dilated cardiomyopathy. The mean time till autonomy gait loss was 36y and the mean CK concentration was 4382 mg/dL.
Conclusion: The clinical characterization of LGMD subtypes is of major importance to increase the information on the progression and clinical characteristics of each of these conditions. It is of utmost importance in optimizing the multidisciplinary care that these patients require.
Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EPO1106

Peculiarities of associations between the neurological status, EEG parameters, and hepatic morphofunctional changes in Wilson's disease

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Background and aims: Unlike other hepatic encephalopathies, in Wilson's disease (WD) its neurological manifestations and impairments of brain functional conditions result both from liver damage and from accumulation of copper in brain, an acute elevation of serum copper levels, and iatrogenic effects.
Methods: During 2012-2017, 40 patients (mean age 24.23±1.90 years old) with WD (E83.01) were evaluated regularly for their neurological status (with the Unified Wilson's Disease Rating Scale (UWDRS)), EEG parameters (indices, powers, ratios), and hepatic morphofunctional changes (liver parenchyma stiffness (LPS)).
Results: Dynamically some patients had changes on EEG with unchanged LPS parameters, whereas other patients had signs of deterioration/improvement of liver morphofunctional conditions, which were not reflected in EEG parameters. Moreover, patients with a poor outcome (7 persons) had a various degrees of hepatic damages, but similar EEG changes. Correlation between LPS and delta/alpha-ratio was not found (r=-0.002), but delta/alpha-ratio correlated with UWDRS scores (r=0.40). Similarly, UWDRS scores demonstrated stronger than LPS correlation with alpha-index (r=-0.397 vs r=-0.049), power of alpha-activity (r=-0.491 vs r=-0.193), and a specific power (r=-0.453 vs r=-0.226). There was a weak correlation between UWDRS scores and LPS (r=0.32).
Conclusion: In WD, a close association between hepatic morphofunctional changes and EEG changes was characteristic only for the WD hepatic form; for other WD forms, this association was complex, as poor outcomes can be occurred not only in cirrhosis, but in initial stages of liver fibrosis. The LPS median value in WD was not a reliable classifier of EEG changes and a marker of neurological manifestations.
Disclosure: Nothing to disclose

EPO1108

Neuropsychiatric Manifestations of adult-onset Rheumatoid Arthritis

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Background and aims: Rheumatoid arthritis (RA) is an autoimmune disease that mainly affects synovial joints but also has an impact on other organ systems. Neuropsychiatric manifestations (NP) are quite common in RA, involving both the central and peripheral nervous system.
Methods: We performed complete rheumatological and neurological evaluation using ACR- EULAR 2010 Classification Criteria, DAS28, Health Assessment Questionnaire-Disability Index (HAQ-DI). Immunological blood tests include RF, Anti-CCP, Anti-MCV, we also performed lumbar puncture, vascular biopsy, neuropsychological testing, Doppler sonography, EMG and EEG, brain MRI/CT.
Results: A total of 150 patients were observed in the period of 2 years /2015-2017/-85 female, (57%), 65 men (43%). NP manifestations include: brain involvement, depression, anxiety, cognitive dysfunction, headache, seizures, cerebrovascular disease, cranial nerve involvement, movement disorders such as Parkinson's disease, atlantoaxial subluxiation, acute myelitis, compressive neuropathy, mononeuritis multiplex and polyneuropathy.
Conclusion: About 70% of patients with RA present with NP manifestations. Potential causes include systemic inflammatory process, neural compression due to bone and joint destruction, side effects of medications. There is a high correlation between the presence of neuropsychiatric symptoms and disease activity, disease duration and treament with DMARDs, corticosteroids or biologics.
Disclosure: Nothing to disclose

EPO1109

Developing a framework to optimise the ongoing assessment of ATTR-amyloidosis

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Background and aims: Transthyretin-related amyloidosis (ATTR) presents in many different forms and with considerable variation in signs and symptoms and across geographic locations. There are important differences in TTR gene mutations, which in turn are associated with different phenotypes. Even within a specific gene mutation, phenotypes are not always uniform. Many diagnostic tests and investigations are not useful for adequately assessing treatment outcomes or identifying thresholds of disease progression. For optimal patient management, we must consider the changing status of a diagnosed and treated patient, and how to understand the rate of progression of disease.

Methods: A structured follow-up that targets specific signs and symptoms was proposed as an appropriate framework, within which, minimum clinical criteria for disease progression could be defined. No formalised approach had been developed to date.

It was agreed that the different phenotypes observed in clinical practice could help define two major phenotype groups:

A. V30M early-onset

B. Non-V30M and V30M late-onset

Results: Novel techniques as well as the combination of tests (composite scores) should be incorporated within the framework, along with assessment of multiple organ systems. The need to be assessed through a multi-disciplinary approach is key, with patient-reported aspects also deemed as essential components.

Conclusion: A framework outlining the recommended specific tests and investigations is proposed to facilitate in making optimal treatment decisions for physicians managing patients with this fatal, progressive disease.

Disclosure: Support provided by Pfizer Inc, and Medical writing support provided by Synergy Medical Education, UK.

EPO1110

Developing a framework to optimise the ongoing assessment of ATTR-amyloidosis in patients with a cardiac phenotype

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Background and aims: Transthyretin amyloidosis (ATTR) is a progressive, autosomal-dominant disease characterised by deposition of transthyretin-derived amyloid fibrils. Amyloid may deposit in the peripheral and autonomic nerves, as well as heart, gastrointestinal tract, kidneys, and eyes. Accordingly, disease presentation is heterogeneous and considerable variation in signs and symptoms can be observed, based on the TTR gene mutation. ATTR is categorised as a neurologic, cardiologic, or mixed phenotype.

Many tests and investigations for initial diagnosis are not useful for adequately assessing treatment outcomes or identifying thresholds of disease progression in neurological or cardiological manifestations: often due to a 'floor' or 'ceiling' effect where no further measurable change in a given parameter is possible.

Methods: A structured follow-up targeting specific signs and symptoms was proposed as an appropriate framework within which clinical criteria for disease progression could be defined. No formalised approach had been developed to date.

When considering a patient with a cardiologic phenotype, key tests and investigations that could be routinely undertaken to capture the necessary information were considered to build a framework.

Results: New techniques and the combination of tests should be incorporated within the framework, along with assessment of multiple organ systems. The need to be assessed through a multidisciplinary approach, where specialties in cardiology and neurology work closely together, should also be considered.

Conclusion: A framework for addressing cardiac phenotypes, and specific tests and investigations that should be recommended, is proposed. This will facilitate optimal treatment decisions for physicians managing patients with this fatal, progressive disease.

Disclosure: Supported by Pfizer Inc with Medical writing support provided by Synergy Medical Education, UK

EPO1111

A case of disseminated Bartonella henselae infection (cat-scratch disease) with encephalitis in an adult patient

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Background and aims: Bartonella henselae is the primary cause of Cat Scratch Disease (CSD). Bacterial infection due to Bartonella henselae commonly develops in children and young adults following cat/dog contacts and/or scratches. The disease is usually self-limited with rare serious complication. Diagnosis is usually based on serologic tests.
Methods: Here, we present a report of a patient with cat scratch disease who presented with aphasia and altered mental status secondary to encephalitis.
Results: A seventy seven years old male patient admitted to our clinic with speech impairment and confusion. In his past medical history no underlying illness was known. He had a history of respiratory tract infection that has not healed for about two months. Physical and neurological examination revealed word substitution errors, trapped aphasia, purpuric rash on the arms and right supraclavicular lymphadenomegaly. Brain MRI showed no acute changes and no contrast enhancement. The EEG findings showed doubtful hypersynchrony on the basis of widespread organization disorder in bilateral frontosentrotemporal regions. Cerebrospinal fluid tests showed normal glucose, high protein levels and 40 leukocytes. CSF viral PCR, tuberculosis tests, CSF cultures were all negative. Right supraclavicular biopsy material showed necrotizing granulomatous lymphadenitis. After antibiotic administration, the patient's symptoms and aphasia resolved. The patient had a history of contact and stratch with kittens. Bartonella henselae serology titers were IgG positive (>1:320) and IgM negative.
Conclusion: We recommend consideration of CSD in the differential diagnosis of any adult with a history of lymphadenopathy, recent contact with a cat who presents with neurological complications.
Disclosure: Nothing to disclose

EPO1112

Low level of consciousness as a debut of Macrophage Activation Syndrome

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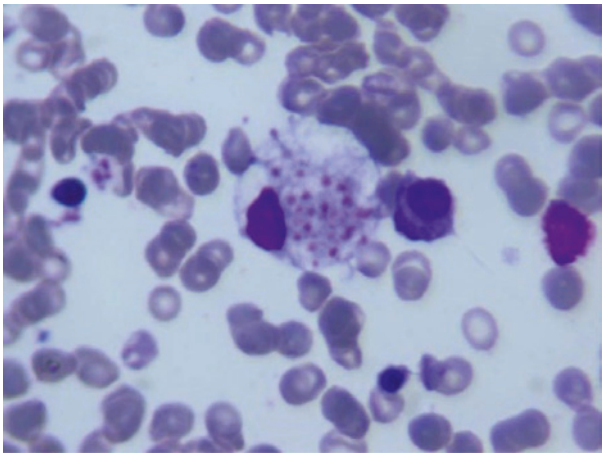
Background and aims: The syndrome of macrophage activation (SMA) is an unusual syndrome that can appear related to neoplasms, infectious diseases and autoinmune diseases. Mortality related to the syndrome is high, consequently, a high index of suspicion must be maintained and treatment mus be started early.
Methods: A 42-year-old man was studied for febrile symptoms with adenophaties and hepatosplenomegaly over 3 weeks with diagnostic suspicion of Still's disease of the adult, and stars with deterioration of the level of consciouness, tonic-clonic movements in both upper-limbs. The analysis taken the following mosninrg revealed an LDH and Triglycerids levels increased, as well as ferritin of 150,000. Lumbar puncture was performed with aseptic meningitis and an EEG that reports epileptic status, so the patient was finally intubated and admitted to the ICU.
Results: With these data, with suspicion of SMA, a FNAB of bone marrow was performed, and it confirmed the presence of hemophagocytosis in bone marrow. Inmediately treatment was initiated with Inmunoglobulins cycles as well as antiepileptic drug with clinical improvement in 3 days and complete recovery un 3 weeks after subsequent corticoid therapy.



Hemophagocytosis in bone marrow

Conclusion: SMA is a syndrome that must be suspected and treated early. It is important to consider it in all patient with systemic infection, rheumatic or haematological

disease that starts with high fever, elevation of LDH and triglycerids, and ferritin levels>1000. One third of the patients occurs with neurological symptoms (seizures, meningism, cranial nerve palsies, decreased state of consciousness, ect). The treatment of choice is corticoids at high doses, Inmunoglobulins cycles or ciclosporines.
Disclosure: Nothing to disclose

EPO1113

Erdheim-Chester Disease as a rare cause of progressive ataxia

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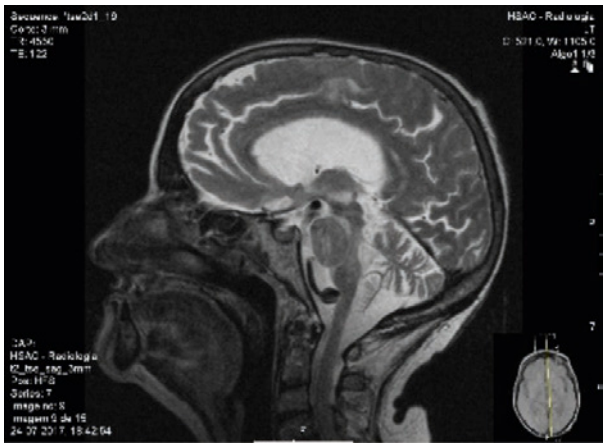
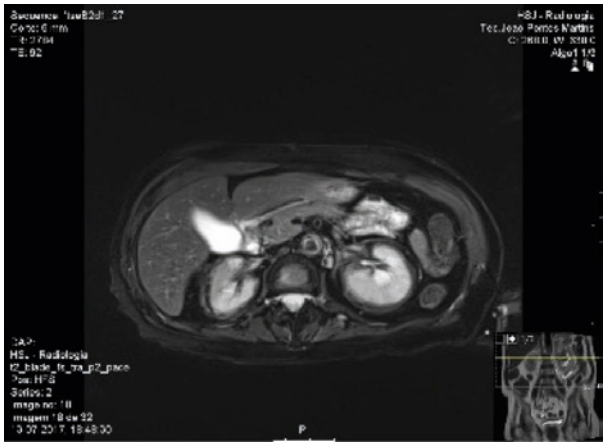
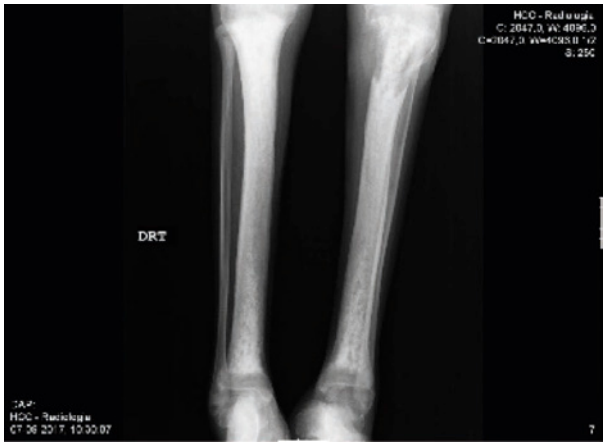
Background and aims: Erdheim-Chester disease(ECD) is a form of non-Langerhans' cell histiocytosis, with clonal proliferation of histiocytes of monocyte-macrophage descent. Skeletal involvement is pathognomonic, and presentation varies from focal to multiorganic, life-threatening disease. CNS involvement is present in half the cases and worsens prognosis.
Methods: Case Report
Results: 66-year-old female progressively developed gait ataxia and dysarthria. At first medical contact (2014), the remaining neurological and physical examination were unremarkable. Complementary exams directed at hereditary, infectious and autoimmune causes of ataxias were innocent. During the following years general and neurological status worsened, with multiple hospital admissions due to renal disease and multiple-site infections.
Echocardiogram revealed a thickened aortic wall and chest CT showed bilateral ground-glass opacities; at that time, these were considered non-specific.
In 2017, renal function and neurologic status worsened and the patient was re-admitted. Neurological examination revealed generalized hypotonia and tetraparesis, severe truncal and limb ataxia, hyperreflexia, dysarthria, dysphagia and altered ocular movements. Tibial radiographies showed bilateral diametaphyseal osteosclerosis; abdominal MRI revealed extensive retroperitoneal fibrosis with infiltration of perirenal fat. Brain MRI showed bilateral orbitary/supratentorial tumefactive lesions, T2/FLAIR hypersintensities of the mesencephalon, pons and cerebellum, generalized atrophy and diffuse white-matter disease.
Renal fascia biopsy was compatible with ECD. The patient was started on IFN-alfa and BRAF mutation study is underway.



Sagital T2



Abdominal T2



Tibial XRay

Conclusion: ECD is a rare and widely unknown disease with a variable course. CNS involvement may precede the classical skeletal signs, making ECD a complex and demanding diagnosis. We suggest adding this clinical entity to the workup of rare causes of progressive ataxia.
Disclosure: Nothing to disclose

EPO1114

A rare case of central nervous system involvement following the onset of multiplex multineuritis in an otherwise typical case of acute eosinophilic granulomatosis with polyangiitis

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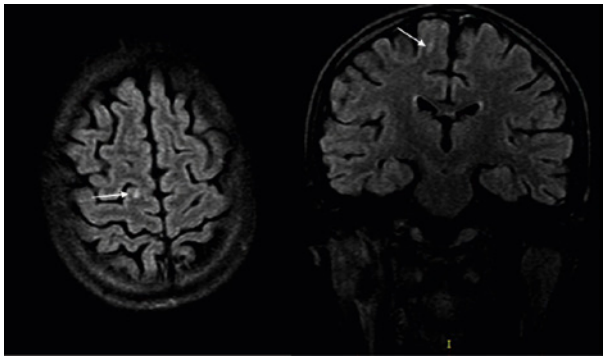
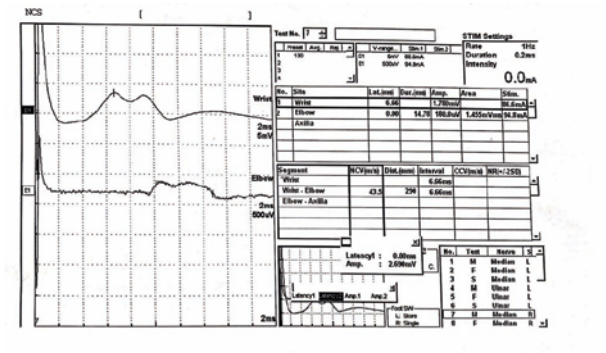
Background and aims: Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome, CSS) is a rare life-threatening immune-mediated vasculitis. In Europe, its annual incidence is less than 3.7 per million. The peripheral nervous system is affected in up to 75% of cases, while central nervous system (CNS) involvement is uncommon (8-14%). We report a rare case of acute CSS presenting with multineuritis multiplex followed by lower limb monoparesis caused by a CNS lesion.
Methods: A 31-year old man without any medical history except for the recent onset of asthma, presented with weight loss, haemorrhagic alveolitis, sinusitis, vasculitic skin lesions, intestinal ulceration, inflammatory syndrome and eosinophilia, accompanied by multiplex mononeuritis with sensory and motor symptoms. He was diagnosed with CSS and high dose methylprednisolone and cyclophosphamide were started. A few days later his neurologic condition worsened due to left lower limb paresis without other signs. Brain magnetic resonance imaging was performed, revealing a small ischemic lesion in the right precental gyrus. Ancillary investigations excluded other aetiologies. The case was compatible with small cerebral vessel vasculitis in the context of CSS, therefore no therapeutic adjustment was required.



Axial fluid-attenuation inversion recovery MR image (right) revealing small ischemic lesion located in the right precentral gyrus. Coronal fluid-attenuation inversion recovery MR image (left) showing the same lesion, oval-shaped, suggestive of perivascular localization.



Nerve conduction study graphic, which reveals decreased amplitude of muscle compound action potentials on proximal compared with distal left median nerve stimulation (conduction block) and temporal dispersion of compound muscle action potential.

Results: Cyclophosphamide was continued for 6 applications, attaining remission. Subsequently, azathioprine was started. After 1 year, the patient had complete resolution of neurological deficits and after two years, continued to be asymptomatic.
Conclusion: Sudden onset of neurological impairment in people with CSS should prompt the consideration of CNS involvement directly related or accompanying the disease. Coexisting peripheral nevritis may hinder the clinical diagnosis, therefore a high awareness index is advised.
Disclosure: Nothing to disclose

EPO1115

Acute autonomic neuropathy and Waldenstrom disease: a case report

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Background and aims: Acute idiopathic dysautonomia is an uncommon syndrome consisting of sympathetic and parasympathetic dysfunction, which can be pure or associated with sensory or sensorimotor impairment. It can be primary or associated with various diseases such as diabetes mellitus, amyloidosis, paraneoplastic syndrome and Sjögren's syndrome. The monophasic clinical course, the presence of previous infections in many cases and an albuminocytologic dissociation suggest an immuno-mediated pathogenesis similar to Guillain-Barré syndrome.
Methods: We report a case of acute autonomic and sensory neuropathy and Waldenstrom's macroglobulinemia treated with intravenous immunoglobulin (IVIg).
Results: A 42-old-year man presented with subacute autonomic dysfunction, consisting on abnormal perspiration, erectile dysfunction, urinary retention and diarrhea with loss of 17kg. He also complained of feet paresthesia.
Nerve conduction studies showed a moderate sensitive axonal neuropathy, and abnormal Sudoscan electrochemical skin conductances. Skin biopsy confirmed the loss of unmyelinated fibers. Lumbar puncture showed an albuminocytologic dissociation (proteins 81 mg/dl and 1 cell/mm3). The diagnosis of acute autonomic and sensory neuropathy was evoked. Biological investigations revealed a Waldenstrom macroglobulinemia, with monoclonal IgM Kappa protein. The patient received 2 courses of intravenous immunoglobulin with total recovery of both autonomic and sensory dysfunction.
Conclusion: Several types of neuropathies have been described in WD, but the relationship between Acute autonomic neuropathy has not been reported. We describe the first case of acute autonomic neuropathy associated with Waldenstrom disease.
Disclosure: Nothing to disclose

Sunday, 17 June 2018

Cerebrovascular diseases 2

EPO2001

The role of admission cholesterol levels on short- and long-term survival after ischaemic stroke.

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Background and aims: Ischaemic stroke (IS) remains a leading cause of death and disability worldwide. Blood-based biomarkers have been used to identify patient-subgroups with increased risk for recurrent vascular events and death. Cholesterol has been studied in stroke and an inverse association to mortality has been reported. In our study, we aim to further investigate the role of admission cholesterol and its subfractions in short- and long-term survival after IS.
Methods: Our study is a retrospective, hospital-based, follow-up cohort of all patients with IS admitted in the stroke unit between January 2005 and February 2016. Of 3753 patients evaluated, 2364 had available cholesterol values. Time of observation was calculated from admission until death or until the end of observation period (May 1st, 2017). Logistic regression analysis, and Cox proportional hazard analysis were used for short- and long-term mortality investigation respectively.
Results: During a median follow-up period of 44 months, 842 of 2364 patients (36%) died. Of those, 113 patients (median age 84 years, IQR 10; 42% males) died within the first month. Patients with low cholesterol were older and had more vascular comorbidities. Increasing low density lipoprotein (LDL) cholesterol was independently associated with decreased 1-month mortality (OR 0.7; 95% Confidence Interval 0.51-0.96; p=0.03). Cholesterol levels were not associated with long-term mortality.
Conclusion: Our results show a possible association between low LDL levels at admission after IS and increased short-term mortality, that may be a marker of less severe stroke and more favourable outcome. No association was confirmed between cholesterol and long-term mortality.
Disclosure: Nothing to disclose

EPO2003

Posterior reversible encephalopathy syndrome associated with accidental intravascular injection of local anaesthetics

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Medical University of Graz, Department of Neurology, Graz, Austria

Background and aims: Posterior reversible encephalopathy syndrome (PRES) is an increasingly recognised acute neurological disorder with various precipitating conditions. Endothelial dysfunction is the pathophysiological key factor of PRES, and a frequent overlap with reversible cerebral vasoconstriction syndrome (RCVS) has been reported. We here present a series of three recently observed cases where PRES occurred immediately after accidental intravascular injection of amino-amide type local anaesthetics.
Methods: Single centre retrospective case series from a primary and tertiary care university hospital.
Results: Case 1: PRES/RCVS with altered vigilance, bilateral blindness and right-sided hemiparesis in a 74-year-old female patient after periradicular high cervical injection of ropivacaine for chronic neck pain.
Case 2: PRES/RCVS with associated refractory status epilepticus and cerebral air embolism in a 47-year-old male patient after dental anaesthesia with lidocaine.
Case 3: PRES with altered vigilance, bilateral blindness and left-sided hemiparesis in a 74-year-old male patient after periradicular cervical injection of ropivacaine for chronic cervicalgia. All three patients had an onset with severe clinical symptoms including reduced consciousness and were therefore admitted to the neurointensive care unit. MRI served to identify the presence of vasogenic oedema in a typical pattern and its subsequent resolution. Functional outcome at the time of hospital discharge was good in all cases (modified Rankin Scale scores of 0, 1, and 2, respectively).
Conclusion: Acute neurological symptoms immediately after the application of local anaesthetics should raise the suspicion of PRES/RCVS. Accidental intravascular drug injection is the most likely cause. Particular caution is required when local anaesthetics are administered in well-vascularised regions.
Disclosure: Nothing to disclose

EPO2004

Mechanical trombectomy in acute basilar artery occlusion.

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[1]Medical University Lublin-Clinical Hospital No.4, Department of Neurology, Lublin, Poland, [2]Medical University of Lublin, Department of Clinical Genetics, Lublin, Poland

Background and aims: Research suggest that mechanical trombectomy (MT) and intravenous trombolysis (ivT) are safe and effective treatment options in patients with acute basilar artery (BA) occlusion. However, optimal choice is still equivocal. This study gives retrospective assessment of MT efficacy in acute BA occlusion.
Methods: In the group of 107 patients treated with MT between Jan 2016 and Dec 2017 we found 7 patients with acute BA occlusion. In all patients CT angiography confirmed BA occlusion before MT.
Results: In MT-treated patients frequency of acute BA occlusion in 6.5%. Clinical characteristics is depicted in Tab. Median age was 75 years. Median NIHSS score at admission was 21 points. In 5 patients BA patency restitution was accompanied by neurological improvement. In 1 patient, despite complete BA reperfusion, neurological condition remained severe due to complete stroke in posterior circulation. In 1 patient BA patency was not restituted and patient died due to circulatory insufficiency. Median NIHSS score after MT was 5 points. Median time from stroke onset to BA reperfusion was 318 minutes. In all cases BA patency was restored with aspiration catheter. In 3 cases MT was preceded by ivT.
Conclusion: MT provides effective treatment method in patients with acute BA occlusion. The main factor that influences final clinical outcome seems to be restoration of BA patency. It must be emphasized that despite relatively long time interval between stroke onset and BA patency restoration substantial clinical improvement was observed.
Disclosure: Mechanical trombectomy treatment is performed by a team of hihgly specialized interventional neuroradiologists from Department of Interventional Radiology and Neuroradiology of Medical University of Lublin, Poland: Roman T, Sojka M, Górnik M, Pyra K, Jargiełło T. Stroke team in Department of Neurology of Medical University of Lublin is supervised by Szczepańska-Szerej H.

EPO2005

Safety and Efficacy of Cerebrolysin in Early Post-stroke Recovery: A Meta-analysis of Nine Randomized Clinical Trials

N. Bornstein[1], A. Guekht[2], J.C. Vester[3], W.-D. Heiss[4], V. Homberg[5], V. Rahlfs[3], E. Gusev[6], O. Bajenaru[7], B.O. Popescu[7], D. Muresanu[8]
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Background and aims: This meta-analysis combines the results of nine ischemic stroke trials, assessing efficacy of Cerebrolysin on global neurological improvement during early post-stroke period. Cerebrolysin is a parenterally administered neuropeptide preparation approved for treatment of stroke.
Methods: All included studies had a prospective, randomized, double-blind, placebo-controlled design. The patients were treated with 30-50 ml Cerebrolysin once daily for 10-21 days, with treatment initiation within 72 hours after onset of ischemic stroke. Data Sources: For five studies original analysis data were available for meta-analysis (individual patient data analysis), for four studies aggregate data were used. Study Selection: The combination by meta-analytic procedures was pre-planned and the methods of synthesis were pre-defined under blinded conditions. Search deadline for the present meta-analysis was December 31st, 2016.
Results: The nonparametric Mann-Whitney (MW) effect size for NIHSS on day 30 (or 21), combining the results of nine randomized, controlled trials by means of the robust Wei-Lachin Pooling Procedure [MERT], indicated superiority of Cerebrolysin as compared with placebo (MW 0.60, $P<0.0001$, $N=1879$). The combined number-needed-to-treat (NNT) for clinically relevant changes in early NIHSS was 7.7 (95% CI 5.2 to 15.0). The additional full scale ordinal analysis of mRS at day 90 in moderate to severe patients resulted in MW 0.61 with statistical significance in favour of Cerebrolysin (95% CI 0.52 to 0.69, $P=0.0118$, $N=314$). Safety aspects were comparable to placebo.
Conclusion: Our meta-analysis confirms previous evidence that Cerebrolysin has a beneficial effect on early global neurological deficits in patients with acute ischemic stroke.
Disclosure: Nothing to disclose

EPO2006

The reliability of prehospital diagnosis of stroke or transient ischemic attack

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[1]Institute of Psychiatry and Neurology, Ist Department of Neurology, Warsaw, Poland, [2]Medical University of Warsaw, Warsaw, Poland

Background and aims: Early and correct suspicion of acute cerebrovascular accident (CVA) is necessary for shortening time to reperfusion treatment. Our aim was to evaluate the reliability of prehospital diagnosis of stroke or transient ischemic attack made by healthcare professionals referring patients directly to a neurological Emergency Department (ED).
Methods: This retrospective analysis included all consecutive patients referred between January 2014 and December 2014 by ambulance physicians, paramedics or outpatient physicians to a neurological ED providing care for the population of 300–350 thousand inhabitants of a highly urbanized area. We calculated sensitivity and positive predictive value (PPV) with 95% confidence intervals (95%CI) for each group of healthcare professionals and compared the proportions of undetected CVAs.
Results: During the study period there were 690 patients with confirmed CVAs, including 639 formally referred by healthcare professionals. The highest sensitivity for detection of any CVA was observed among ambulance physicians (96%, 95%CI: 92-98%), followed by paramedics (85%, 95%CI: 80-90%, $p<0.001$) and then outpatient physicians (74%, 95%CI: 70-79%, $p<0.001$). PPV for stroke was 83% (95%CI: 77-87%) among ambulance physicians, 73% (95%CI: 65-80%) among paramedics and 56% (95%CI: 47-64%) among outpatient physicians.
Conclusion: Ambulance physicians are highly sensitive in diagnosing any CVA. Their prehospital diagnosis of stroke was correct in 8 of 10 cases, and only in 7 of 10 cases if made by paramedics, which indicates the necessity of two-way communication between ambulance and the stroke team before arrival at the ED. Suboptimal sensitivity urges additional training for paramedics and primary care physicians.
Disclosure: Nothing to disclose

EPO2007

Body Mass Index, Waist-to-Hip Ratio and Body Surface Area in patients with acute central nervous system ischemia in north-eastern Poland – preliminary examination.

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[1]Medical University of Białystok, Neurology, Białystok, Poland, [2]Białystok, Poland, [3]Warsaw University of Life Science, Faculty of Applied Informatics and Mathematics, Warsaw, Poland, [4]Medical University of Białystok, Neurology-Student research group, Białystok, Poland, [5]Medical University of Białystok, Neurology, Bialystok, Poland

Background and aims: Obesity is an important risk factor for stroke and probable predictor of functional outcome following ischemic stroke. The aim of our study was to measure and compare body mass index (BMI), Waist-to-Hip Ratio (WHR) and Body Surface Area (BSA) in patients with acute central nervous system ischemia in north-eastern Poland.
Methods: A total of 104 (63 male and 41 female) patients diagnosed with acute central nervous system ischemia were included. This was a retrospective pilot study of patients admitted in the last 3 months of 2017. Standard norms for BMI and gender specific norms for WHR were used as references.
Results: The patients' age ranged from 31 to 94 years (the average age of men and women was 71.1 and 69.06 years respectively). The average BMI for both sexes was 28.7, the average WHR was 0.98. BMI above 24.9kg/m² was present in 72.12% and WHR above normal in 83.65% of patients. More male than female had WHR above normal values. Among patients with BMI above the norm BSA, calculated by Du Bois formula, was about 2.04m² for men and 1.82m² for women.
Conclusion: In the majority of patients with acute central nervous system ischemia in north-eastern Poland WHR, BMI and BSA are significantly increased.
Disclosure: Nothing to disclose

EPO2009

Large vessel occlusions with low NIHSS-Frequency, clinical course and outcomes in a tertiary stroke center

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Background and aims: Most patients with acute large vessel occlusions (LVO) such as occlusion of carotid-T or proximal middle cerebral artery (MCA) present with severe stroke symptoms and according to large randomized clinical trials there is a clear indication for iv-thrombolysis in combination with mechanical recanalisation. However, there is a small number of patients with LVO with mild symptoms only. Not much is known about frequency, clinical course and outcome of these patients.
Methods: Consecutive patients with acute infarcts in the MCA-Territory and initial CTA were assessed for presence and site of vessel occlusions. Patients with initial NIHSS ≤4 and Occlusion of Carotid-T, M1-3-Segments of the MCA were assessed for treatment, clinical course and outcome at discharge.
Results: 1869 patients with acute stroke were referred to our hospital from 01/2012-09/2014. Of these, 1046 had ischemic stroke in the MCA territory and 936 obtained CTA or MRA on admission. Large vessel occlusions (LVA) were present in 432 patients and 343 subjects showed up within a therapeutic time window for IVT and/or MR. 99 patients had LVO and NIHSS≤4 (23% of all LVO) and secondary deterioration occured in13 (13%) of these patients. Due to different times from onset and contraindications patients were treated differently: secondary prevention only in 3; IVT in 1; MR in 4; IVT+MR in 5.
Conclusion: LVO with mild stroke NIHSS≤4 was not rare (23%). In 13% of these patients, without specific treatment on admission, secondary deterioration occured. These patients need special attention and monitoring in order to immediately start treatment when deterioration occurs.
Disclosure: Nothing to disclose

EPO2010

withdrawn

EPO2011

Intraplaque hemorrhage in symptomatic and asymptomatic progressive carotid artery stenosis–a pilot study

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Background and aims: Intraplaque hemorrhage (IPH) belongs to potential mechanisms of unstable plaque development. Study aims to compare the IPH occurrence in patients with asymptomatic stable (ASS), asymptomatic progressive (APS) and symptomatic (SS) carotid artery stenosis >50%.
Methods: Serial duplex ultrasound (DUS) in a 6-month period and magnetic resonance imaging (MRI) using axial 3DT1w sequence were used for IPH detection in patients with carotid stenosis. Stenoses in patients with ipsilateral stroke/transient ischemic attack within previous 4 weeks or acute ischemic lesion on diffusion-weighted MRI were evaluated as symptomatic. Stenoses with progression of >10% since last DUS examination were evaluated as progressive. Echolucent part of atherosclerotic plaque >8 mm2 on DUS and hyperintensity on 3DT1w-MRI were evaluated as IPH. Differences in IPH occurrence between ASS, APS and SS patients were statistically evaluated.
Results: Totally 32 patients (18 males, mean age 71.3±7.7 years) were enrolled during 18 months; 5 patients with ASS, 18 with APS and 9 with SS. MRI examination was not performed in 3 ASS and 1 SS patient. IPH was detected using DUS/MRI in 1 (20%)/2 (40%) of ASS patients, 9 (50%)/8 (53%) of APS patients, and 5 (56%)/4 (50%) of SS patients ($p>0.05$ in all cases). IPH on both DUS and MRI were detected in none of ASS patients, 5 (28%) APS patients and 3 (33%) SS patients ($p>0.05$ in all cases).
Conclusion: No significant difference in IPH occurrence was found between ASS, APS and SS patients. Totally 200 patients will be enrolled to the ongoing study.
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Disclosure: Supported by grants MHCR 17-31016A, 16-30965A.

Child neurology/developmental neurology

EPO2013

X-linked Adrenoleukodystrophy: a metabolic disorder in young male psychiatric patients

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Background and aims: X-linked adrenoleukodystrophy (XALD) is a rare disorder of peroxisomal fatty acid beta-oxidation which leads to the accumulation of very-long-chain fatty acids (VLCFA) in body tissues, and is caused by mutations in ABCD1 gene. Clinical picture results from the affection of central nervous system, adrenal cortex, and testicular Leydig cells, while the onset may be in childhood, adolescence, or adulthood. Unlike the childhood-onset XALD which is mainly a rapidly progressive neurologic disorder, the adult-onset forms have variable initial manifestations. We describe a case of adult-onset XALD which remained undiagnosed for almost a decade as presented with pure psychiatric features years prior to the appearance of the neurologic symptoms.
Methods: A male patient was diagnosed with schizoaffective disorder at 23 years of age. No other symptoms existed at the time and no neurologic work-up was performed. A slowly progressive limb weakness and instability appeared eight years later, thus prompting extensive neurologic, radiologic, metabolic, and genetic investigations.
Results: Neurologic assessment revealed bilateral pyramidal and cerebellar signs. No endocrine dysfunction was found. Specific white matter lesions were seen on magnetic resonance imaging of the brain, which, along with the finding of elevated serum VLCFA values and the confirmation of a known mutation in ABCD1 gene, proved the diagnosis of XALD in the patient.
Conclusion: Adult-onset XALD may persist as a psychiatric illness long before the onset of the other XALD-related symptoms. Therefore, early screening for XALD in young male psychiatric patients helps in reducing the diagnostic errors, enables proper genetic counselling and timely therapeutic decisions.
Disclosure: Nothing to disclose

EPO2015

Acute Necrotizing Encephalopathy: applying the diagnostic criteria to two cases

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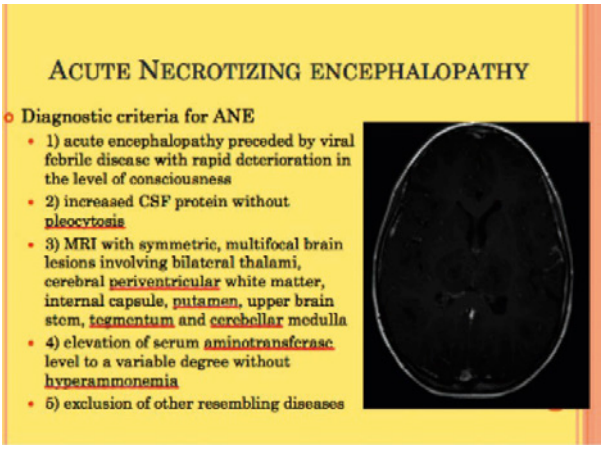
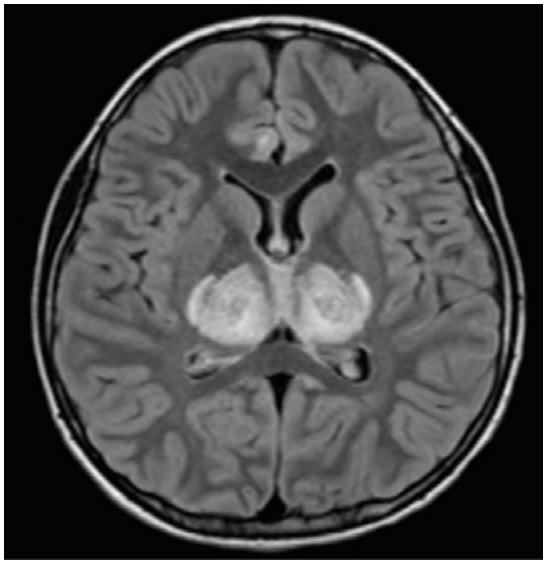
Background and aims: Acute necrotizing encephalopathy (ANE) is a rare para-infectious inflammatory process that causes rapid coma in previousy healthy children following viral illness. The hallmark radiographic feature is bilateral restricted diffusion of the deep gray matter with punctate hemorrhage. The pathogenesis is thought to be cytokine mediated breakdown of the blood brain barrier. Early and aggressive immunotherapy is the treatment of choice; however, treatment may be delayed in cases where the diagnosis is not clear. In this paper, I apply the diagnostic criteria established by Mizuguchi et al (1995) for ANE to elucidate pitfalls in diagnosis and treatment.

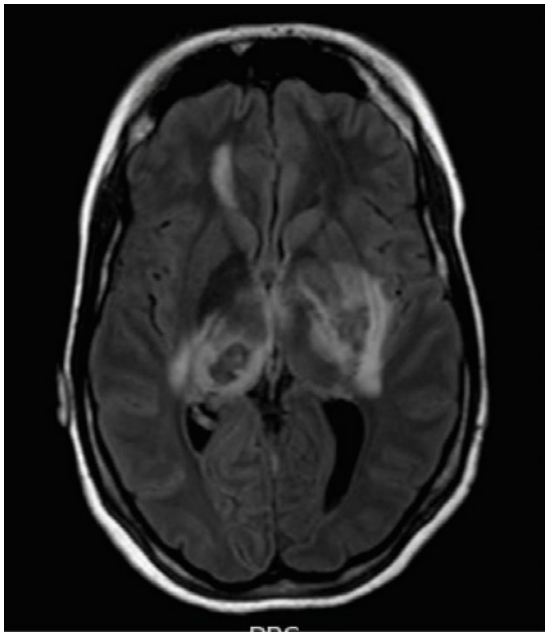


Mizuguchi diagnostic criteria

Methods: Two patients with influenza and radiographic findings consistent with ANE presented to Vanderbilt Children's Hospital in 12/2017. The Mizuguchi diagnostic criteria were applied and the cases shared all 4 criteria, although one patient was ultimately found to have a straight sinus thrombosis and ANE was ruled out as it is a diagnosis of exclusion.



Patient one axial flair MRI



Patient two axial flair MRI

Results: Patient one was treated with high dose steroids, PLEX and IVIG, and is now walking, talking and feeding herself. Patient two was treated for her venous sinus thrombosis and continues to have significant deficits, most notably bilateral CN VI palsies.

Conclusion: The Mizuguchi criteria help clinicians move quickly to life saving immunotherapy where delay in treatment can be the difference between life and death. It is important to exclude other resembling diseases, specifically venous sinus thrombosis, as this can be a mimicker of this rare disease.

Disclosure: Nothing to disclose

EPO2016

Spinal cord lesion in a 5-year-old girl with LHON G3460A mtDNA mutation

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Background and aims: Leber's Hereditary Optic Neuropathy (LHON) is a mitochondrial disease characterized by visual loss consequent to optic nerves atrophy. In some cases, LHON is associated with heterogeneous neurological extra-ocular manifestations, referred as "Leber plus syndrome", and rarely to a multiple sclerosis (MS)-like syndrome. We described a large Italian family with the G3460A mtDNA mutation, six of them presenting with LHON. A 5-year-old girl who carried the mutation was referred to clinical examination for an acute spinal cord lesion, mimicking a spinal cord vascular injury.

Methods: PCR-RFLP and Sanger sequence.

Results: The girl presented in Emergency department after acute back pain, followed by tetraparesis and impaired bladder control. Brain and Spinal cord Magnetic Resonance Imaging (MRI) showed hyperintense signal alterations in T2- weighted sequences and restricted diffusion in Diffusion Weightened Imaging (DWI) sequences in the anterior portion of spinal cord from C6 to D2, suggesting anterior spinal artery territory involvement, but inflammation could not be excluded. Angio-Computed Tomography (CT) was normal. Autoimmunity and thrombofilia screening yielded negative findings. Anti-AQP4 and anti-MOG resulted negative. An ecocardiography assessed normal heart and aorta features. A control spinal cord MRI together with 31Phosphorus- Spectroscopy was performed 10 days later, showing the complete regression of alterations and no abnormal metabolites.

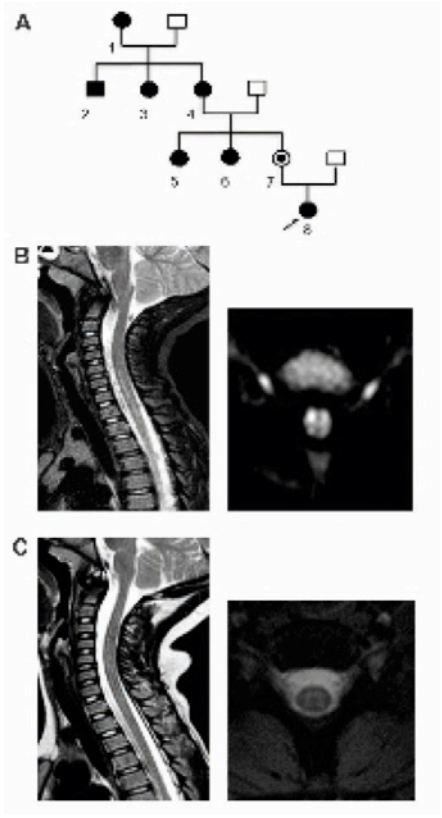

Fig.1

Conclusion: Aspirin was introduced at low doses, and high dose Methilprednisolone and Idebenone were administered. A mechanism of energetic dysfunction similar to stroke-like cannot be excluded. Our case reports a novel infantile clinical manifestation associated to G3460A mtDNA mutation, broadening the clinical spectrum of this disease.
Disclosure: Nothing to disclose

EPO2017

Symptomatic Brain Telangiectasias in Ataxia-Telangiectasia: from brain MRI to the anatomopathological findings

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Background and aims: Ataxia telangiectasia (AT) is an autosomal recessive genetic disease caused by mutations in the ATM gene. It is a multisystemic disorder characterized by progressive cerebellar ataxia, conjunctival and dermal telangiectasias, immunodeficiency with recurrent sinopulmonary infections and predisposition to malignancies. Some of the patients that survive till adulthood present MRI brain lesions, of unknown nature, but proposed to be telangiectasias. We present a case where autopsy findings were indeed consistent with brain telangiectasias. Furthermore, this is the first reported case where these lesions were symptomatic.
Results: A 31-year-old woman with classical AT phenotype was admitted for a 1-week history of headache suggestive of intracranial hypertension. Brain MRI revealed multiple nodular enhancing lesions with extensive oedema causing a 7mm midline shift. A malignancy was suspected and brain biopsy was scheduled. However, after some days of clinical stability, the patient quickly deteriorated. She became progressively stuporous with signs of brainstem compression and eventually died. The autopsy revealed that the nodular lesions were cerebral telangiectasias.
Conclusion: Recent reports that include adult patients with AT revealed the presence of nodular lesions in brain MRI. It is proposed that they are brain telangiectasias associated with microbleeds, gliosis and oedema. The anatomopathological study of our patient confirms that these are indeed brain telangiectasias. Moreover, to our knowledge, there are no reported cases where brain telangiectasias were responsible for intracranial hypertension. In adult AT patients the differential diagnosis of brain space-occupying lesions should not only include malignancies and infectious complications, but also brain telangiectasias.
Disclosure: Nothing to disclose

EPO2020

Proposed practical recommendations of stress management for headaches in children and adolescents

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Background and aims: Stress is considered to be the most common factor reported to trigger headaches in children and adolescents. Although tension-type headache and migraine are the two most common types of headache in children and adolescents, they are often untreated, ignoring their stressful background. Since stress-induced alterations of the stress system are involved in the onset and maintenance of headaches, we suggested that practical stress management could be used for prevention and therapy of stress effects of childhood and adolescence.
Methods: We conducted a systematic literature review from 1989 to December 2017 in databases: MEDLINE, EMBASE, Scopus, and Web of Science. Supplementary citations were recognized through the references of relevant articles. All English-language studies were evaluated for for health-care professionals involved in stress-related headache management and health promotion programs.
Results: 17 of 52 studies were included; 8 randomized-controlled trials, 6 non controlled and 1 prospective (total of 767 patients). An integrative plan is delivered through lifestyle improvement and biopsychosocial modifying stress response techniques. Healthy dietary choices, sleep hygiene, and regular exercise, although limited, are effective for young sufferers. Biopsychosocial therapies such as relaxation, biofeedback, hypnosis, yoga, cognitive behavioral therapy, and acupuncture focus at stress physiological and behavioral relief.
Conclusion: Stress management techniques are effective to moderate the effects of stressors and reduce distress, by normalizing stress responses the sensitive stages of childhood and adolescence. We suggest a stress-related headache management to empower children to make healthy choices in order to improve their lifelong well-being and quality of life
Disclosure: Nothing to disclose

Clinical neurophysiology

EPO2021

Evaluation of motor impulsivity in Huntington Disease with a choice reaction time task and brain metabolic (PET 18FDG) imaging

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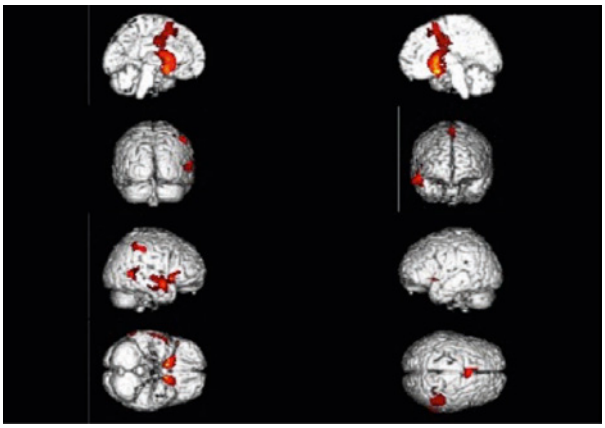
Background and aims: Impulsivity is an early behavioral change in Huntington disease (HD), experimentally described as an urge to act/react and/or as the impossibility to stop and correct this impulse. Our aim was to determinate which component of impulsivity was early affected in HD.
Methods: 11 symptomatic genetically proved HD patients (5≤motor UHDRS≤ 35) and 17 controls performed a choice reaction time task (Simon Task) with electromyographic (EMG) recordings of bilateral muscle agonists. Common behavioral measures of performance and "EMG-augmented" data were analyzed, in particular those reflecting expression and suppression of subthreshold muscle impulses. Assessment of cognitive functions, impulsive behavior (UPPS scale) and a brain PET-TDM 18FDG at rest were also performed.
Results: While HD patients had a higher impulsivity score in the UPPS scale (p<005), they didn't make more errors or partial errors (subthreshold of wrong muscle impulses) than controls (p=018). Correction rate was similar in both groups (p=064). Partial errors latency was similar in both groups (p=016) but correction time was significantly longer in HD patients (p<001). This correction time was significantly correlated with the TMTB time score (p<0001) and inversely correlated with the Mattis (p<0001) and Stroop test (p<001) performances. Striatal metabolism was inversely correlated with the correction time (p<005) and with Stroop (p<005) and TMTB time (p<005) performances.
Conclusion: A dissociation between motor impulsivity and impulsive personality (UPPS scale) seems to exist because the former may more likely be linked to an executive motor control dysfunction than a complex personality disorder. Besides, psychotropic treatments may interact with the task.



PET 18FDG in HD : 5 hypometabolic clusters (bilateral striata, bilateral frontal medial cortex, right inferior parietal cortex and right temporal lateral cortex)

Disclosure: Nothing to disclose

EPO2022

Fatigue is associated with impaired intracortical inhibition in patients with progressive multiple sclerosis: a transcranial magnetic stimulation study

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Background and aims: Fatigue is one of the most reported symptoms in people with multiple sclerosis (MS), affecting up to 75% of patients. In relapsing patients, fatigue has been associated to imbalance between intracortical motor excitatory and inhibitory circuits, with conflicting results. We aimed at testing this hypothesis in patients with progressive MS (PMS), compared to healthy controls (HC), using double-pulse transcranial magnetic stimulation (TMS).

Methods: We enrolled 45 patients (F=22 age=49.24±7.41, median EDSS=6.0, range=4.0-6.5) with PMS. Patients were divided into 3 groups according to Fatigue Severity Scale (FSS) score: no-fatigue (MS-NF;FSS≤4.0), borderline-fatigue (MS-bF;4.0<FSS<5.0) or fatigue (MS-F;FSS≥5.0). Short-interval-intracortical-inhibition (SICI) (interstimulus interval, ISI 1, 3ms) and facilitation (ICF, ISI 10, 15ms) to TMS was tested in patients and in 9 aged-matched HC (F=6 age=51.6±4.34).

Results: Groups did not significantly differ in age, EDSS, motor evoked potentials, walking performance and symptomatic treatment. Significant difference in best inhibition at SICI was found among groups (Kruskal-Wallis, p=0.017), in particular between HC vs MS-bF and vs MS-F (Mann-Whitney p=0.01, p=0.039) and between MS-NF vs MS-bF and vs MS-F (p=0.021, p=0.049). No significance was found between HC vs MS-NF and MS-bF vs MS-F. No significant difference was found at ICF.

Conclusion: In progressive MS, fatigue might be associated with impaired GABAergic intracortical circuits in primary motor cortex, with relative preservation of excitatory activity. Even if this mechanism might not be causative, these data, consistent with findings in relapsing MS, shed more light about the pathogenesis of fatigue in progressive MS.

Disclosure: M. Pisa, S. Gelibter, M. Fichera, A. Giordano, R. Chieffo, M Congiu, M. Comola have nothing to disclose. G. Comi has recieved compensation for consulting services and / or speaking activities from Novartis, Teva, Sanofi, Genzyme, Merck, Biogen, Roche, Almirall, Celgene, Forward Pharma L. Leocani has received compensation for consulting services and/or speaking activities from Novartis, Merck, Biogen, Roche, Almirall. V. Martinelli received honoraria for consulting services or speaking activities from Biogen, Merck KGaA, Bayer, Teva, Novartis, and Genzyme. Part of this work was supported by FISM, Fondazione italiana Sclerosi Multipla-Via Operai, 40-16149 Genova

EPO2023

withdrawn

EPO2024

Posterior auricular muscle response: observations in brainstem lesions

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Background and aims: Posterior auricular muscle response (PAMR) is a myogenic potential recorded over posterior auricular muscle (PAM) after auditory stimulation. Its circuit is formed by cochlear and facial nerves with the generator in the brainstem. Here, we investigated whether addition of posterior auricular muscle response (PAMR) examination would add an additional use in determining or localizing isolated brainstem lesions since the importance of blink reflex (BR) in determining or localizing brainstem lesions is known. Our hypothesis was that examination of both reflexes would increase the clinical utility.
Methods: We included 34 patients with isolated brainstem lesions (multiple sclerosis, ischemic stroke and cerebellopontine angle schwannoma) and 41 healthy subjects. PAMRs were recorded over posterior auricular muscle (PAM) after auditory stimulation. BR was elicited by the electrical stimulation of the supraorbital nerve.
Results: PAMR was present in 82.9% of healthy subjects whereas presence was quite low in the patient group (38.2%, p=0.001). Mean latency of PAMR was delayed in patients compared to healthy subjects (p=0.001). BR was obtained in all healthy subjects whereas prolonged latencies or absence of BR was observed in the patient group. There were no differences according to the different etiologies or localization.

Table 3. Blink reflex and PAMR parameters in patient subgroups according to different etiologies.

	CPA Tm n=2	Stroke n=14	MS n=18	p
R1 abnormality n (%)				0.599
Normal	2 (100)	9 (64.3)	9 (50.0)	
Asymmetrical long	-	4 (28.6)	5 (27.8)	
Bilateral absent	-	1 (7.1)	-	
Unilateral absent	-	-	2 (11.1)	
Bilateral prolonged	-	-	2(11.1)	
R2 abnormality n (%)				0.889
Normal	2 (100)	10 (71.4)	11 (61.1)	
Asymmetrical long	-	2 (14.3)	4 (22.2)	
Bilateral absent	-	-	-	
Unilateral absent	-	-	1 (5.6)	
Bilateral prolonged	-	2 (14.3)	2 (11.1)	
R2C abnormality n (%)				0.650
Normal	1 (50.0)	9 (64.3)	11 (61.1)	
Asymmetrical long	1 (50.0)	2 (14.3)	1 (5.6)	
Bilateral absent	-	-	-	
Unilateral absent	-	1 (7.1)	2 (11.1)	
Bilateral prolonged	-	2 (14.3)	4 (22.2)	
PAMR abnormality n (%)				0.948
Normal	1 (50.0)	5 (35.7)	7 (38.9)	
Asymmetrical long	-	-	-	
Bilateral absent	1 (50.0)	4 (28.6)	6 (33.3)	
Unilateral absent	-	3 (21.4)	4 (22.2)	
Bilateral prolonged	-	2 (14.3)	1 (5.6)	

CPA, cerebellopontine angle; MS, multiple sclerosis

Blink reflex and PAMR parameters in patient subgroups according to different etiologies.

Table 1. Demographical and clinical features of patients and healthy subjects.

	Patients n=34	Healthy subjects n=41	p	Stroke patients n=14	MS patients n=18	Tumor patients n=2
Age, y	44.3±17.4	43.5±12.1	0.808	59.3±13.9	32.2±8.6	55.0±22.6
Gender, M/F	19/15	15/26	0.095	5/9	8/10	0/2
MR localization, n (%)						
Mesencephalon	0 (0)	-	-	0 (0)	0	0
Pons	20 (58.8)			10 (71.4)	10 (55.5)	0
Bulbus	7 (20.6)			2 (14.3)	5 (27.8)	0
Pons-bulbus	5 (14.7)			2 (14.3)	3 (16.7)	0
Cerebellopontine angle	2 (5.9)			0 (0)	0 (0)	2 (100)

MS, multiple sclerosis; M, male; F, female

Demographical and clinical features of patients and healthy subjects.

Table 2. Blink reflex and PAMR parameters in patients and healthy subjects.

	Patient group n=34	Healthy subjects n=41	p
R/R1 latency	11.6	10.1	0.000
L/R2 latency	11.4	10.1	0.010
R/R2 latency	37.5	32.7	0.001
L/R2 latency	38.5	32.5	0.000
R/R2C latency	39.3	33.1	0.000
L/R2C latency	39.7	32.9	0.000
R/PAMR latency	11.5	9.3	0.001
L/PAMR latency	11.4	9.3	0.001
R1 abnormality n (%)	14 (41.2)	0 (0)	0.000
Asymmetrical/long	9 (26.5)		
Absent bilaterally	1 (2.9)		
Absent unilaterally	2 (5.9)		
Long bilaterally	2 (5.9)		
R2 abnormality n (%)	11 (32.3)	0 (0)	0.001
Asymmetrical/long	6 (17.6)		
Absent bilaterally	0 (0)		
Absent unilaterally	1 (2.9)		
Long bilaterally	4 (11.8)		
R2C abnormality n (%)	13 (38.2)	0 (0)	0.000
Asymmetrical/long	4 (11.8)		
Absent bilaterally	0 (0)		
Absent unilaterally	3 (8.8)		
Long bilaterally	6 (17.6)		
PAMR			
Normal	13 (38.2)	34 (82.9)	0.001
Absent bilaterally	11 (32.4)	5 (12.2)	
Absent unilaterally	7 (20.6)	2 (4.9)	
Long bilaterally	3 (8.8)	0 (0)	

Blink reflex and PAMR parameters in patients and healthy subjects.

Conclusion: Although presence of PAMR is quite high, its absence does not always indicate a pathology. But prolonged latencies almost always suggest an involvement of PAMR pathway. Likewise, absent PAMR with an abnormal BR provides information for the involvement of brainstem facial nucleus or proximal part of the facial nerve.
Disclosure: Nothing to disclose

EPO2025

Exploring the neurophysiological basis of balance impairment in multiple sclerosis patients

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Background and aims: Balance impairment is very common in multiple sclerosis (MS), and it has a deep impact on quality of life. However, the causes of MS-related unbalance remain unclear. Some authors hypothesized that the main mechanism is a dysfunction in the lower limbs sensorimotor control. Aim of the present study is to evaluate, by evoked potentials (EP), the contribution of motor and somatosensory pathways on balance performance in MS patients.

Methods: Patients underwent brain and spine MRI and clinical evaluation. Balance was assessed by Tinetti Scale (TS). Disease severity was measured by EDSS. The functionality of central somatosensory and motor pathways was tested by somatosensory EP (SEP) and motor EP (MEP), respectively. OLS regression with robust standard errors of TS on EP was employed, controlling for gender, age, MS type, EDSS, and spine MRI findings.

Results: 40 patients were included. 19 patients (47.5%) had balance impairment. SEP were abnormal in 18 patients (45%). MEP were abnormal in 14 patients (35%). 27 patients (67.5%) had spinal cord lesions.

Linear regression model revealed negative significant correlations between TS and EDSS ($p<0.01$) and between TS and central conduction time at SEP ($p<0.05$). No significant correlation was found between TS and spine MRI findings, and between TS and MEP.

Table 1
OLS Regression of Tinetti Scale

Model	N = 40	F(7,32) = 8.00	Prob > F = 0.000	R^2 = 0.669
Variable	**Coefficient**	**Standard Error**	**t stat**	**p value**
Gender (M=1)	0.9403	0.6427	1.46	0.153
Age	-0.0408	0.0319	-1.27	0.212
SM Type (RR=1)	0.9469	0.6151	1.54	0.134
EDSS	-0.8728	0.2116	-4.12	0.000
Spinal MRI (Y=1)	-1.2751	0.747	-1.71	0.097
MEP	-0.1212	0.0892	-1.36	0.183
SEP	-0.1788	0.0807	-2.22	0.034
Constant	28.175	1.5575	14.88	0.000

Conclusion: In MS, balance impairment is related to a dysfunction of lower limbs somatosensory ascending pathways conveying proprioceptive and somatosensory information. More in general, EP are useful in the study of pathophysiology of unbalance and seem to be more sensitive than MRI in assessing sensorimotor pathways functionality.

Disclosure: Nothing to disclose

EPO2027

The relationship between callosal transfer and anxiety in multiple sclerosis: A transcranial magnetic stimulation study

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Background and aims: Among the frequently encountered symptoms in multiple sclerosis (MS) stand anxiety and depression. They could occur at any time during the disease course and can severely compromise the patients' functioning. Nevertheless, no single study has addressed the neurophysiological underpinnings of these symptoms.

Methods: Fifty consecutive MS patients aged between 18 and 75 years participated in the study protocol. Patients were excluded if they were on any pharmacological intervention that could affect cortical excitability measures. Anxiety and depression were assessed by means of the Hospital Anxiety and Depression Scale (HADS). Cortical excitability measures were recorded using transcranial magnetic stimulation (TMS) and included resting motor threshold, motor evoked potentials, contralateral silent period, interhemispheric inhibition, short-interval intracortical inhibition and facilitation at different interstimuli intervals, as previously described. Correlation analysis was employed to assess the relationship between HADS scores and TMS variables.

Results: Patients had a mean age of 51.82±12.72 years and a mean physical disability score of 5.52±1.64. Their depression scores ranged from 0 to 14 (mean±SD: 6.08±3.66) and their anxiety scores ranged from 1 to 15 (mean±SD: 5.82±3.42). A significant direct correlation was found between anxiety scores and interhemispheric inhibition ($r=0.43$, $p=0.003$).

Conclusion: The results of the current work highlight the relationship between anxiety and callosal transfer and are consistent with those obtained in a previous study. Compared to MS patients with low anxiety scores, those with higher scores seem to exhibit a relatively more efficient callosal transfer, a finding that merits further assessment.

Disclosure: SSA declares having received travel grants or compensation from Genzyme, Biogen, Novartis and Roche. AC gave expert testimony for CSL Behring, Novartis, received grants from Biogen, Novartis, CSL Behring, GE Neuro, Octapharma, and gave lectures for Genzyme. JPL, UP and MAC: Nothing to disclose.

Epilepsy 2

EPO1036

Seizure-free 6 months follow-up after surgical treatment in a Lennox-Gastaut syndrome patient: a case report.

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Background and aims: We report the case of a 7-year old that developed different type of seizures (atypical absences, epileptic "spasms", tonic and clonic seizures) together with a cognitive decline. Before age of 5, she had an unremarkable history. EEGs showed multifocal interictal abnormalities (predominant in right fronto-temporal region), as well as bilateral slow sharp-and-waves and paroxysmal fast rhythms. Electro-clinical features were consistent with a Lennox-Gastaut syndrome (LGS).
Methods: Brain-MRI, cerebrospinal fluid, metabolic and genetic analyses didn't show any abnormalities. PET-FDG showed a hypo-metabolism of left temporal and right superior-frontal regions. 3D-FLAIR brain-MRI allowed identification of a right fronto-polar dysplasia. Patient was refractory to several anti-epileptic drug treatments and ketogenic diet. Intracranial monitoring confirmed pluri-focal right frontal seizures. Therefore, a right fronto-polar disconnection surgery was realized.
Results: At 6-month follow-up, patient was seizure free and cognitive improvement was noted as well.
Conclusion: LGS is an age-related epileptic encephalopathy that may be cryptogenic or symptomatic, the latter having a worse prognosis. Resective surgery can have encouraging results, especially when seizure onset zone is confounded to one lobe or a limited area in the brain. With respect to cognitive function, the younger the patient at surgery or the shorter the interval between seizure onset and surgery, the better the cognitive outcome. We report here a case of medically refractory LGS with a complete remission after surgical treatment. This case highlights the importance of surgery for symptomatic LGS.
Disclosure: Nothing to disclose

EPO2029

Esclicarbazepin in the treatment of patients with refractory and super-refractory status epilepticus

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Background and aims: Refractory status epilepticus (SE) is a life-threatening condition with limited therapeutic options. New antiepileptic drugs should be investigated in refractory SE in order to improve treatment of this condition. Eslicarbazepine (ESL) is a new sodium channel blocker, which efficacy have not yet been investigated in refractory SE. Our aim was to analyze data on treatment of SE with ESL.
Methods: In terms of the Mainz Epilepsy Registry (MAINZ-EPIREG) we analyzed data on the efficacy and safety of ESL in treatment of refractory and super-refractory SE.
Results: Five patients with refractory or super-refractory SE have been treated with ESL. The mean age of patients was 62 ± 7 years. The median number of antiepileptic drugs administered prior to initiation of ESL was 4. The mean duration of SE prior to initiation of ESL was 2 days. Initial dose of ESL was 800mg, titrated to a daily dose of 1200 to 1600mg. SE was resolved in 2 of 5 patients (40%) within 36 hours after initiation of ESL. No serious adverse effects have been recorded.
Conclusion: According to our data, ESL may prove useful in the treatment of SE. Farther trials are encouraged to investigated ESL in larger populations of patients with SE.
Disclosure: Nothing to disclose

EPO2030

Gamma oscillation in EEG recordings in patients with epilepsy.

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Background and aims: Gamma waves in the EEG record include frequencies between 30 and 100 Hz. Due to the increasing possibilities of registration by computerized EEG apparatus, more research on the significance of gamma waves in various physiological and disease states has appeared, and one of the more promising discoveries was the statement that the seizure discharges present in patients with epilepsy may be preceded by increased oscillations of EEG activities with a gamma frequency. The aim of our study was to record gamma oscillations in EEG records in epileptic patients and to evaluate their clinical relevance for better monitoring of patients' treatment.

Methods: The research material consisted of 10 EEG records of epilepsy patients and 10 patients with no CNS findings. The research was done in our diagnostic EEG laboratory with EEG apparatus EBNeuro (32-channel). The EEG EBNeuro Neurotravel is equipped with the company's EEG Galileo .NET software. We also used our own application for EEG analysis and evoked potentials averaging, written in C ++ (fig.1).

Fig.1. A fragment of the EEG curve of a 14-year-old woman suffering from epilepsy. We used our own C ++ application to analyze the curve; oscillation of gamma waves in the O1 lead (left occipital region).

Results: We found that gamma oscillations are present in EEG recordings of patients with epilepsy in contrast to healthy individuals. They are often accompanied by interictal discharges in the EEG record and may precede them.

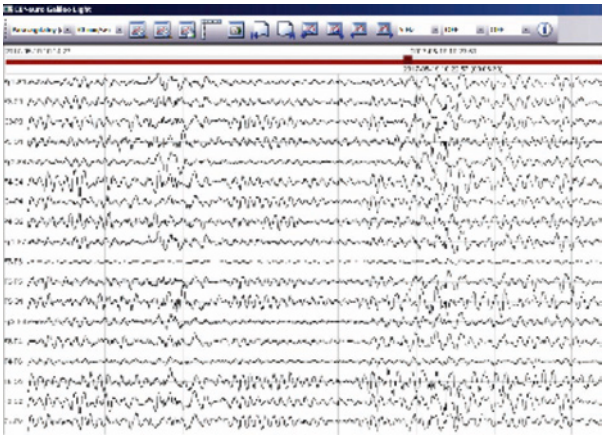

Fig.2. A fragment of the EEG record of a 23-year-old woman suffering from epilepsy. The record made during the treatment shows generalized discharges of a series of high-voltage free waves theta 3.5-6Hz and spike-and wave discharges against the background of regular alpha with a frequency of about 9-10Hz.

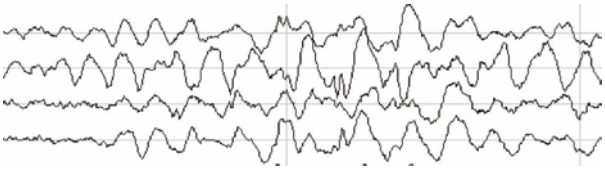

Fig.3. Fragment of the EEG curve of the patient, which is shown in Fig. 2. Gamma oscillations accompanying epileptic discharges.

Conclusion: Gamma oscillations are more frequent in EEG recordings in patients with epilepsy in comparison with the records of healthy people. They are often accompanied by interictal discharges in the EEG and can precede them. Registration of gamma oscillations requires increasing the routine frequency of EEG signal sampling and effective elimination of artefacts.

Disclosure: Nothing to disclose

EPO2031

Screening tools for depression and adverse events in epilepsy-experiences from clinical practice

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Background and aims: Depression is the most frequent comorbidity in people with epilepsy (PwE). Adverse events (AE) of antiepileptic drugs (AEDs) are frequent as well, particularly with add-on AEDs. Aim of the present study was to identify PwE suffering from depression and AE of AED and to evaluate its impact on quality of live (QoL).
Methods: All patients attending the local epilepsy outpatient clinic were asked to fill a questionnaire. This included LAEP, NDDI-E, ET5, EQ-VAS and questions regarding current seizure frequency. Questionnaires filled between October 2015 and December 2016 were included. An inclusion criterion was diagnosis of epilepsy. In case of multiple attendances, the first filled questionnaire was included only.
Results: 509 questionnaires were included. 20.4% showed significant AEs (LEAP>44), increasing with the number of AEDs. Negative correlation on LAEP was found for Lacosamide, Gabapentin and Perampanel. Screening for depression was positive for 18.3% in ET (cut-off >15) and 15.3% in NDDI-E (cut off >13). 11.2% had a clinical diagnosis of depression and a further 12.2% another psychiatric co-morbidity. 20.6% were on regular psychiatric medication. QoL correlated with seizure freedom but not with seizure frequency. Almost 30% of the variance of QoL depended on depression, AEs of AED and seizure freedom in the last year.
Conclusion: QoL in PwE depends on seizure control but also on comorbidity of depression and AEs of AEDs. Screening tools help to identify PwE with comorbidity, which might respond well to treatment, and with AEs, which might require a change in AEDs.
Disclosure: Nothing to disclose

EPO2032

The effects of periodic discharges on the prognosis of patients with status epilepticus

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Background and aims: It is important to predict prognosis of status epilepticus (SE). The aim of this study was to assess the prognostic significance of PDs on the functional outcome of patients with SE and the occurrence of refractory status epilepticus (RSE).
Methods: The author analyzed the clinical history, neuroimaging data, routine EEG and continuous video-EEG monitoring records of consecutive patients with SE. We selected patients with PDs in EEG records which included more than 50% of epochs that were composed of more than 50% seconds with PDs. We excluded patients with anoxic brain damage, SE with simple partial seizures, absence SE or incomplete medical records. Functional outcome at the time of hospital discharge was assessed by Modified Rankin Scale (MRS).
Results: Among 86 consecutive patients with SE, fourteen patients were excluded. In 72 patients with SE, 31 had PDs in EEG. Thirty eight out of 72 had good functional outcome (MRS 0-3) and 34 had bad functional outcome (MRS 4-6). The presence of PDs (p=0.033, odd ratio 3.651, 95% CI 1.107-12.040) and stuporous or comatose mentality at presentation (p=0.044, odd ratio 3.351, 95% CI 1.036-10.840) were independent risk factors for bad functional outcome in multivariate analysis. The occurrence of RSE was significantly higher in patients with PDs (p=0.001, odd ratio 11.059 95% CI 2.788-43.872).
Conclusion: PDs is an independent predictive factor of bad functional outcome and the occurrence of RSE, so patients with SE and PDs should be given early and rigorous management.
Disclosure: Nothing to disclose

EPO2033

Temporal lobe epilepsy with amigdala enlargement.

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Background and aims: Temporal epilepsy with amygdala enlargement (TE-AE) is a distinct electroclinical entity that is becoming increasingly recognized. Focal cortical dysplasia, low grade tumors, and seizure-related changes have been reported as probable causes. An autoimmune cause, even with negative antibody testing, raises the possibility of immunotherapy in these cases.We report the clinical characteristics and therapeutic response of a series of 18 patients with TE-AE.
Methods: Patients with focal epilepsy and amygdala enlargement after MR visual inspection were included. Volumetric analysis was performed in order to confirm the findings.
Results: We found 18 patients with amygdala enlargement after visual inspection and excluded one after volumetric analysis. Mean age at epilepsy onset was 40.4 years old. Seizures were classified as temporal (10 mesial, 4 lateral), extratemporal (2) and unclassified (1) according to the corresponding semiology. 3 patients had another identifiable cause (100% ipsilateral to AE) and 1 patient's amygdala enlargement proved reversible after removal of a cavernoma. Antibody testing was negative in all 5 patients tested. Neuropsychological testing was performed and found to be abnormal in 6/6 patients. Psychiatric disorders were reported in 6 patients.
Conclusion: TL-AE is an emerging epileptic syndrome with certain identifiable features (late onset, neuropsychological abnormalities, and mood disorders). Amygdala enlargement can be seizure-related and other lesions should be searched for.
Disclosure: Nothing to disclose

EPO2034

Personality Disorders in Temporal Lobe Epilepsy

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Background and aims: Personality Disorder (PD) is defined as a pattern of inflexible and maladaptive personality traits that cause functional disability or subjective suffering. They consist of 10 types, grouped into 3 clusters-A (Schizoid, Schizotypal, Paranoid), B (Borderline, Narcissistic, Histrionic, Antisocial) and C (Dependent, Avoidant and Obsessive Compulsive). People with epilepsy (PWE) are at greater risk of suffering from PP with prevalence's that may reach 75%.
Our aim is to analyze the frequency and type of PD, in a sample of PWE, accompanied at the Reference Center for Refractory Epilepsy of Hospital de Santa Maria (CHLN).
Methods: Retrospective analysis of pre-surgical evaluation of 121 people with refractory epilepsy (RE). The personality assessment was done using the Millon Multiaxial Clinical Inventory-II. A score > 85 was considered for the definition of PP. When scores > 85 were obtained on more than one type of PP it was considered "Not Otherwise Specified" (NOS). The types of PP and their frequency were analyzed according to the location of the epileptogenic zone (temporal vs. extra temporal).
Results: 70% of those with ER had at least one of the PD types. The most frequent types were PD NOS (40; 47%), followed by Obsessive PD (17; 20%) and Dependent PD (14; 16%). No statistically significant differences were found regarding the epileptogenic zone (p=0.297).
Conclusion: In our population, the prevalence of PP in PCE is much higher than that described in the general population. They may be associated to either the psychological or biological factors.
Disclosure: Nothing to disclose

EPO2036

Anti-NMDA receptor encephalitis triggered by epilepsy surgery

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Background and aims: Anti-NMDA receptor (NMDAR) encephalitis is a nosological entity associated with antibodies directed against the glutamatergic NMDAR.
Herpes simplex virus 1 (HSV1) is a common cause of viral encephalitis. It may be reactivated by brain surgery with a latency of many years after the index event. A recently described complication of HSV1-encephalitis is induction of anti-NMDAR-encephalitis.
So far, brain surgery has not been described as a trigger of anti-NMDAR-encephalitis in patients post-HSV1-encephalitis.
Methods: We report on a patient who had suffered from HSV1-encephalitis as a child. 37 years later, anti-NMDAR encephalitis was triggered by epilepsy surgery.
Results: A 40-year-old male patient presented at our hospital for epilepsy surgery. He suffered from drug-resistant frontal lobe epilepsy post-childhood HSV1-encephalitis. Postoperatively, the patient developed semiologically new seizures and focal neurological symptoms. FLAIR-MRI showed progressive bilateral hyperintensities. Cerebrospinal fluid (CSF) analysis revealed slight lymphocytic pleocytosis. HSV1-PCR in the CSF was negative and there was no improvement on virostatic therapy. Serum and CSF NMDAR-antibodies returned positive, and immunosuppressive therapy with rituximab and cyclophosphamide led to significant improvement of the clinical and imaging parameters.
Conclusion: To our knowledge, this is the first published case of anti-NMDAR encephalitis triggered by brain surgery. Two pathomechanisms are feasible:
1) HSV1 encephalitis was triggered by epilepsy surgery with subsequent induction of anti-NMDAR encephalitis.
2) Anti-NMDAR encephalitis was directly induced by brain surgery.
We favor the latter hypothesis and argue that intracellular antigens may have been released by surgical trauma, triggering an autoinflammatory cascade. We discuss the consequences for indicating brain surgery in patients post-HSV1-encephalitis.
Disclosure: Nothing to disclose

EPO2037

Epilepsy treatment gap in Cameroon

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Background and aims: The availability of AEDs differs between high-income countries and low and middle ones. In many Sub-Saharan African countries, like Cameroon, the coverage is very low and limited (carbamazepine, phenytoin, phenobarbital and valproic acid). Despite other AEDs as lamotrigine have been added to the WHO List of Essential Medicines (2017), they are not available in most of these countries yet.
The objective of our study was to increase our knowledge about the management of epilepsy by general healthcare providers (GHP) in Cameroon.
Methods: A four-day training course in neurology was organized for GHP by Spanish neurologists in Cameroon. During the course, we investigated the availability and management of AEDs in the country through a questionnaire.
Results: Of the 42 GHP, 88.1% would use medicines to treat epilepsy. 76.2% knew the existence of only one to three AEDs. Regarding the management: 21.4% reported using haloperidol, 69% carbamazepine, 73.8% valproic acid, 88.1% phenobarbital and 35.7% phenytoin. Most of them (92.9%) would maintain AEDs during pregnancy, considering carbamazepine (38%), valproic acid (33,4%), phenobarbital (38.2%), haloperidol (4,8%) and phenytoin (7.2%) good choices for pregnant women. No mention was made to any other antiepileptic drugs, including lamotrigine.
Conclusion: Most of the GHP use medicines to treat epilepsy, but only a few AEDs are available. These results raise concerns about the lack of procurement and distribution of AEDs in many countries. Further studies inquiring into the hurdles of this reduced access to new generation AEDs are needed.
Disclosure: Nothing to disclose

Infectious diseases; Sleep disorders

EPO2038

The Impact of a Specialist Joint Neurology/Infectious Diseases Outpatient Clinic in Managing HIV-infected patients with Neurological Problems

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Background and aims: A specialist, tertiary Neuroinfectious Diseases (NeuroID) clinic, where patients are seen jointly by a Neurologist and Infectious Diseases physician was set up in 2005 to address neurological problems in patients with infectious diseases. A joint discussion involving investigation, diagnosis and management of patients remains the main approach of this clinic.
Methods: We conducted a retrospective case review of all patients attending the NeuroID clinic between the 1st of January 2011 until the 31st December 2012.
Results: 61 patients were seen in the NeuroID clinic during the dates studied. 40 (66%) of these patients were known to be HIV positive. Patients with HIV infection were on average older had fewer known neurological conditions, compared to those without HIV. Epilepsy, peripheral neuropathy and memory impairment were the most common neurological comorbidities. The majority of patients had good HIV control (89% had an undetectable HIV viral load).
Patients with HIV infection were mostly referred due to undiagnosed neurological symptoms, most commonly neuropathic sounding pain, focal motor symptoms and paraesthesiae. HIV positive patients had on average more investigations (mean of 2.6 compared to 0.9). 83% of HIV positive patients had atleast one new diagnosis made in the NeuroID clinic. Common new diagnoses in HIV positive patients were movement disorders, HIV associated neurocognitive disease and myeloradiculopathy.
Conclusion: At least one new diagnosis was made in the clinic in 83% of HIV-infected patients demonstrating the benefit of a specialised integrated approach in managing HIV-infected patients with neurological disease.
Disclosure: There is no commercial or institutional support to disclose for this research.

EPO2039

Stroke in HIV Patients: 41 cases in the neurology department of Ignace Deen Hospital

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Background and aims: The literature suggests a strong association between Human Immunodeficiency Virus (HIV) and stroke. Although HIV infection is endemic in sub-Saharan Africa, few authors are interested in this association. The aims is to evaluate the frequency of HIV infection during stroke, describe the clinical and paraclinical aspects of this association
Methods: This was a prospective study of the descriptive and analytic type that included for 12 months all subjects admitted to the neurology department of the Conakry University Hospital for a stroke with HIV positive serology (Western Blot confirmed Elisa) and who agreed to participate after counseling. Sociodemographic, clinical, paraclinical and progressive data (National Institutes of Health Stroke Scale(NIHSS) and modified RANKIN scores) were collected for each patient. The statistical significance level was fixed at 0.05.
Results: Forty-one out of 423 (9.69%) had positive HIV serology. In this population, the mean age was 48.56±10 years; the female sex was predominant (Sex ratio=1.3). More than half of the patients had no cardiovascular risk factors. The clinic was superimposable to that found in the general population; however, the fever was constant. Ischemic strokes predominated and the area of the superficial sylvian artery was the most concerned. Stroke occurred at all stages of HIV infection; the prognosis at the acute phase was severe.
Conclusion: the occurrence of stroke in HIV is still underestimated in Africa. It is necessary to systematize retroviral serology (VRS) in patients with stroke.
Disclosure: Nothing to disclose

EPO2040

Interferon via Ommaya reservoir in Subacute sclerosing panencephalitis(SSPE): A success story

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Background and aims: SSPE is a chronic progressive and fatal neurological disorder usually in children due to persistent measles virus infection of CNS characterised by myoclonic jerks, cognitive decline and typical EEG findings.
Our aim was to treat SSPE and assess the efficacy of interferon-alpha injected through intraventricular route via Ommaya reservoir .
Methods: Our prospective study was conducted in Department of Neuromedicine, CNMC between 1.5.16-30.4.17. Twenty (20) children with a probable diagnosis of SSPE as per Dyken's criteria were included and evaluated for H/O measles infection, vaccination, symptoms of cognitive decline and myoclonic jerks and were investigated through CSF study (anti-measles antibody titre), EEG and neuroimaging. All were treated by body weight adjusted doses of Inj. Interferon alpha through intraventricular route for 6 weeks via Ommaya reservoir .
Results: The mean age was 9.4 yrs. M:F ratio was 3:2. 8 had past H/O measles and 4 were vaccinated. 12 were in Jabbour stage III B and 8 in stage III A. All 20 patients had positive measles antibodies in CSF and titres were more than 1:4 in CSF and 1:250 in serum. 16 children had typical periodic discharges in EEG. Following interferon therapy coupled with oral Ribavirin for 1 month after discharge , modest clinical improvement was noted as per Jabbour staging.
Conclusion: Although no curative treatment is available for this degenerative disease, interferon therapy provides ample hope and intraventricular route obviates the need for twice weekly lumbar punctures which is both painful and cumbersome.
Disclosure: Nothing to disclose

EPO2041

First case report of Herpes Simplex Virus Encephalitis During Immunosuppressive Treatment of Autoimmune Hepatitis.

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Background and aims: Herpetic encephalitis (HE) causes high morbidity and lethality. Immunosuppressive therapies have spread during the last decades, and it has been demonstrated that they worsen outcomes in patients with HE. In a review of the literature, we have not found any case of HE associated with the immunosuppressive treatment of Autoimmune Hepatitis (AH). Here, we describe a patient with AH, who developed HE during immunosuppressive treatment, and share our experience in the management of these specific patients.
Methods: We report a case of HE in a patient with AH on azathioprine (AZA) therapy. A literature review was performed with search items including "encephalitis" and "immunosuppression" in the thesaurus of Medline.
Results: We found just one series comparing immunosuppressed patients and immunocompetent ones both with HE, and one case report with HE on AZA in Crohn's disease. Our patient presented with prodromal syndrome and severe focal deficits, which is not consistent with literature. However, absence of CSF pleocytosis and atypical MRI manifestations were. AZA was suspended and acyclovir therapy was completed for 21 days. Liver profile did not worsen and patient considerably improved, remaining at discharge with mild dysarthria and persisting currently with no immunosuppressive therapy and with hepathology follow up.
Conclusion: HE in immunosuppressed patients has particular features. In patients on AZA, this should be discontinued and restarted again if indicated, preferably after completion of HSE therapy. Individualization and consensus between physicians are key features of management. Further investigation is needed to provide stronger recommendations according to subgroups of patients.
Disclosure: Nothing to disclose

EPO2042

Gliomatosis cerebri mimicking PML in an immunocompromised patient.

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is a feared complication in immunosuppressed patients. Indeed PML most frequently develops in a context of HIV, malignancy or medication induced immunosuppression. The diagnosis is made based on clinical and radiological findings and often confirmed by highly specific CSF JC-virus PCR.

Results: We present the case of a 48-year-old man with a medical history of Crohn's disease and multiple preceding immunosuppressive treatments in the past few years (azathioprine, adalimumab, methylprednisolone). After starting a new treatment with infliximab (TNF-alfa blocker) there was a progressive generalized malaise. 4 months later he presented at the emergency department with complaints of headache, transient visual obscurations, urinary urgency, aphasia and mild right hemiparesis. Imaging showed multifocal white matter lesions with a mild mass effect. IV corticosteroid treatment, in suspicion of TNF-A mediated demyelination, was started immediately without significant improvement. Later JC-virus PCR on CSF was positive (560 copies/mL) and a diagnosis of PML was made. As a progressive deterioration was present further examinations showed papilledema and a spinal lesion. A second lumbar puncture could not detect JC virus anymore, a brain biopsy was performed but was inconclusive. 2 months later the patient died and autopsy revealed a diffuse infiltrative astrocytoma WHO grade III.

Conclusion: As a conclusion, we like to emphasize the differential diagnosis of PML and diffuse glioma (gliomatosis cerebri). Intracranial hypertension and spinal lesions are highly atypical of PML and JC-virus PCR specificity is not 100%.

Disclosure: Nothing to disclose

EPO2043

B-amyloid metabolism disregulation in sleep disorder

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Background and aims: Recent studies have demonstrated that sleep disorders are associated with cognitive dysfunctions and nocturnal sleep modifies B-amyloid metabolism.Obstructive Sleep Apnea Syndrome (OSAS) is characterized by repeated episodes of upper airway obstruction during sleep that result in intermittent hypoxemia and arousal. Periodic limb movements in sleep (PLMD) are repetitive, stereotypical involuntary movements of the lower extremities that appear during sleep. These sleep disorders are very frequent, in particular in elderly patient.This study aimed at evaluating CSF B- amyloid metabolism in patients with OSAS and PLMD.

Methods: We enrolled patients affected by OSAS and PLMD compared with controls. Both patients and controls underwent nocturnal polysomnographic monitoring and lumbar puncture to determine CSF levels of amyloid-β1-42, amyloid-β1-40, total (t-)Tau, and phosphorylated (p-)Tau.

Results: We recruited 20 OSAS patients, 12 PLMD and 10 controls. The OSAS group had lower levels of B-Amyloid compared to PLMS subject and controls. Furthermore PLMD patients showed lower levels of B-Amyloid compared to controls. Sleep structure was altered in both group of patient in a similar way.

Conclusion: This report showed alteration of CSF biomarkers in both OSAS and PLMD patients. However, beta-amyloid dynamics were more altered in OSAS group possibly because these patients show

both alterated sleep structure and intermittent hypoxemia, while PLMS group presents only alteration of sleep architecture.

Disclosure: Nothing to disclose

EPO2044

Transcranial Magnetic Stimulation reveals cognitive impairment in obstructive sleep apnea syndrome

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Background and aims: Patients with obstructive sleep apnea syndrome (OSAS) show neurocognitive impairment, but the exact mechanisms that cause cognitive dysfunctions remain unknown. The cholinergic system is known to play a key role in all attentional processes and cognitive functions. A transcranial magnetic stimulation (TMS) protocol may give direct information about the function of some cholinergic circuits in the human brain; this technique relies on short latency afferent inhibition (SAI) of the motor cortex. The objective of this exploratory study was to test the hypothesis that impaired cognitive performances in OSAS patients are associated with a dysfunction of the cholinergic system, as assessed by SAI.
Methods: We applied SAI technique in a group of 13 patients with OSAS and compared the data with those from a group of 13 age-matched healthy subjects. All the patients underwent a sleep study, an extensive neuropsychological evaluation, and TMS examination.
Results: Mean SAI was significantly reduced in our OSAS patients when compared with controls. The neuropsychological evaluation showed impairments in most cognitive areas in the OSAS patients. SAI values were strongly correlated with the neuropsychological test scores.
Conclusion: These findings suggest that the cognitive deficits in OSAS may be, at least in part, secondary to alterations in cholinergic neurotransmission, presumably caused by nocturnal hypoxemia. TMS studies may shed light on the pathophysiological mechanisms of the cognitive disturbances in OSAS patients.
Disclosure: Nothing to disclose

EPO2045

Delayed diagnosis in narcolepsy

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Background and aims: Sleep disorders are very prevalent in the population. However, narcolepsy is one of the most infrequent, classificated as a rare disease. We describe the reasons of the delayed diagnostic of our patients with narcolepsy, attended in the Multidisciplinary Unit of Sleep Disorders of the Infanta Sofía University Hospital in Madrid, Spain.
Methods: Retrospective observational descriptive analysis of 30 patients, diagnosed with narcolepsy, attended in the consultation of Neurology of our center from October 2012 to December 2017. We reviewed the sex, the age of the patients to the diagnosis in specialized consultation, and the beginning of the symptoms, the time of delay of diagnosis, the reasons for consultation, and the patient´s previous information search in Internet or social networks.
Results: 601 patients attended in our consult between 2012 and 2017, 30 have narcolepsy, 17 with cataplexy, 13 without it. 15 Men, 15 women. The delayed diagnostic time from the onset of symptoms was 11.8 years. The main reason for consultation was the labor repercussion. 33.33% of the patients had consulted their symptoms using Internet or social networks.
Conclusion: The main reason for consultation in our series is the labor repercussion, including driving. The diagnosis of 30 patients of the potential 70-90 that we should have (in relation to the population of our health area), despite our experience and interest in this pathology, and that only 33.33% of patients had consulted previously their symptoms using Internet or social networks, suggest the need to make this disease better known to the general population.
Disclosure: Nothing to disclose

EPO2047

Kleine-Levin-Syndrome in Pregnancy: A Case Report

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Background and aims: Kleine-Levin syndrome (KLS) is a rare sleep disorder, predominantly affecting males during adolescence. We report a female patient with recurrent episodes of hypersomnia and a long sleeping episode during pregnancy.

Methods: A 26-years-old female patient is presented with recurrent episodes of hypersomnia, starting at the age of 12, shortly before menarche.

Results: Sleep episodes occurred in a frequency of 2-3/year with varying duration, the longest being 3 weeks in 2008, when the patient presented at our clinic the first time. In addition, altered perception and cognitive dysfunction were present, but no hyperphagia or hypersexuality, fulfilling the criteria of the international classification for sleep disorders. Polysomnography, actigraphy and MSLT showed normal results during asymptomatic phases. Encephalopathy was excluded by laboratory results, normal cMRI and normal hypocretin-1 level in cerebrospinal fluid.

After 2010, the episodes became less frequent and shorter until 2017, when the patient developed hypersomnia lasting from the 8th to the 18th week of pregnancy. Polysomnography showed a sleep duration of >14 hours with normal sleep architecture, 8 sleep cycles. Genetics confirmed HLA positivity for HLA DQB1*0201 with maternal transmission. For 2 weeks the patient was treated with i.v. infusions and s.c. heparin to prevent dehydration and thrombosis. The patient slowly became more vigilant and mobile without using any medication because of pregnancy.

Conclusion: This is the first case of KLS with a dramatic hypersomnia episode during pregnancy. Sleep studies and HLA-results are presented and discussed together with pathophysiology.

Disclosure: Nothing to disclose

Movement disorders 2

EPO2049

Trust the Patient not the Doctor: Health-related Quality of Life in Cervical Dystonia

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Background and aims: Non-motor symptoms are a feature of cervical dystonia and can affect quality-of-life, despite effective therapy with botulinum toxin. It has been postulated, disordered subcortical mechanisms related to the interpretation of salient emotional stimuli might be a factor in their pathogenesis.
Methods: We prospectively collected data on health-related quality-of-life(HrQoL) and anxiety and depression measures in patients with cervical dystonia attending a University Hospital specialist clinic. Cervical Dystonia Impact Profile–58(CDIP-58) assessed HrQoL; mood disorder was assessed via Beck Anxiety Index(BAI-II) and Beck Depression Index(BDI-II); dystonia severity was assessed using the TWSTRS-2 severity-scale and pain-scale
Results: The 38 patients who completed all assessments indicated: 1): HrQoL measured by the CDIP-58 inversely correlated with depression by the BDI($r2=0.39$; $p< 0.0001$), anxiety by BAI-II($r2=0.43$; $p< 0.0001$). 2):HrQoL measured by the CDIP-58 significantly inversely correlated with the TWSTRS Pain scale($r2=0.30$; $p=0.0004$) but not with dystonia severity measured by TWSTRS-2($r2=0.09$; $p=0.064$). 3):The TWSTRS–2Severity-Scale correlated weakly with the BAI($p=0.037$), and the CDIP sub scales sleep($r2=0.13$; $p=0.02$), Head & neck ($r2=0.24$; $p=0.002$), pain($r2=0.13$;$p=0.026$).
Conclusion: Initial findings from this patient cohort suggest that self-report measures, are a valid measure of the impact of cervical dystonia in everyday life highlighting the importance of psychological symptomatology in . These findings also question the sensitivity and relevance of the measurement of dystonia severity by physicians using the TWSTRS–2 severity-Scale.
Disclosure: Nothing to disclose

EPO2050

Complications and side effects of DBS surgery in patients with Parkinson's disease

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Background and aims: DBS is effective surgical treatments in advanced PD. DBS is a minimally invasive procedure but may be burdened by complications due to the surgical procedure, to the hardware and side effects (SE) during the chronic stimulation. The frequency of complications and SE depends on the experience of an multidisciplinary team and surgical methods of the DBS center.
To study complications and SE of DBS surgery in PD patients in Belarus.
Methods: 48 patients have undergone surgery for PD since 2011. 26 male and 22 female, mean age 55.5±7.4. There are 30 patients–II stage of H&Y, 18–with III-IV. 36 patients with DBS STN, 8–DBS Gpi, 3–DBS Vim, 1–DBS STN LE, Gpi RE.
Results: Complications due to the surgical procedure: pneumocephaly in one patient with transient decrease in strength in the right hand and motor aphasia, in another patient ischemia in the left subthalamic nucleus with hemiballism in the right limbs. Complications due to the hardware: migration of IPG in one patient, lead migration in one patient, IPG infection in two patients, chronic erosion with local infection at the scalp in two patients. SE dysphonia/dysarthria in 5 patients, gait and balance disturbances (freezing) in 8 patients, transient paresthesias in DBS STN patients, weight gain in 38 patients, personality and mood changes in 5 patients.
Conclusion: The incidence of complications and SE of DBS surgery in PD patients in Belarus is comparable with other DBS center with surgical team's experience and methods of operation.
Disclosure: Nothing to disclose

EPO2051

Screening Adults with Neurodegenerative Disorders for Niemann-Pick type C Disease: A retrospective study of a large cohort of a Greek tertiary Academic center

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Background and aims: Niemann–Pick type C (NPC) disease is a rare fatal lysosomal storage disease of autosomal inheritance, resulting from mutations in NPC1 or NPC2 genes. Disease presentation has a broad clinical spectrum, ranging from a neonatal rapidly fatal disorder to an adult onset neurodegenerative disease. Recently, patients aged over 50 years, with the late form of the disease, have been increasingly described, indicating that many patients in this spectrum may remain unrecognized. We retrospectively accessed with the NPC-Suspicion Index (NPC-SI) adults with neurodegenerative diseases for further biochemical evaluation for NPC.
Methods: We conducted a chart review of symptom presentation in 1000 patients during the period of 2012-2017. Of those 117 'suspected NP-C' cases, plasma oxysterols (OxTs) and chitotriosidase (ChT) levels were determined. Lyso-SM-509 was additionally measured in six patients, and one patient, with the highest OxT and ChT levels, was genetically tested.
Results: Out of 1000 patients, 72.6% were classified as low, 21% as moderate and 6.4% as high likelihood in the NPC–SI. Eight patients presented with elevated OxT, and 10 with increased ChT levels. Lyso-SM-509 and genetic testing were negative.
Conclusion: NP-C in adults may be extremely rare in Greece. The NPC–SI is more sensitive than specific, since other more common neurodegenerative disorders presented with gaze palsy abnormalities and/or an ataxia syndrome, scoring high in the NPC –SI, are prevalent. Plasma OxT and ChT are not NP-C specific, while methodological issues, such as cut-off levels, should be considered in order to improve screening specificity.
Disclosure: Nothing to disclose

EPO2052

Sleep disorders and other non-motor symptoms in a cohort of p.A53T alpha-synuclein (SNCA) mutation carriers.

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Background and aims: Parkinson's disease (PD) has a long prodromal phase with non-motor signs which form the pre-clinical phase of the disease. Asymptomatic carriers of the p.A53T mutation in the SNCA gene represent a population at high risk for developing PD. Non-motor symptoms, and in particular sleep disorders, have not been sufficiently assessed in such subjects. Thus, the aim of this study was to evaluate non-motor symptoms in asymptomatic p.A53T carriers and sleep disorders in both asymptomatic and symptomatic carriers.
Methods: Seven asymptomatic p.A53T carriers underwent UPDRS III, Epworth Sleepiness Scale, RBDSQ, UPDRS I, UPDRS Ia, SCOPA-AUT, QUIP, UPSIT, GDS and MOCA. Five of them underwent DAT Scan and four polysomnography (PSG). We have also assessed eight symptomatic carriers with PSG, Epworth Sleepiness Scale, RBDSQ and MOCA.
Results: DAT Scan was normal in all 5 asymptomatic carriers tested. Cognition and olfactory function were within normal limits, except for one case of relatively advanced age with a marginal MOCA and a very low UPSIT score. All seven asymptomatic subjects reported anxiety, four reported bowel and urinary dysfunction, and five mild depression. As far as sleep disorders are concerned, six out of eight symptomatic and only one asymptomatic carrier, treated with antidepressants, had polysomnographic evidence of REM Sleep Behavior Disorder (RBD) or REM Sleep without Atonia (RWA).
Conclusion: Certain non-motor symptoms may antedate nigrostriatal dopaminergic degeneration in p.A53T SNCA-related Parkinsonism. RWA or frank RBD seem not to precede motor symptoms, but to manifest in the majority of symptomatic carriers who already have motor dysfunction.
Disclosure: Nothing to disclose

EPO2053

Normal substantia nigra echogenicity in suspected Parkinson's Disease: False negative or true negative results? A follow-up study

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Background and aims: Substantia nigra hyperechogenicity (SN+) as detected by Transcranial Sonography (TCS) is useful for Parkinson's Disease diagnosis, although a proportion of 15% false negative results of unknown significance exists. However, most TCS studies are transversal, and diagnosis of PD may change during follow-up.

Methods: We analysed our prospective database of TCS (December 2012-January 2015): patients with sufficient bone window, to whom TCS was performed because of suspected PD, with a minimum follow-up of three years were selected and classified regarding basal SN echogenicity (SN+/SN-). Clinical variables were compared with appropriate statistical tests.

Results: 149 patients (104 SN+, 45 SN-), with mean age of 71 years (25-90) and 46 months (36-60) follow-up were included. Male sex was more frequent in SN+ group (69 vs. 51%, p 0.03). There were no differences in atypical sonographic features, non-motor symptoms or family history. At the end of follow-up, PD diagnosis was retained by 88% in SN+ vs. 55% subjects in SN- group (p:0.000016). Conversely, final diagnosis of Atypical Pakinsonism (AP) (7% vs. 20%, p:0.016) and essential tremor (3% vs. 11%, p:0.004) were more frequent in SN- group. Dopaminergic therapy response was associated with baseline SN+ (87% vs. 53%, p:0.000011), as were abnormal DaT-scans (91% vs 59%, p:0.009).

Conclusion: Our patients with suspected PD and baseline normal SN echogenicity responded less to PD therapy and converted to a diagnosis different from PD more frequently than SN+ subjects. In this setting, normal SN appears to be a caveat for clinicians to check for AP features during follow-up.

Disclosure: Nothing to disclose

EPO2054

Tolerability, Pharmacokinetics and Pharmacodynamic Effects of ODM-104 a Novel Catechol-O-Methyltransferase Inhibitor, after Single Escalating Doses in Healthy Subjects

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Background and aims: ODM-104 is a novel Catechol-O-methyltransferase (COMT) inhibitor aimed at the treatment of Parkinson's disease in combination with levodopa and an aromatic amino acid decarboxylase (AADC) inhibitor. The objectives of this first-in-man study were to evaluate the tolerability, pharmacokinetics and pharmacodynamic effects (COMT inhibition in erythrocytes) of ODM-104 following single oral doses in healthy male volunteers.

Methods: This was a randomised, double-blind, placebo-controlled, single-dose escalation study with an alternating 3 panel crossover design and 8 dose levels (2, 10, 25, 50, 100, 200, 400 and 800 mg). There were 6 study subjects on ODM-104 treatment and 3 subjects on placebo at each dose level. Each subject received active treatment or placebo for a total of 2 or 3 periods.

Results: ODM-104 was well tolerated at all doses tested. The absorption of ODM-104 was rapid, tmax was achieved in 0.8-2.2 h. Systemic exposure of ODM-104 and its main circulating metabolite increased in an approximately dose-proportional manner. The terminal elimination half-life of ODM-104 was 4.2-21.1 h. Maximum COMT inhibition by ODM-104 was dose dependent, ranged from 22% (2 mg) to 87% (800 mg), and reached statistical significance at all doses tested. In similar setting 200 mg of entacapone has produced maximum COMT inhibition of 38-65%. After ODM-104 the COMT inhibition lasts substantially longer than after entacapone.

Conclusion: ODM-104 was well tolerated and presented rapid absorption and close to dose-proportional kinetics. ODM-104 produced clear and long lasting COMT inhibition.

Disclosure: The study was sponsored by Orion Pharma

EPO2055

Cerebrospinal fluid flow dynamics in Huntington's disease using phase contrast MRI: a pilot cross-sectional study

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Background and aims: The objective of this study was to generate pilot data on cerebrospinal fluid (CSF) flow dynamics in Huntington's disease (HD) using phase contrast MRI (PCMRI), to inform the design of future intrathecal drug trials in HD.
Methods: We performed a prospective cross-sectional analysis of 10 age- and gender-matched healthy controls and 10 manifest HD gene expansion carriers. All participants underwent extensive clinical evaluation and cardiac-gated PCMRI at the level of the Aqueduct of Sylvius, T1 and T10. CSF velocities and flow measurements were derived using a semi-automated method. The influence of age, gender, CAG repeat-length, serum osmolality, whole-brain volume, and ventricle volume on these measurements were tested using Spearman correlations or Fisher's exact tests. Group comparisons between healthy controls and manifest carriers were achieved via two-sample Wilcoxon rank-sum tests. All tests were two-sided with a significance level of 0.05, and corrected for multiple comparisons.
Results: Twenty participants were recruited, and no significant age- and gender-imbalances were found. None of the studied covariables was found to have an effect on the CSF velocities and flow measurements after corrected for multiple comparisons. No apparent differences were found between study groups in regards to CSF velocities and flow measurements.
Conclusion: Although under-powered, our pilot results add to the view that CSF dynamics are not altered in HD. These results need external validation but offer reassurance that clinically-relevant disease-related alterations in CSF flow, that might justify dose-adjustments of intrathecal drugs, are very unlikely to exist.
Disclosure: Nothing to disclose

EPO2056

Movement disorder specialists' determination of eligibility for device aided treatment in advanced Parkinson's disease: Results from the OBSERVE-PD study

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Background and aims: To characterize the clinical and non-clinical features of PD patients considered to be eligible or ineligible for device-aided treatment by movement disorder specialists.
OBSERVE-PD was a cross-sectional, observational, multicenter study. A previous analysis reported that physicians judged 51% of the PD patients in participating movement disorder centers as 'advanced'.
Methods: This is a post-hoc analysis of the clinical and non-clinical characteristics of 'advanced' PD patients judged eligible or ineligible for device-aided treatment by the treating physician. Device-aided treatments included levodopa-carbidopa intestinal gel, also known as carbidopa-levodopa enteral suspension, apomorphine SC infusion, and Deep Brain Stimulation. Patients were analyzed using descriptive statistics.
Results: 66% (n=876) of advanced PD patients were considered eligible for device-aided treatment. Device-aided treatment-eligible patients were on average(SD) 66.0 years(9.2) (mean PD duration: 12.2 years(5.5). Device-aided treatment-ineligible patients had a mean(SD) age and PD duration of 70.6(9.1) and 8.6(5.5) years, respectively. Reasons for lack of device-aided treatment use primarily included: patient needing more decision making time (43%) and patient refusal (28%). No patients stated cost or lack of reimbursement as reasons for lack of use [table1]. Of the 876 'advanced' and eligible PD patients, 383(44%) had ongoing device-aided treatment, 163(19%) began device-aided treatment during the study visit, and 330(38%) had no device-aided treatment planned [table2].

Table 1. Reasons for device-aided treatment (DAT) ineligibility

Reason for DAT-ineligibility	n (% of 460)
Patient needs more time to decide	143 (43%)
Patient refusal	94 (28%)
Cognitive related issues	27 (8%)
Psychiatric related issues	23 (7%)
Comorbidities	20 (6%)
Age	12 (4%)
Lack of caregiver/family support	11 (3%)
Motor function related issues	6 (2%)
Cost/reimbursement	0 (0%)
Other reason	45 (14%)

[a]Multiple entries for each patient were possible

DAT = device-aided treatment

Table 2. Baseline characteristics of DAT-eligible and DAT-ineligible 'advanced' PD patients

Baseline characteristics	Ongoing DAT (N=383)	DAT-eligible (Total N=876) Planned DAT (N=183)	Not Planned (N=330)	DAT-Ineligible (Total N=460)
Demographics				
Age, years, mean (SD)	65.1 (8.7)	64.3 (9.0)	67.9 (9.6)	70.6 (9.1)
Gender, female, n (%)[a]	145 (38%)	61 (37%)	132 (40%)	186 (40%)
Caregiver support, yes, n (%)[a]	278 (73%)	109 (61%)	242 (74%)	286 (63%)
Medical history				
PD duration, years, mean (SD)[a]	14.2 (5.6)	10.1 (4.7)	11.1 (5.7)	9.6 (5.5)
Motor fluctuations, yes, n (%)[a]	335 (92%)	154 (84%)	323 (96%)	338 (74%)
Motor fluctuation duration, years, mean (SD)[a]	7.2 (4.3)	4.2 (2.8)	4.4 (3.5)	3.3 (2.8)
Comorbidity, yes, mean (SD)[a]	327 (85%)	135 (85%)	301 (91%)	431 (94%)
Time since referral to center, years, mean (SD)[a]	5.2 (5.5)	2.7 (3.7)	4.7 (4.8)	4.0 (4.8)

[a]DAT ongoing N=384, DAT planned N=164, DAT not planned N=332, [b]DAT ongoing N=399, DAT planned N=162, DAT not planned N=328, DAT ineligible N=455; [c]DAT ongoing N=372, DAT planned N=160, DAT not planned N=322; [d]DAT not planned N=332, DAT-ineligible N=448; [e]DAT-ongoing N=351, DAT-planned N=137, DAT-ineligible N=334; DAT-not planned N=312; [f]DAT-ongoing N=305, DAT-planned N=118, DAT-not planned N=231, DAT-ineligibility N=340, DAT = device-aided treatment

Conclusion: This analysis shows a trend for advanced PD patients judged device-aided treatment-ineligible to be older individuals, with shorter disease duration, however direct statistical comparisons were not performed. Device-aided treatment-ineligibility was primarily related to patient refusal/needing additional time to decide.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO2057

Prevalence and Correlates of Anxiety & Depression in Cervical Dystonia

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Background and aims: Non-motor symptoms, anxiety and depression are prominent in Cervical Dystonia and can affect quality-of-life, despite therapy of motor symptoms with botulinum-toxin. Our aim was to assess the prevalence and severity of mood disorder in our Cervical Dystonia population attending the botulinum toxin clinic and to assess their effect on quality-of-life.

Methods: We prospectively collected data on anxiety, depression measures in patients with cervical dystonia attending clinic. Health related quality-of-life (HrQoL) was assessed using the Cervical Dystonia Impact Profile–58 (CDIP-58); mood disorder was assessed using the Beck-Anxiety-Index (BAI-II), Beck-Depression-Index (BDI); Dystonia severity was assessed using the TWSTRS-2 severity-scale and pain-scale.

Results: A cohort of 70 patients (50 women) with cervical dystonia were surveyed; 28/70(40%) reported symptoms of anxiety using the BAI. In 66 patients who completed the BDI-II, 30(45%) reported symptoms of depression; 18/66(27%) had BDI-II scores indicating moderate-to-severe depression. 40/70(57%) patients reported depression and/or anxiety. A weakly significant correlation between anxiety, measured by the BAI and the TWSTRS pain scale (R2=0.163; p=0.0006) but no correlation with the TWSTRS–2 severity scale (R2=0.024; p=0.2 . Similarly depression measured by the BDI–II correlated weakly with the TWSTRS pain scale (R2=0.151; p=0.001) but no correlation with the TWSTRS–2 severity scale (R2=0.009; p=0.44).

Conclusion: Significant findings of (57%) patients with cervical dystonia have concurrent anxiety and/or depression. The lack of correlation with disease severity, and low correlation with pain suggests non-motor symptoms may have pathogenic mechanisms unrelated to motor-disorder.

Disclosure: Nothing to disclose

EPO2058

Safety and Efficacy of Levodopa-Carbidopa Monotherapy in Patients With Advanced Parkinson's Disease

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Background and aims: To evaluate the efficacy/safety of levodopa-carbidopa intestinal gel (LCIG) daytime monotherapy (with/without nighttime oral carbidopa/levodopa) vs polytherapy (LCIG with >1 adjunctive therapy) in patients with advanced Parkinson's disease (APD).

Treatment of motor complications often requires multiple adjunctive PD therapies. Continuous administration of LCIG reduces motor complications associated with oral levodopa, while potentially simultaneously reducing pill burden.

Methods: LCIG was administered continuously 16 hours/day via percutaneous endoscopic gastrojejunostomy (PEG-J) to patients with APD in two phase 3 studies. In the first study, a 52-week open-label extension of a 12-week double-blind study (patients received either LCIG or oral carbidopa/levodopa), both groups received LCIG, and adjunctive therapies could be tapered off. In the second study, a 54-week, open-label study of LCIG, adjunctive therapies were allowed after week 4.

Results: Study 1 included 30 patients on LCIG daytime monotherapy and 32 patients on LCIG polytherapy. In study 2, of 324 patients with PEG-J placement, 248 (76.5%) were on LCIG daytime monotherapy (of these, 90 patients received no overnight oral carbidopa/levodopa). Total daily levodopa dose increased with LCIG use in all groups. In both studies, patients on daytime LCIG monotherapy experienced similar reductions in "Off" time and improvements in "On" time compared with patients receiving LCIG polytherapy. Adverse events were similar for both groups.

Conclusion: Daytime LCIG monotherapy and polytherapy demonstrated similar efficacy/safety profiles in two phase 3 studies in patients with APD, suggesting that LCIG monotherapy can provide a more simplified treatment option with similar efficacy for appropriate patients.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO2059

Effect of levodopa-carbidopa intestinal gel on dyskinesia: Design of an open-label, randomized multicenter 12-week study in advanced Parkinson's disease patients

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Background and aims: To examine the effect of levodopa-carbidopa intestinal gel (LCIG, designated carbidopa-levodopa enteral suspension in the US) treatment relative to that of optimized medical treatment (OMT) on dyskinesia in advanced Parkinson's disease (PD) patients.

LCIG, delivered continuously via percutaneous gastrojejunostomy, reduces wearing off of levodopa therapy in advanced PD patients, but data on dyskinesia are limited. The DYSCOVER (dyskinesia comparative interventional trial on LCIG versus oral medication) study will be the first interventional, randomized study investigating the efficacy of LCIG on dyskinesia in advanced PD patients.

Methods: Sixty LCIG-naïve advanced PD patients with severe motor fluctuations and dyskinesia will be enrolled in movement disorders centers in accordance with local product label. Prior to recruitment, patients will have reached the maximum therapeutic effect of oral anti-PD therapies. Patients will be randomized (LCIG treatment group or OMT group) for 12-weeks of treatment with scheduled study visits. Subjects randomized to OMT will continue their current anti-PD medication regimen.

Results: The primary efficacy outcome will be the mean change from baseline to week 12 in the Unified Dyskinesia Rating Scale (UDysRS) total score. Key secondary endpoints include "On" time without troublesome dyskinesia, the 8-item PD Questionnaire (PDQ-8), the Clinical Global Impression of Change assessment, the Unified PD Rating Scale (UPDRS) part II score, "Off" time, and UPDRS part III score. Adverse events will be monitored.

Conclusion: Robust evidence is lacking for device-aided medical treatments in advanced PD. This study is designed to determine whether LCIG is an effective management strategy for the treatment of dyskinesia in advanced PD.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

Movement disorders 3

EPO2060

Regional Diffusion of Botulinum toxin to Contralateral Facial Musculature and its Effects on Neuromuscular Junction after Repeated Injections

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Background and aims: Hemifacial spasm (HFS) is characterized by initially progressive, involuntary, irregular, clonic or tonic movements of muscles innervated by the seventh (facial) cranial nerve on one side of the face. Treatment of this condition primarily includes botulinum toxin injections. It is generally agreed that diffusion of botulinum toxin occurs, but the extent of the spread and its clinical importance are disputed. The twitching on the contralateral facial sides in some of the patients with hemifacial paralysis, whose having treatment of botulinum toxin for years prompted us to investigate the spreading effect.

The aim of the stduy is to investigate the whether there is a regional diffusion and effect on neuromuscular junction in the contralateral facial mucles after repeated injections.

Methods: The study was designed as prospective randomized and were evaluted 19 female, 20 male patients (19-65 years) diagnosed with hemifacial spasm. Parameters of efficacy and diffusion (CMAP; SFEMG; MCD and jitter analysis) in both orbicularis oculi muscles were assessed at baseline, before botulinum toxin injection and 4 weeks following injection.

Results: CMAP of the threated orbicularis oculi muscles was significantly reduced. Contralateral CMAP reduction was observed too. Jitter analysis was performed, in order to assess neuromuscular transmission failure in the contralateral orbicularis oculi, at baseline before botulinum toxin injection and 4 weeks after the injection.

Conclusion: The results showed the mean jitter value was significantly increased. We observed higher jitter values in patients receiving repeated treatment for years.

Disclosure: Nothing to disclose

EPO2061

Longitudinal development of nigral iron load in Parkinson's Disease

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Background and aims: Iron accumulation in the substantia nigra (SN) is discussed to be an important factor in the pathogenesis of Parkinson's disease (PD). We for the first time investigated longitudinal changes of nigral iron load measured by Quantitative Susceptibility Mapping (QSM), a highly iron-sensitive MRI method.

Methods: We included 52 PD-patients (36 male, mean age 62.6±10.7; mean disease-duration 4.1 years) and 29 healthy controls (HC) (13 male; mean age 68.1±9.1). All subjects underwent a clinical examination and a 3T MRI scan at baseline and after a follow-up period of approximately 2 years. For group comparisons we performed ANOVAs, corrected for age, gender and between-scan-time.

Results: QSM values in total SN, SN pars compacta (SNc) and SN pars reticulata (SNr) were significantly higher in PD compared to HC ($p<0.001$) at baseline and follow-up. There were no significant group differences in longitudinal QSM-change. QSM values in PD tented to increase in SNc and decrease in SNr, in HC they tended to decrease in SNc and SNr. There was no significant correlation for QSM change and change in clinical parameters (MDS-UPDRS, FTM-tremor rating scale, Non Motor symptoms questionnaire, MMSE, LED).

Conclusion: We confirmed higher nigral iron load in PD compared to HC. However there was only a not significant trend for stronger shortterm longitudinal increase of iron concentration in SNc in PD compared to HC. This might be due to relatively long baseline disease-duration in our PD subjects and suggests nigral iron accumulation as an early factor in the pathogenesis of PD.

Disclosure: Nothing to disclose

EPO2062

Dysphagia predicts poor outcome in late-stage Parkinson's disease

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Background and aims: Few data exists on the rate of clinical progression of disability milestones and prognostic factors for Parkinson's disease (PD) patients who have entered a very late stage of disease. Our aim was to to evaluate the clinical progression and prognostic factors of a late-stage PD (LSPD) population.
Methods: 50 LSPD patients (Schwab and England ADL Scale <50 or Hoehn Yahr Stage >3 in MED ON) and 17 advanced (AD) PD patients matched for age at disease onset underwent an acute levodopa challenge test and an extensive cross-sectional clinical assessment for motor, non-motor symptoms (NMS), quality of life (QoL) and caregiver burden. LSPD patients were also assessed at one year follow-up.
Results: LSPD patients present a more severe clinical picture, with prominent axial motor and NMS, that negatively influenced QoL. LSPD and ADPD patients' MDS-UPDRS-III score significantly improved after levodopa ($p < 0.001$), respectively 18% and 53% (Table 2). The magnitude of levodopa response significantly correlated with motor complications in LSPD. After one-year, 20% of LSPD patients were dead. Overall, after 1 year follow-up there was still clinical worsening of motor symptoms (worsening of MDS-UPDRS-III mean±SD 7.7±10.3) and NMS although heterogeneous. Nevertheless, motor fluctuations and dyskinesias improved. Functional independence worsened. Dysphagia severity at baseline significantly predicted a poor outcome (death, institutionalization or HY 5).
Conclusion: LSPD patients still present a significant, although heterogeneous, progression in motor and non-motor features. Dysphagia severity influences the progression of additional disability milestones.
Disclosure: Nothing to disclose

EPO2063

Differences between early-onset and "normal"-onset Parkinson's Disease in Greece: Data analysis of the Hellenic Biobank of Parkinson's Disease

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Background and aims: The aim of this study is to compare clinical characteristics and environmental exposures between early-onset (≤50 years) and "normal"-onset (>50 years) PD.
Methods: Our data derived from the Hellenic Biobank of PD, consisting of blood samples, clinical and lifestyle information of PD cases and controls during 2006-2017. Cases with A53T mutation in SNCA or mutations in GBA1 gene were excluded. OR and 95% CI were calculated for each factor. Quantitative variables were analyzed with Mann-Whitney test and Spearman's correlation coefficient.
Results: 98 patients with early-onset and 469 patients with "normal"-onset PD were included. Early-onset PD was associated with family history of PD (OR=1.613, 95% CI=1.019-2.555) and cigarette smoking (OR=2.013, 95% CI=1.240-3.268). Smoking years were not associated with onset age of PD (p=0.182). Dystonia and motor complications were more common in early-onset PD (OR=4.665, 95% CI=2.612-8.329, OR=2,858, 95% CI=1.809-4.514 respectively). The mean disease and dopaminergic treatment duration were longer in early onset PD ($p<0.001$, $p<0.003$ respectively). There were no associations between onset age of PD and gender, coffee consumption, pesticide exposure, tremor, bradykinesia, rigidity, gait disturbances, postural instability, autonomic dysfunction, dementia, depression or psychosis.
Conclusion: Family history, cigarette smoking, dystonia and motor complications are more common in early-onset PD in this Greek cohort. The longer disease and dopaminergic treatment duration may explain the more common motor complications in early-onset PD. The stronger genetic influences in younger ages may explain the "loss" of negative association with smoking in early-onset PD.
Disclosure: Nothing to disclose

EPO2064

Symptoms of peripheral neuropathy in Idiopathic Parkinson's Disease: prevalence and impact on quality of life; a case controlled study

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Background and aims: Neuropathic symptoms (NS) are commonly reported in Parkinson's Disease (PD), but robust data on the epidemiology of such symptoms are lacking. The present study sought to investigate the prevalence and determinants of peripheral NS in Idiopathic PD (IPD) and ascertain the effects of such symptoms on the patients' quality of life(QoL).
Methods: Patients with IPD and age- and gender-matched controls were screened for NS, using the Michigan Neuropathy Screening Instrument (MNSI). The impact of NS on QoL was investigated using the 36-Item Short Form Survey(SF-36).
Results: 52 patients and 52 age and gender matched controls were recruited.NS were reported more frequently in patients with IPD than in controls(82.7% versus 44.2%, $p<0.001$). Mean MNSI total score was 3.2±2.2 for IPD compared to 1.4±1.4 for controls($p<0.001$). No significant relationships were found between PD-related clinical characteristics(i.e. disease severity and duration, duration of exposure to levodopa, cumulative levodopa dose etc) and the presence of NS.
Significant correlations were found between the number of NS and emotional role limitations(Spearman's rho -0.484), physical functioning(Spearman's rho -0.473), physical role limitations(Spearman's rho -0.373), energy/fatigue (Spearman's rho -0.299), mental health(Spearman's rho -0.231) and the general health perception(Spearman's rho -0.338).
Conclusion: Our results support the notion of a greater prevalence of NS in IPD patients compared to the general population, which, at least in part, may be secondary to large and/or small fibre peripheral neuropathy. This warrants further investigation in larger studies that include detailed neurophysiological assessments.
Disclosure: Nothing to disclose

EPO2065

Pain in Idiopathic Parkinson's disease: prevalence and impact on quality of life; a case controlled study

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Background and aims: Pain is a frequent non-motor symptom of Idiopathic Parkinson's Disease(IPD). We sought to investigate the prevalence of overall pain and more specifically peripheral neuropathic pain(PNP) in IPD, and ascertain any impact of PNP on quality of life(QoL).
Methods: Patients with IPD and age- and gender-matched controls were screened for overall pain using the King's Parkinson's Pain Scale(KPPS). PNP was assessed using the Michigan Neuropathy Screening Instrument(MNSI). QoL was assessed using the 36-Item Short Form Survey(SF-36).
Results: 51 patients and 51 controls were recruited. The prevalence of overall pain was similar between the two groups(88.2% versus 94.1%, $p=0.487$). However, patients with IPD presented with higher KPPS scores in fluctuation-related(4.9±6.9 vs 1.1±2.6, $p<0.001$), nocturnal(6.6±7.5 vs 1.7±4.2, $p<0.001$) and oro-facial(0.6±2.0 vs 0.0±0.0, $p=0.040$) domains.
When looking specifically into PNP, patients with IPD were experiencing more PNP compared to controls(35.3% versus 13.7%, $p=0.011$).
After adjusting for age, gender, disease duration and overall KPSS score, PNP was significantly correlated with physical functioning(Spearman's rho -0.290), emotional role limitations(Spearman's rho -0.319) and general health perception(Spearman's rho -0.342) domains of SF-36.
Conclusion: PNP is very prevalent in IPD and has a significant impact on the QoL. The aetiology of such pain requires further studies. The presence of burning pain is suggestive of small fiber neuropathy, but is not captured by the KPSS alone, and therefore a revision of the KPSS is needed.
Disclosure: Nothing to disclose

EPO2066

SPG15 with Levodopa-responsive parkinsonism and peak-dose dyskinesia

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Background and aims: Hereditary spastic paraplegias are a heterogeneous group of neurodegenerative pathologies clinically classified in pure and complex forms. Recently, cases of SPG11 and SPG15 with parkinsonism have been reported. In juvenile cases with pyramidal and extrapyramidal signs the differential diagnosis remains a challenge.
Results: Two portuguese sisters, with unremarkable family history, developed a spastic paraparesis and akinetic-rigid parkinsonism in their second decade of life. Soon after the introduction, levodopa became essential to maintain their functionality. Their condition progressively worsened, with mental deterioration, marked spastic paraparesis, ataxia, epilepsy and important extrapyramidal signs: moderate-severe bradykinesia, rigidity, tremor and dystonia. Upon levodopa dose escalation, peak dose dyskinesia appeared (after 3 years under 450 mg/day of levodopa) and were managed with dose reduction and amantadine. Metabolic, infectious, neoplastic and immunological investigations were normal/negative. Genetic study for levodopa-responsive dystonia was negative (GCH1 and TH genes) as were the study of Parkin, PINK1 and DJ-1 genes. Cerebral MRI showed symmetrical T2 hypersignal of the periventricular white matter and thinning of the corpus callosum; I-Ioflupane SPECT revealed nigro-striatal degeneration. Broadening the genetic pursue, and after a normal spatacsin gene sequenciation, the molecular study of the ZFYVE26 gene demonstrated a homozygous pathogenic mutation.
Conclusion: There are only two reports of parkinsonism as a feature of SPG15, both with nigro-striatal loss in I-ioflupane SPECT and partially beneficial levodopa treatment. Our case adds to the existing literature the occurrence of levodopa-induced dyskinesia and strengthens the evidence of SPG15 as a cause of autosomal recessive spastic parapaplegia with levodopa-responsive parkinsonism.
Disclosure: Nothing to disclose

EPO2067

Acute sensorimotor neuropathy as a complication of Duodopa® treatment

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Background and aims: Duodopa® is a modern treatment for advanced Parkinson's disease (PD) administrated via PEG-J by means of a tube connected to an external pump. Duodopa® is delivered continuously in small quanta preventing large plasma level fluctuations and thus suppressing disabling motor complications related to oral treatment in advanced stages of PD.
Methods: We describe the case of a 66-year-old female with a 16-year history of PD with progressive severe motor and psychiatric complications. Due to complications and inefficacy of oral dopaminergic treatment, the patient has been treated with Duodopa®.
Results: In October 2016, Duodopa® was initiated with a positive subjective and objective effect. After successful titration, PEG-J was inserted and patient was released home. During two months she observed worsening of Parkinson symptoms, the dose of Duodopa was increased. In January 2017 pains, paraesthesia and weakness of the lower limbs developed. EMG confirmed acute severe sensorimotor polyneuropathy. The level of vitamin B12 and folate were normal. Due to the normal EMG finding prior to the Duodopa® titration, it was thought of acute neuropathy as a complication of Duodopa® treatment. The Duodopa treatment was discontinued, the patient transferred back to oral dopaminergic treatment. However we observed an improvement in sensory and motor symptoms in four weeks, EMG finding had nearly normalized in six months.
Conclusion: Acute polyneuropathy is one of the rare complications of Duodopa® treatment. The pathogenesis is not clear; it may be changes of the metabolism of vitamin B6, B12, homocysteine or methylmalonic acid.
Disclosure: Supported by GAČR 16-13323S and Progress Q27.

EPO2068

Localisation of Deep Brain Stimulation electrodes within Subthalamic Nucleus and its impact on Non-Motor Symptoms in Patients with Parkinson's Disease

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Background and aims: Deep brain stimulation (DBS) has clear effect on motor symptoms of Parkinson's disease (PD). Recently an effect on non-motor symptom (NMS) has been studied. Subthalamic nucleus (STN) is the most common target of DBS. According to experimental studies, STN consists of sensorimotor, limbic and associative part. The aim of our study was to evaluate the impact of localization of DBS electrodes within the STN on improvement of NMS in patient with PD.
Methods: Each STN was divided using software system SureTune to thirds that represent their sensorimotor, associative and limbic part. DBS electrodes were divided into groups according to the localisation of their tip. Electrodes with tip outside STN were excluded. Non-motor and motor symptoms were then evaluated by using 8 standard questionnaires preoperatively, one month and four months after DBS. Finally, the correlation between position of the tip of the electrode and change of NMS and MS for each side was calculated.
Results: From 43 evaluated electrodes, 1 was placed in limbic, 31 in associative and 11 in sensorimotor part. The first two group were integrated. There was no significant difference in NMS change in groups on both sides. After four months there was only significantly bigger improvement in MDS UPDRS in electrodes localised in limbic/associative part than in sensorimotor part on the left side.
Conclusion: Our pilot study has not proven correlation between position of the tip of the electrode and change of NMS, which could be due to low amount of electrodes. Further research with more patient must be done.
Disclosure: Supported by IGA_LF_2017_039

EPO2069

Carrier mediated delivery system bearing Dopamine for effective management of parkinsonism

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Background and aims: Delivery of drug and sustaining it in effective concentration in brain is challenging due to blood brain barrier (BBB). In the present investigation, amino acid coupled liposomes bearing dopamine-HCl were prepared to deliver drug to the brain utilising receptor-mediated transcytosis for effective management of parkinsonism.
Methods: L-lysine stearylamine conjugate (LSC) was synthesized & LSC coupled liposomes bearing dopamine HCl was prepared by lipid cast film method. Formulations were analysed for average vesicle size, drug entrapment, in-vitro drug release and in-vivo efficacy of the formulations was assessed by measuring the reduction in the degree of drug induced catatonia in albino rats.
Results: Average particle size was found in the range of 1.92-0.80mm. There was increase in the size for coupled liposomes due to the inclusion of LSC in liposomal bilayers. The percent encapsulation efficiency decreased from 46.82±2.17% in uncoupled to 38.13±1.18% in coupled liposomes. The in-vitro drug release after 24hrs was 58.9±2.94% with uncoupled while the coupled liposomes showed 43.7±2.18% drug release. The lower value for coupled formulation could be due to the retardation of drug release caused due to the incorporation of LSC in the liposomal bilayers, which enhanced the structural integrity of the bilayer. In-vivo study reveals that the animals receiving uncoupled liposomes showed partial reduction and animals that received coupled liposomes showed almost complete reduction in catatonia.
Conclusion: Fluoresence study clearly indicates the uptake of 6-CF in blood vessels and accumulated in brain. This could be due to enhanced uptake of Lysine coupled liposomes through amino acid transporters present at BBB surface
Disclosure: Nothing to disclose

EPO2070

Tolerability, pharmacokinetics and pharmacodynamic effects of ODM-104 a Novel Catechol-O-Methyltransferase Inhibitor, after escalating repeated doses in healthy subjects

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Background and aims: ODM-104 is a novel Catechol-O-methyltransferase (COMT) inhibitor aimed at the treatment of Parkinson's disease in combination with levodopa and an aromatic amino acid decarboxylase (AADC) inhibitor. The objectives of this study were to evaluate the tolerability, pharmacokinetics and pharmacodynamic effects (effects on levodopa pharmacokinetics) of ODM-104 following repeated oral doses in healthy male volunteers.
Methods: This was a randomised, double-blind, placebo-controlled, repeated-dose escalation study with parallel group design and crossover comparison to entacapone. At each ODM-104 dose level (10, 25, 50, 100, 200 mg) 6 subjects were on active treatment and 3 on placebo. The subjects received ODM-104 or placebo q.i.d for 7 days. All subjects received levodopa/carbidopa (100/25 mg or 100/65 mg) combined with entacapone (200 mg) q.i.d for 1 day before starting the ODM-104/placebo treatment and with ODM-104/placebo q.i.d during the last treatment day.
Results: ODM-104 was well tolerated at tested dose levels. The maximum concentration (Cmax) and exposure (AUC0-24h) of ODM-104 increased in a dose-dependent manner. The Cmax appeared mainly after the 2nd or 3rd daily dose. The terminal elimination half-life of ODM-104 was 6.6-10 h. ODM-104 accumulated slightly. The increase in levodopa exposure (AUC0-24h) had an ODM-104 dose-dependent trend. 100 and 200 mg doses of ODM-104 produced significantly higher levodopa AUC0-24h than 200 mg of entacapone. The effect was evident with both carbidopa doses.
Conclusion: ODM-104 was well tolerated, presented close to dose-proportional kinetics and slight accumulation during 7 days q.i.d dosing. ODM-104 produced significantly higher levodopa exposure than entacapone.
Disclosure: The study was sponsored by Orion Pharma.

MS and related disorders 3

EPO2071

Oxidative stress parameters in relapsing-Remitting Multiple Sclerosis (RRMS) patients before and after corticosteroid therapy

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Background and aims: Oxidative stress is implicated in the pathophysiology of multiple sclerosis (MS). The aim of our study was to investigate the effect of corticosteroid therapy on oxidative stress parameters in RRMS patients during remission and during relapse (before and after the corticosteroid treatment).
Methods: The study included 60 RRMS patients in relapse and 30 in remission. Prooxidative-antioxidative balance (PAB), nitrate and nitrite as a pro-oxidants and total antioxidative status (TAS), paraoxonase, transferrin, bilirubin and uric acid as antioxidants were measured in plasma in remission (Control), before (Group I) and a day after corticosteroid therapy (Group II).
Results: Statistically significant difference was found among Group I, Group II, Control in PAB values (150.3 vs 133.8 vs 127.4 HKU) and nitrate and nitrite production (4.42 vs 3.93 vs 3.63 μmol/L), having lower levels of pro-oxidants after corticosteroid treatment and in remission. Antioxidants were significantly decreased after corticosteroid therapy-TAS (911.9 vs 810.5 vs 977.2 μmol/L), paraoxonase activity (395.3 vs 368.2 vs 422.4 U/L) uric acid (263.1 vs 206.1 vs 279.2 μmol/L), bilirubin (11.89 vs 10.64 vs 12.07 μmol/L) and transferrine values (2.51 vs 2.41 vs 2.61 g/L), being the highest in a remission.
Conclusion: Our results showed increased levels of pro-oxidants and higher antioxidant activity in relapse, while remission was characterized with lower pro-oxidant and the highest antioxidant activity. Corticosteroid therapy resulted in decreased production of free radicals and consequent lessen antioxidant activity.
Disclosure: Nothing to disclose

EPO2073

Pupillometry enhances the detection of optic nerve damage in multiple sclerosis without a history of optic neuritis: prediction of Visual evoked potential latency

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Background and aims: The present study was conducted to investigate alterations in the pupillary light response measured by automatic pupillometry and to assess its potential associations with latency prolongation of the visual evoked response (VEP) in non-ON RRMS patients.
Methods: We investigated P100 latency and pupillometry parameters including neurological pupil index (NPi), pupil size (PS), minimum size of pupil (MinPS), percentage change of pupil size (CH), Constriction Velocity (CV), Maximum of Constriction Velocity (MCV), Dilation Velocity (DV) and latency (LAT) from 62 non-ON RRMS and 80 control. Independent-samples t-tests were run, first to determine pupillometry differences between the right eye of cases and controls and then, to determinate differences across age-matched controls and cases while p100 latency was in normal range. To assess P100 latency variation in terms of EDSS and pupillometry variables, right eyes of non-ON cases were quantified through multiple regression.
Results: The mean comparison of case and control subjects showed statistically significant differences of -0.56, p=.002; -0.24, p=.01; -3.18, p=.015; -0.53, p=.01 for PS, MinPS, CH, MCV, respectively. And under normal p100 classification,it was revealed that there were statistically significant differences of -0.77, p=.007; -5.38, p=.006; -0.78, p=.015 for PS, CH and MCV, respectively. EDSS and CH statistically significantly predicted P100 $p<0.005$, $R2=18.3\%$.
Conclusion: Pupillary light response parameters are affected by the pathophysiologic process in MS disease even in the absence of ON and latency prolongation of VEP. CH alongside EDSS can predict p100 latency with a medium effect size.
Disclosure: Nothing to disclose

EPO2074

Evaluation of brain atrophy in early Multiple Sclerosis by corpus callosum index

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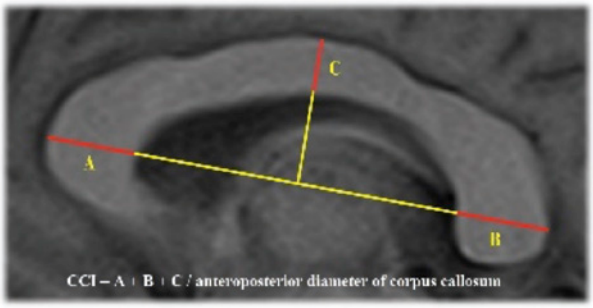
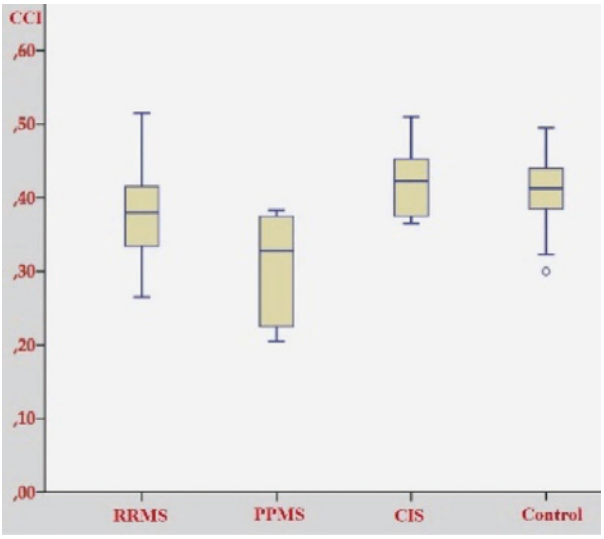
Background and aims: Neurodegeneration has emerged as a significant phenomenon in Multiple Sclerosis (MS) even in the earliest stage of the disease. Recently, the corpus callosum index (CCI) has been described as a reliable biomarker correlated with whole brain volume and long-term disability. Our aim is to assess the applicability of CCI in newly diagnosed patients.
Methods: We prospectively enrolled 76 patients who were studied between October 2012 and August 2016 with a new diagnosis of CNS demyelinating disease. The control group consisted of 101 age-matched healthy controls. CCI was obtained in 241 brain MRI by manual measurements (on a conventional best mid-sagittal T1W, T2 and FLAIR).



Results: Among the 76 patients in the study (29% males, 71% females, mean age 37.4 years), 82.9% filled the criteria for relapsing-remitting MS (RRMS), 6.6% for primary progressive MS (PPMS) and 10.5% were diagnosed with Clinically Isolated Syndrome (CIS). Their mean CCI was 0.373 (SD 0.05, CI95%). In the control group (64% females, mean age 37.7 years), mean ICC was 0.411 (SD 0.03, CI95%). There was a reduction in mean CCI observed in both groups of MS patients, markedly in PPMS group (0.303), but also among RRMS patients (0.372), when compared to healthy controls. No differences between CIS patients (0.421) and controls (0.411) were observed.



Conclusion: Our study confirms a reduction in CCI in the early stages of MS. This method could be a useful alternative to volumetric measurements, which are almost restricted to clinical trials nowadays
Disclosure: Nothing to disclose

EPO2075

Optical coherence tomography is less sensitive than visual evoked potentials in clinically isolated syndrome suggestive of Multiple Sclerosis

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Background and aims: Visual evoked potentials (VEPs) and optical coherence tomography (OCT) can detect demyelination and neurodegeneration in the visual pathway, with higher sensitivity of VEPs reported in clinically definite MS and first-ever optic neuritis. Our aim was to compare the sensitivity of VEPs and OCT in patients with Clinically isolated syndrome–CIS suggestive of MS.
Methods: 71 patients with CIS (43 females, mean age 34.3 + 9 years) underwent VEPs and OCT with measure of VEP latency and of thickness of the peripapillary retinal nerve fibre layer (RNFL) in both eyes.
Results: Considering all patients, VEPs were abnormal in 43.7% and OCT in 15.5% of patients; 8 patients (11.3%) had both abnormal VEPs and OCT, 23 (32%) had abnormal VEPs only, 3 patients (4.2%) had abnormal OCT only (McNemar's Chi squared 13.885, p=0.0002). Considering optic neuritis at presentation (n=24, 33.8%), VEPs were abnormal in 22 (91.7%) patients and OCT in 7 (29.2%). In patients without ON, abnormal VEPs were found in 9 patients (19.1%) and OCT in 4 (8.5%).
Conclusion: Our findings of a higher sensitivity of VEPs in CIS are consistent with previous literature in MS and isolated optic neuritis. OCT adds little to VEPs in detecting visual pathway involvement, particularly in patients without optic neuritis. Longitudinal monitoring is required to assess comparative value of the two methods in proving optic nerve involvement as an indicator of dissemination in space and their prognostic value on conversion to MS.
Disclosure: Nothing to disclose

EPO2076

Unmet needs of patients transitioning to secondary progressive Multiple Sclerosis: qualitative findings for a resource development

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Background and aims: About 50% of relapsing multiple sclerosis (MS) patients convert to secondary progressive (SPMS) 15 years after clinical onset. Despite the complexity and potential impact of this transition, no targeted interventions to promote patients' wellbeing are available. Managing the Transition to SPMS (ManTra) aims to develop and assess the efficacy of a user-led resource for newly diagnosed SPMS patients. Here, we describe a key project phase: assessment of the experiences and needs of SPMS transition.
Methods: We performed: personal semi-structured interviews with 15 recently diagnosed SPMS patients; three focus groups (with patient significant others, neurologists, and other MS health professionals [HPs] across Italy). Interviews and focus groups were audio-recorded, transcribed verbatim, and analysed (framework method).
Results: Data analysis revealed 62 sub-categories, grouped into 10 categories and four themes: 'Awareness of the transition'; 'Transition'; 'Reaction to disease progression'; 'Resources'. All stakeholders agreed on the following unmet needs: management of SPMS at the MS Centre; psychological support; HP training; communication/ information; job/welfare.
Conclusion: We observed a general lack of communication of the transition by neurologists and low awareness by SPMS patients who massively used defensive mechanisms. All stakeholders unanimously asked for improved management at the MS center, provision of psychological support, specific HP training, access to more information, dedicated worker protection policies and job outplacement

in this disease phase. Our findings will be combined with those of the ongoing German qualitative study. An online survey (>400 recently diagnosed Italian and German SPMS patients) will follow to substantiate needs on a large, independent sample.

Disclosure: This study is supported by the Fondazione Italiana Sclerosi Multipla (FISM, grant 2015/R/22 to AS).

EPO2077

Baseline characteristics of the CASTING Study population: a Phase IIIB Trial evaluating Ocrelizumab in patients with relapsing-remitting Multiple Sclerosis and suboptimal response to disease-modifying therapies

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Background and aims: Patients with relapsing-remitting Multiple Sclerosis (RRMS) often experience disease activity despite receiving a disease-modifying therapy (DMT). Ocrelizumab demonstrated superior efficacy versus interferon-beta-1a in two Phase III trials (OPERA I/II [NCT01247324]/[NCT01412333]) in patients with relapsing MS. We report baseline characteristics of RRMS patients enrolled in CASTING, a prospective, multicentre, single-arm Phase IIIb study (EudraCT: 2015-005597-38) evaluating the efficacy and safety of ocrelizumab in patients who had a suboptimal response to an adequate course of a DMT.

Methods: Eligibility criteria included disease duration ≤10 years, ≥6 months prior treatment with one or two DMTs, Expanded Disability Status Scale (EDSS) of 0.0–4.0 at screening, and discontinuation of the most recent DMT due to suboptimal disease control (≥1 relapse, or ≥1 T1 gadolinium-enhancing lesion or ≥2 new/enlarging T2 lesions). Patients receive intravenous ocrelizumab 600mg/24 weeks (≥4 doses [96 weeks]; first dose, 2×300mg separated by 14 days).

Results: In total, 681 patients (64% female) from 16 European countries were enrolled. Mean (SD) baseline age was 34.2 (8.6) years and duration since first MS symptom onset was 5.0 (2.7) years; median (range) EDSS score was 2.0 (0.0–6.0). 61% and 40% of patients had received one versus two DMTs prior to enrolment, respectively. The most commonly used DMT immediately before enrolment was dimethyl fumarate (25%). The most frequent qualifying event for study inclusion was MS relapse while on previous DMT.

Conclusion: The CASTING study will describe the efficacy and safety of ocrelizumab treatment in patients who had ongoing disease activity while receiving another DMT.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

EPO2078

Teriflunomide (Aubagio®) International Pregnancy Registry: enrolment update

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Background and aims: Teriflunomide, approved for the treatment of relapsing forms of MS, is contraindicated in pregnancy based on embryo-foetal toxicity in rats and rabbits. Despite requirements for effective contraception use during teriflunomide clinical trials, a small number of pregnancies occurred. Outcomes of these pregnancies suggested no signal for human teratogenicity. The International Teriflunomide Pregnancy Exposure Registry will record birth defect rates in teriflunomide-exposed pregnancies, and these will be compared with those reported by the European Surveillance of Congenital Anomalies (EUROCAT).

Methods: The International Teriflunomide Pregnancy Exposure Registry is an ongoing, voluntary, multinational, prospective, observational, exposure-registration study. Pregnant women with MS exposed to teriflunomide at any time after Day 1 of their last menstrual period until pregnancy end can enrol. National coordinators liaise with healthcare professionals for data collection and patient enrolment. Target recruitment for statistical analysis: 196 women to achieve 104 live births, providing 80% power to detect a 3.95-fold increase in risk ratio of birth defects associated with teriflunomide exposure vs EUROCAT. Data collected include birth defects and infant characteristics during the first year of life.

Results: As of April 2017, 14 patients have enrolled from 7 European countries; 6 babies have been born with no abnormalities reported; there was 1 elective termination, which was not motivated by results of prenatal tests or concerns for potential birth defect. Updated enrolment data will be presented.

Conclusion: This registry will provide outcomes from teriflunomide-exposed pregnancies; these data will help physicians to provide better counselling for women exposed to teriflunomide during pregnancy.

Disclosure: Study supported by Sanofi.

EPO2079

Clinical profile and treatment pattern of Neuromyelitis Optica Spectrum Disorder (NMOSD) patients in Western India.

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Background and aims: To study clinical profile, treatment pattern and outcomes in NMOSD patients in Western India.
Methods: Clinical profile at onset, follow up and relapses, anti-aquaporin(AQ4) antibody status, imaging were recorded. Relapses on first line immunomodulatory therapy(IMT) and whether relapsed patient was shifted to another IMT after relapse on first agent, was recorded.
Results: 40 NMOSD patients were followed up for a period ranging between 6 months to 5 years. Age ranged between 10-65 years. 6 were males and 34 females. Presentations were longitudinally extensive transverse myelitis(LETM) in 23/40, followed by optic neuritis(ON) in 13/40, area postrema Syndrome(APS) in 1/40, acute brainstem Syndrome(ABS) in 2/40, and one patient had a long lesion extending from medulla to cervical cord(APS+LETM). 37 were AQ4 antibody positive. First line IMT was Azathioprine(Aza) in 30/40, Mycophenolate(MMF) in 7/40 and Rituximab(RTX) in 2/40 patients. One patient did not receive any IMT. So, 37 patients received oral therapy as first line, of which 14 relapsed. 9/14 of the patients who relapsed on oral IMT were switched to RTX.
Conclusion: LETM and ON were the commonest clinical manifestations at onset. We did not come across patients presenting with acute diencephalic syndrome (ADS) and symptomatic cerebral syndrome (SCS). Apprehension towards injection and cost were the factors affecting IMT decision, so majority received oral agents Aza/ MMF as first line therapy. 35% patients relapsed on oral therapy and the trend was to shift from oral therapy to RTX after relapse on oral agent. No relapses were seen once the patient went on RTX.
Disclosure: Nothing to disclose

EPO2080

On the different etiologies of isolated myelitis: a McDonald's 2010 and 2017 criteria comparative study

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Background and aims: Myelitis refers to an inflammatory process of the spinal cord. We present a series of patients with a first episode of myelitis with the aim of describing the clinical and radiological characteristics of its different etiologies and to analyse which of them would meet McDonald's Criteria 2010 and 2017 for a diagnosis of multiple sclerosis.
Methods: Retrospective and descriptive study including all patients with a first episode of myelitis from two tertiary hospitals in Madrid, Spain, between January 2007 and January 2017.
Results: We identified 49 patients with myelitis (22 men/27 women) with an average age of 43. 67% presented sensory and motor symptoms. The lesions were mainly: unaccompanied, with cervical location (51%) and with gadolinium enhancement (63%).The CSF showed inflammation in all cases by the presence of pleocytosis (38%) or oligoclonal bands (53%). Idiopathic myelitis had worse functional outcome at discharge compared to demyelinating (mRS 1.9 vs 1.2).Of all cases of myelitis identified as clinical isolated syndrome or idiopathic etiology (n=41), 7 of them met McDonald's 2010 criteria (17%), 7 met McDonald 2017 criteria (by OCB and typical lesions in brain MRI, 17%), with a change in the previous diagnosis and management.
Conclusion: A higher mean age, in the presence of motor and sensory symptoms, the absence of OCB and a normal brain MRI were significantly related to idiopathic myelitis. In patients with suspected demyelinating etiology, new Mc Donald's 2017 criteria permitted to change the diagnosis in 17% of patients, being able to diagnose multiple sclerosis.
Disclosure: Nothing to disclose

Neurogenetics 1

EPO2081

First clinicogenetic description of Parkinson's disease related to S107L GBA1 mutation

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Background and aims: Mutations in the glucocerebrosidase gene (GBA1) are the most common genetic risk factor for Parkinson's disease (PD). Phenotypic characterisation of GBA1-related PD has been challenging, in part due to differential impact of distinct GBA1 mutations.
The aim is to provide a phenotypic description of two patients with PD heterozygous for the GBA1 mutation S107L. This mutation has not previously been reported in patients with PD.
Methods: Motor and non-motor symptoms (NMS) of PD were evaluated using established rating scales and questionnaires. The genotype was determined by sequencing all exons of GBA1.
Results: Two half-brothers, both heterozygous carriers of S107L exhibited an early PD onset with several NMSs, although rapid progression of motor symptoms was observed in only one.
Conclusion: In these patients, heterozygosity for S107L was associated with an early onset of PD with NMS.
Disclosure: Nothing to disclose

EPO2082

Common and rare genetic variants associated with wearing-off and dyskinesia in Parkinson's disease

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Background and aims: Patients with Parkinson's disease (PD) typically show excellent therapeutic response to dopaminergic medications, but the majority develop late motor complications, including wearing-off and levodopa-induced dyskinesia (LID). Etiology of wearing-off and LID is still unclear. Furthermore, onset time and clinical features of wearing-off and LID are very heterogeneous among patients with PD. Therefore, we aimed to identify the genetic variants that are associated with the occurrence of wearing-off and LID in patients with PD.
Methods: Genomic data was produced using the Korean Chip (K-CHIP), Affymetrix Axiom KORV1.1, which contains imputation genome-wide association study (GWAS) grid and other GWAS loci, functional variants of nonsynonymous exome, pharmacogenetics variants, variants in genes involved in absorption, distribution, metabolism and excretion (ADME) of drugs, and expression quantitative trait loci (eQTL), in 1,070 PD patients.
Results: The SNP rs118109628 showed the most significant association with the occurrence of wearing-off within 5 years after PD onset. The SNP rs144125291 showed the most significant association with the occurrence of LID within 5 years after PD onset. There are several other genomic variants that showed associations with the occurrence of wearing-off or LID within 5 years after PD onset.
Conclusion: This study identified new loci associated with wearing-off and LID within 5 years after PD onset. Further studies are needed to confirm our findings.
Disclosure: This study was supported by a grant of the Korea Healthcare Technology R & D Project, Ministry of Health & Welfare, Republic of Korea (HI17C0328).

EPO2083

Neurocognitive assessment of patients with Chronic Neuronopathic Gaucher's Disease type 3-Norrbottnian form

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Background and aims: The Norrbottnian type of chronic neuronopathic Gaucher Disease type 3 (GD3) worldwide is rare but it is rather frequent in northern Sweden. We aim to describe the neurocognitive profile of patients with Norrbottnian GD3.
Methods: The Repeatable Battery of Neurocognitive Assessment (RBANS) was used to assess cognition in 10 patients (5 males/5 females). Disease severity was assessed with the use of modified Severity Scoring Tool (mSST).
Results: The mean age of our GD3 cohort was 40.9 years (±11.67) and the mean for years of education was 13.25 (±1.83) years. Half of the patients had been diagnosed with epilepsy and were treated with antiepileptic medications. The mean score for mSST was 10.4 (±5.25). Overall, regarding RBANS, the patients scored lower than average in all domains: Immediate Memory (Mean Index Score (MIS) 74.6±15.14), Visuospatial/Constructional (MIS 79.1±20.29), Language (MIS 82±13.78), Attention (MIS 56.4±15.54) and Delayed Memory (MIS 75±21.92). The total average score was also lower than normal (MIS 62.3±15.84).
Conclusion: The group consists of relatively young multisymptomatic patients. The overall assessment of cognition revealed low scores with the group performing worse than the 4% of the healthy population. However, the deficit was even more obvious in attention where the patients scored the lowest and the group value lies below the 2% of healthy population. Memory, both immediate and delayed, was also affected but to a lesser degree and so was visuospatial and constructional ability.
Disclosure: Nothing to disclose

EPO2084

withdrawn

EPO2085

X-linked Charcot-Marie-Tooth disease and multiple sclerosis: emerging evidence for a possible association

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Background and aims: X-linked Charcot-Marie-Tooth disease (CMTX) is a hereditary neuropathy caused by mutations in GJB1, a gap-junction protein expressed in Schwann cells and oligodendrocytes. Subclinical and clinical CNS involvement can be observed in CMTX. To date, three patients developing CNS demyelination compatible with multiple sclerosis (MS) have been individually reported.
Methods: The Neurogenetics Unit, Eginition Hospital, Athens provides genetic testing for Greek patients with suspected CMTX. Over 20 years, 70 patients (36 males) with GJB1 mutations have been identified. These were assessed for clinical features suggestive of MS. Additionally, 16 CMTX patients without suspected MS underwent brain MRI. Serum from available patients with CMTX and MS was tested for anti-AQP4, MOG and ganglioside antibodies.
Results: We identified 3 CMTX index-patients, who developed clinical features suggestive of CNS demyelination and fulfilled MS diagnostic criteria. The resulting MS frequency of 4.3% in the CMTX cohort, significantly differed from the highest background MS prevalence (12/10,000) ever reported in Greece ($p=0.00014$). Additionally, one patient not fulfilling MS diagnostic criteria had CSF oligoclonal bands. Brain MRI identified 2 patients (12.5%) with lesions highly suggestive of demyelination. Moreover, 6 patients had subcortical lesions, 10 had callosal hyperintensity, and 13 diffuse white-matter hyperintensity. Patients with CMTX and MS tested negative for anti-AQP4, MOG and ganglioside antibodies.
Conclusion: We have demonstrated a higher-than-expected frequency of MS in CMTX patients and a high frequency of demyelinating lesions on brain MRI in CMTX patients without suspected MS. This provides circumstantial evidence for GJB1 mutations acting as a possible MS risk factor.
Disclosure: Nothing to disclose

EPO2086

Interrupted CAG repeats in ATXN2 gene: an expansion of the genetic spectrum of frontotemporal dementias

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Background and aims: Spinocerebellar ataxia type 2 (SCA2) is caused by an expansion of an unstable CAG trinucleotide repeat in the coding sequence of ataxin-2 (ATXN2) gene. Expansions of 33 or more pure CAG repeats are pathogenic and lead to cerebellar ataxia. Expansion of 33 or more CAG interrupted by one or more CAA motifs leads to isolated dopa-responsive parkinsonism, without cerebellar ataxia or any neurological features. We identified an interrupted ATXN2 expansion of 39 CAG in a patient with predominant cognitive disorders diagnosed as a corticobasal syndrome, and pathological hallmarks of frontotemporal lobar degeneration (FTLD) with TDP-43-positive inclusions type A.
Methods: We describe the clinical and pathological characteristics of this patient.
Results: This study provides several important results: 1) interrupted full-length ATXN2 expansions can produce isolated FTLD phenotype; 2) interrupted expansions are associated with phospho-TDP-43 neuronal cytoplasmic and intra-nuclear 'cat eye' inclusions, and p62 neuronal inclusions in neocortex; 3) no mosaicism has been observed in various brain structures;
Conclusion: Finally, this study provides arguments for a common pathological pathway involving TDP-43, not only in the FTLD and ALS spectrum of diseases, but also in several CAG repeat expansion disorders including ATXN2 interrupted expansion diseases. Most importantly, this case establishes a novel genetic link between FTLD phenotype and ATXN2 gene. It expands the molecular spectrum of FTLD-TDP disorders, and shows that ATXN2 analysis should be performed not only in patients with cerebellar ataxia or parkinsonism but also in FTLD patients or, more largely, in cases with TDP-43 pathology after exclusion of the most frequent FTLD genes
Disclosure: Nothing to disclose

EPO2087

Diagnostic yield of Next-Generation Sequencing (NGS) technology applied to Neurological disorders

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Background and aims: The increasing availability of NGS, coupled with the exponential increase in the description of genetic etiologies for neurological diseases, requires neurologists to be familiar with its strengths and weaknesses.
The aim of our study was to assess the diagnostic yield of NGS studies in neurological disorders at our tertiary center.
Methods: Retrospective descriptive cross-sectional study of consecutive neurological patients for whom a NGS study was ordered, for 18 months.
Results: Of 192 patients included, a definitive molecular diagnosis was reached in 35.4%. The main neurological syndromes represented were: intellectual disability/autism (45.8%), epilepsy (12%), dementia (9.9%) and muscle disease (9.4%).
An additional 19.8% of patients had a result of clinical undetermined significance (CUS), meaning either a variant of unknown significance in a phenotypically suitable gene (PSG) or a probably pathogenic variant not previously described in a PSG in a patient in whom the family segregation revealed the same mutation in one of the healthy parents. Results excluded from the CUS definition were: variants in PSG, variants in heterozygosity in recessive conditions and variants in which the bioinformatics prediction was benign or probably benign.
We found a rate of 5.2% of accidental pathogenic findings unrelated to the symptoms that motivated the NGS study.
Conclusion: Our results, derived strictly from clinical practice, show that in approximately one third of patients with neurological disorders of undetermined etiology a definitive diagnosis can be reached when NGS technology is used. Its cost-effectiveness taking into account its impact on patient management, was not addressed.
Disclosure: Nothing to disclose

EPO2088

Novel pathogenic ITM2B mutation or incidental benign sequence variant? Next Generation Sequencing conundrum

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Background and aims: To illustrate the potential difficulties in interpreting results of next generation sequencing (NGS) panels.
Methods: A man in his fifties became increasingly withdrawn, expressed delusional ideas, and psychiatric diagnosis of depression was made. He progressively developed limb tremors, parkinsonism, falls, and loss of spontaneous verbal output. Various neurodegenerative disorders were considered and excluded after extensive investigation, with residual diagnosis of corticobasal syndrome, possibly tauopathy.
Results: Although there was no family history of similar disorder, blood was sent for the dementia/movement disorder NGS panel. This was negative aside from a sequence change in exon 5 of the ITM2B gene (predicted protein change p.Thr228Ala) located on chromosome 13q14.2, not previously described. It was not apparent whether this represented pathogenic mutation or incidental sequence variant: ITM2B mutations are found in familial British and Danish dementias, conditions characterised as cerebral amyloid angiopathies, but missesne mutations have not previously been described to our knowledge. Hence the biological credibility for pathogenicity of this sequence change was uncertain. Subsequent amyloid (18F florbetapir) PET imaging was negative.
Conclusion: NGS panels enhance the potential to define pathogenic mutations in neurodegenerative disorders, but may also reveal incidental sequence variants of uncertain significance. Interpretation of NGS results can be challenging.
Disclosure: Nothing to disclose

EPO2089

Reversible valproate-induced subacute encephalopathy caused by a mitochondrial DNA variant

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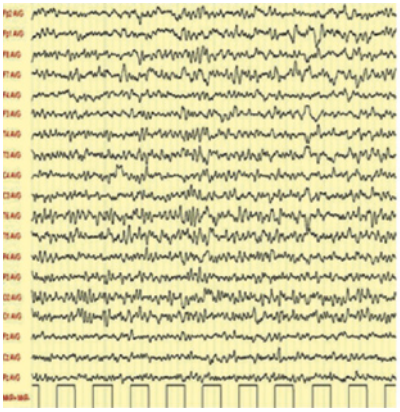
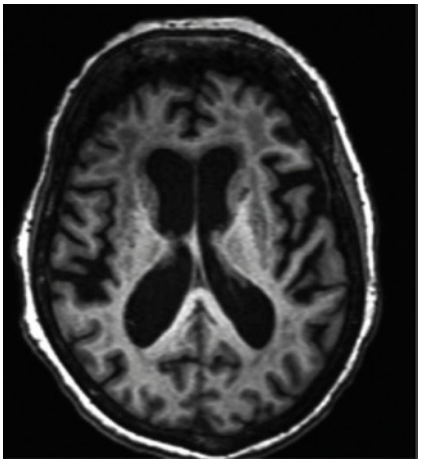
Background and aims: There are several reported cases of patients developing motor and cognitive neurological impairment under treatment with valproic acid (VPA). We describe a woman who developed a subacute encephalopathy after VPA intake, harboring a mitochondrial DNA variant, previously described as causing VPA sensitivity in one pediatric patient.

Methods: A 65-year-old woman developed a progressive, severe neurological deterioration after a three-month treatment with valproate sodium, 800mg daily. Magnetic resonance spectroscopy (MRS), muscle histochemical analysis and assay of mitochondrial enzymatic activities, and mitochondrial DNA sequencing were performed.

Results: Neurological examination showed drowsiness, vertical gaze palsy, inability to either stand or walk, diffuse weakness, increased tendon reflexes. Blood lactate was increased, EEG showed diffuse theta and delta activity, MRI subcortical atrophy and leukoencephalopathy, MRS marked reduction of the NAA spectrum, with a small signal compatible with presence of lactate. Muscle biopsy evidenced a significant variability of the fiber caliber with hypotrophic fibers, presence of ragged red fibers (20%) and reduced COX reactivity. Assay of the muscle enzymatic activities showed multiple deficiencies of the electron transport chain. The nt.8393C>T variant in the MT-ATP8 gene was found in homoplasmy. The patient considerably improved after valproate withdrawal.



EEG showing a slow alpha with theta and delta activity



MRI scan showing cortical atrophy with confluent areas of hyperintensity

	Patient	Control values
CI(NADH dehydrogenase)	1.73	1.56-2.6
CII(succinate malonatedehydrogenase)	0.05	0.07-0.11
CI+CIII (NADH cytochrome coxidoreductase)	0.03 (27.3%)	0.11-0.25
CII+CIII(succinate cytochrome coxidoreductase)	0.01 (20%)	0.05-0.08
CIV(cytochrome coxidase)	0.04 (23.5%)	0.17-0.28
CS(citrate synthase)	10.68	7.80-10.90

Respiratory chain enzyme activities in muscle homogenate. The enzymatic activities of the respiratory chain complexes are expressed as mmol/min/gr muscle tissue and normalized to the activity of citrate synthase, a marker of mitochondrial mass. The percentage of mean residual activity of normal controls is shown in brackets.

Conclusion: The mutation we found has been reported both as a polymorphism and related to the valproate-induced encephalopathy. The present case is the first bearing this mutation in homoplasmy. In case of neurological symptoms after starting VPA therapy, once hyperammonemia and liver failure have been ruled out, mtDNA abnormalities should be considered.

Disclosure: Nothing to disclose

EPO2090

Diagnosis of autosomal recessive spinocerebellar ataxia type-10 (SCAR 10): implications for treatment

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Background and aims: Clinical and imaging features are seldom useful in narrowing the differential diagnosis of autosomal recessive cerebellar ataxias. Next generation sequencing (NGS) has proved its usefulness in establishing a definite diagnosis and enable accurate genetic counselling. SCAR10 is associated with CoQ10 deficit and some case reports have suggested clinical stability with oral supplementation.
Methods: Case report
Results: We present two isolated cases of slowly progressive cerebellar ataxia. Patient#1: A 35-year-old woman with dysarthria, diplopia and gait ataxia, since age 23y. Physical examination showed cerebellar nystagmus, dysarthria, gait and appendicular ataxia, hyperreflexia and bilateral extensor plantar responses. Patient #2: A 51-year-old male with dysarthria, dysphagia, gait ataxia and hyperreflexia starting at 36y of age. Brain MRI revealed global cerebellar atrophy in both cases. Treatable causes of ataxia were investigated, but no abnormalities were detected, besides a CoQ10 deficit in patient #2 (not tested in patient #1). Multiple genetic tests were negative in both cases, including MJD/SCA3, CABC1 (causing CoQ10 deficiency), POLG and FRDA.
A NGS panel showed these patients to be a homozygote (#1) and a compound heterozygote (#2) for pathogenic variants in ANO10, confirming the diagnosis of SCAR10 in both. This prompted treatment with high-dose oral COQ10, resulting in relative stability of cerebellar deficits over more than 5 years, and adequate genetic counselling.
Conclusion: This case highlights the usefulness of NGS in achieving a definite diagnosis in "sporadic" cases of cerebellar ataxia. In rare cases, such as those described here, treatment may be available and result in slowing of disease progression.
Disclosure: Nothing to disclose

EPO2091

New genes on infantile epileptic encephalopathies–five years experience of a terciary center review

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Background and aims: The use of Next Generation Sequencing(NGS), exome and panels, in the previous years has allowed major advances on the identification of causative genes of paediatric epileptic encephalopahies(EE).
Methods: Review of clinical files of children with EE due to new genes identified by NGS since 2012.
Results: We present 10 children (7 boys, 17months-21 years), all presenting with seizures refractory to medical treatment in the newborn period and all evolving to global developmental delay without dysmorphic features or organomegalia. A few distinctive clinical features include global severe hypotonia and scarce spontaneous movements in the child with SLC25A22 mutation and spastic tetraparesis related to KCNQ2, GRIN2A and SCNL2A. The child with MEF2C mutation presents continuous stereotypies and the one with SPTAN1 mutation also shows Rett-like stereotypies but also global chorea and dystonia. One of the 2 children with STXBP1 mutation has autism.
All children presented with global lentification of eletrogenesis except ATP1A3 and multifocal paroxystic activity on EEG. SCNL2A mutation was the only associated with neonatal burst –suppression pattern and ATP1A3 with nonconvulsive status epilepticus.
The only consistent positive response to treatment occurred with the use of ketogenic diet on the children with ATP1A3 and GRIN2A mutations.
Conclusion: The recognition of new causative genes of paediatric EE allows the recognition of suggestive phenotypes, more individualized treatment directed to the dysfunction of codified proteins and paves the way to eventual future genetic treatment. All genes involved code for proteins relevant for synaptic function.
Disclosure: Nothing to disclose

Neuro-oncology

EPO2092

Primary CNS Lymphoma presenting as ophtalmoparesis and facial nerve palsy

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Background and aims: PCNSL is an uncommon variant of non-Hodgkin lymphoma confined to the CNS. Leptomeningeal involvement can occur as a manifestation of systemic lymphoma or synchronously with PCNSL and is exceedingly rare to be found exclusively.

Methods: A 65-year-old woman with history of atrial fibrillation, presented at emergency room, with symptoms of headache, diplopia and imbalance for 3 days. On examination, she had a right abducens nerve palsy, right facial nerve palsy and unsteady gait. No adenopathies were present.

Brain CT and nonenhanced MRI were normal. In the following days, she developed bilateral facial nerve palsy, cervical and lumbar radiculopathies.

Results: A contrast-enhanced MRI revealed bilateral enhancement of the internal acoustic canal, and CSF analysis showed lymphocytic pleocytosis and hyperproteinorraquia. A first flow cytometry immunophenotyping was normal, but a second one revealed malignant lymphocytes supporting the diagnosis of diffuse large B-cell lymphoma. Extensive CSF and serum studies were negative for infectious or systemic autoimmune causes. Body CT and bone marrow aspirate were negative. Initially improved with steroids, the patient developed a severe septic shock due to pneumonia and died 1.5 months later. Upon clinical deterioration, a CT scan revealed multiple mass lesions involving the brain lobes, white matter and cerebellum.

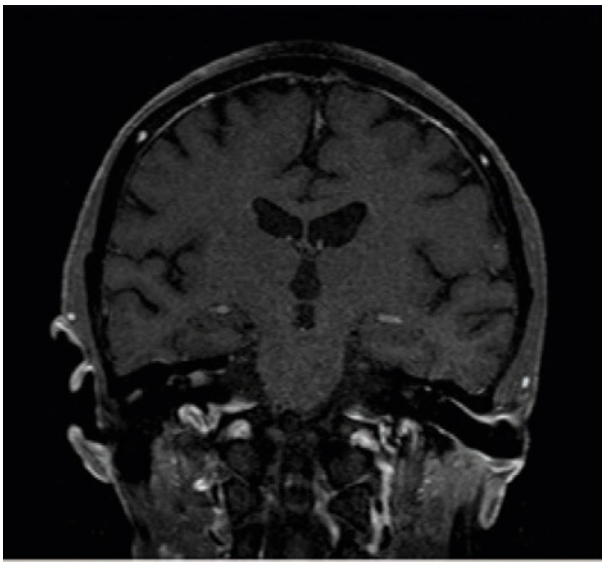

Figure 1: MR imaging with coronal post-gadolinium T1-weighted image with bilateral enhancement of internal acoustic canal.

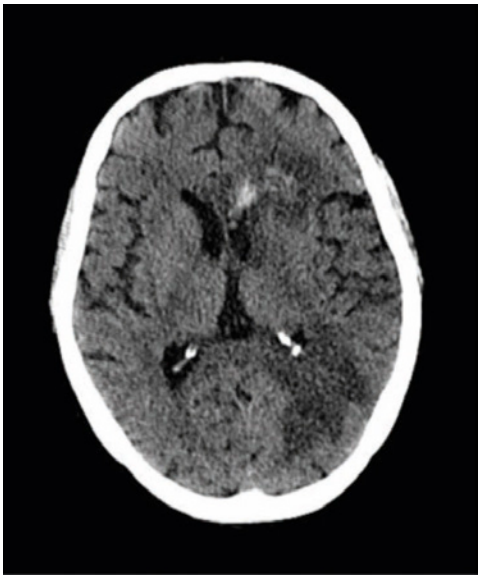

Figure 2: Non-enhanced CT with a hypodense expansive lesion on left striatocapsular region with hyperdense foci compatible with acute intralesional haemorrhage. On left peritrigonal white matter there is a similar lesion, also with haemorrhagic foci (not shown).

Conclusion: Establishing the diagnosis of leptomeningeal involvement from lymphoproliferative disorders can be challenging. In our case, evidence was limited to a subtle contrast enhancement on MRI. Only in a later stage parenchymal lesions could be seen.

We strongly suggest that upon high clinical suspicion, CSF immunophenotyping should be performed and repeated if found negative.

Disclosure: Nothing to disclose

EPO2093

Isolated Castleman's disease affecting the central nervous system presenting as generalized seizure

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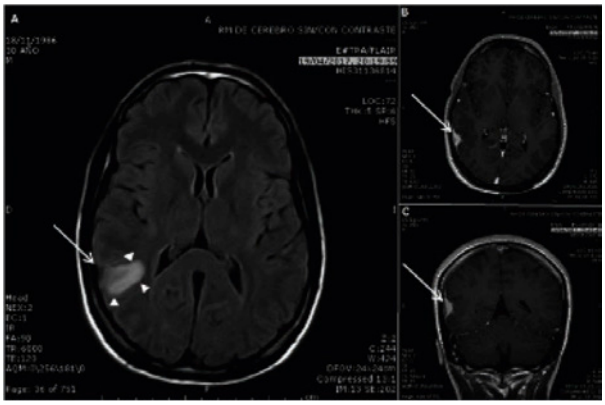
Background and aims: Castleman's disease is a rare pathologic process of unknown etiology, characterized by nonneoplastic lymph node enlargement. His clinical features are classified in two categories, localized and generalized, and two distinct histological patterns are also recognized, the hyaline-vascular and the plasma-cells types. Intracranial involvement is extremely rare. We describe a case of localized intracranial Castleman's disease.

Methods: A 30-year-old-man suffered a generalized tonic-clonic seizure that required intravenous administration of benzodiazepines and phenytoin for control. Neurological examination on admission revealed somnolence, disorientation, and mild left hemiparesis.

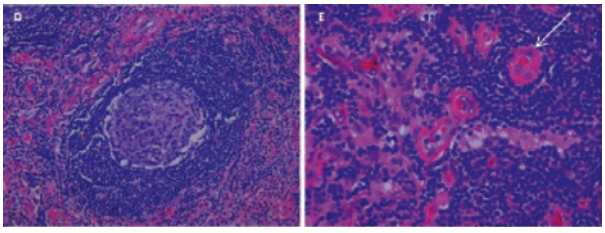
Results: Seizures were subsequently controlled with oral phenytoin therapy, which was subsequently replaced by lacosamide. A body computerized-tomography (CT) examination and cerebrospinal-fluid (CSF) study found no abnormalities.

Brain magnetic resonance (MR) imaging demonstrated an extraaxial mass in the right temporo-parietal convexity that was homogeneously enhanced with gadolinium. Based on the neuroradiological findings, the presumptive diagnosis was convexity meningo-angiomatosis.

A right temporal craniotomy was performed and the dural-based solid mass was resected. Histological examination of the surgical specimens revealed numerous lymphoid follicles with hyalinized vascular proliferation and the diagnosis was the hyaline-vascular type of Castleman's disease.The patient had an uneventful postoperative course. He was discharged without neurological deficit one week after surgery. After follow up for one year, he remained seizure free without evidence of systemic involvement.



A: FLAIR-weighted magnetic resonance (MR) image showing a mass in the right temporo-parietal convexity (arrow). Brain edema surrounding the mass is extensive in comparison to the size of the mass (arrowheads). B, C: T1- weighted (MR) image after contrast administration showing the mass with homogenous enhancement (arrow).



D: Photomicrograph showing rings of lymphocytes surrounding germinal centers. Hematoxylin-eosin stain, original magnification x 80. E: Photomicrograph showing numerous hyalinised vessels (arrow). Hematoxylin- eosin stain, original magnification x 100.

Conclusion: Intracraneal Castleman's is a rare disease that could appear as a solid extracranial mass attached to meninges. It may manifest as seizure or focal signs and it should be considered in the differential diagnosis of meningeal tumors.

Disclosure: Nothing to disclose

EPO2094

Intraspinal intradural nodular fasciitis mimicking glioblastoma metastasis: a case report

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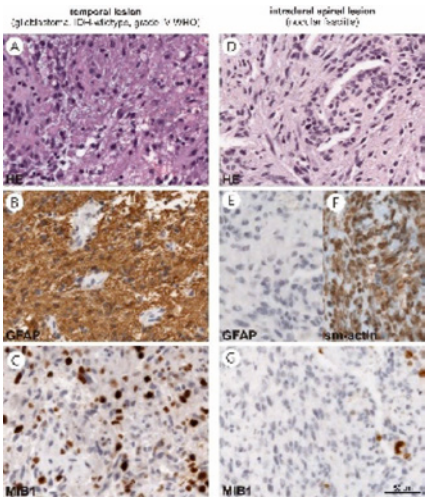
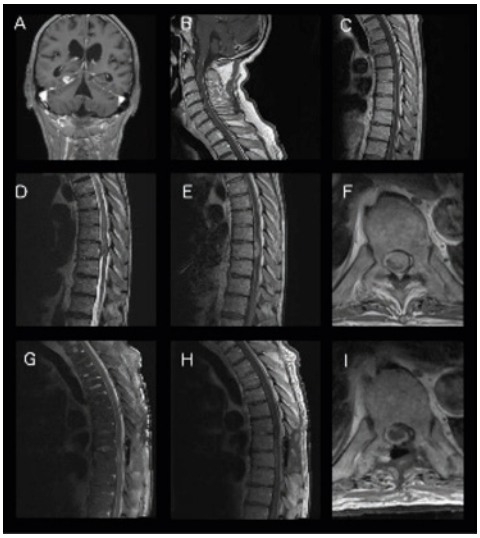
Background and aims: Nodular fasciitis (NF) is a rapidly growing but non-malignant lesion. Due to its rapid growth and unspecific imaging characteristics it is often misinterpreted as a malignant process.
Methods: We report the case of a 78-year-old male patient suffering from a right temporal glioblastoma with radiographic meningeal tumor spread. During the further course of the disease he developed a rapidly progressive paraplegia. An MRI scan showed a contrast enhancing intraspinal intradural lesion with compression of the myelon on segment Th 8/9. With a high suspicion of a spinal metastasis of the known glioblastoma, emergency spinal decompression and resection of the intradural mass was performed.
Results: The resected tissue of the spinal lesion had a total diameter of 1.0cm. There was no specific expression of actin (clone HHF35), calponin, GFAP, STAT6, melan A, pan-CK, EMA, progesterone-receptor and neurofilament. S100 was only focally expressed and CD34 staining was restricted to blood vessels. Thus, a metastasis of the known glioblastoma could be excluded. Additionally, a FISH analysis was performed but failed to show a clear USP6 rearrangement. The lesion was considered to be a reactive proliferation, consistent with a nodular fasciitis.
Conclusion: This patient with a history of a left temporal glioblastoma developed a reactive intraspinal lesion. Although we could not demonstrate an USP6 rearrangement, a characteristic that is often but not always found in nodular fasciitis, we assume nodular fasciitis the most likely diagnosis. To the best of our knowledge, this is the first report of an intraspinal and intradural nodular fasciitis.



The temporal tumor (A-C) showed cells with an astrocytic morphology, expression of GFAP and numerous MIB1-positive cells. In contrast, the spinal lesion consisted of spindle shaped cells. Epitheloid cells were noted (D). This lesion lacked expression of GFAP (E), was immunoreactive for smooth muscle actin (F) and showed MIB1-positive cells (G).



Right-sided multicentric temporomesial contrast-enhancing lesion on postcontrast T1 sequences (A+B) with spinal leptomeningeal tumor spread (C+D). Novel intradural lesion at the level Th8/9 on spinal MRI (E+F). The postoperative images showed a good decompression of the myelon and partial resection in postcontrast T1 and T2 sequences (G+H).

Disclosure: Nothing to disclose

EPO2095

Intravascular Lymphoma of central nervous system – the great imitator

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Background and aims: Intravascular lymphoma (IVL) is a rare variant of extranodal diffuse large B-cell lymphoma restricted to the vascular lumina, affecting preferentially the Central Nervous System and skin, with non-specific clinical manifestations, which pose a diagnostic challenge.
Methods: n/a
Results: Case report: A 59-year-old male with history of stage IV lymphoplasmocytic lymphoma (LPL) 2 years prior to admission, in remission, presented with acute right hemiparesis. After a thorough investigation, he was discharged with a diagnosis of stroke but subsequently progressive gait difficulties and impaired cognitive function ensued. Two months later, general examination was unremarkable and a neurological examination showed multiple-domain cognitive dysfunction, right spastic hemiparesis, and gait instability. The laboratory workup revealed persistently elevated LDH, CPR and ESR. Brain MRI showed bilateral and multifocal (left predominant) hyperintense T2- and T2-FLAIR-weighted white-matter parieto-occipital lesions, also involving the splenium of corpus callosum and right middle cerebellar peduncle, without restricted diffusion or contrast enhancement. CSF examination was negative, including cytological analysis without malignant cells, no intrathecal immunoglobulin synthesis and unremarkable immunophenotyping. Due to clinical progression, brain MRI was repeated 10 days later and revealed bilateral progression of the previous lesions to the temporal and frontal lobes, with diffusion restriction and patchy contrast enhancement. A brain biopsy was performed, confirming the diagnosis of B-cell intravascular lymphoma.
Conclusion: Discussion: It is unclear whether IVL represented a transformation from LPL, or whether it was a de novo lymphoma. Nevertheless, our case should raise awareness for early brain biopsy in cases of progressive neurological deterioration with nonspecific findings in brain MRI.
Disclosure: Nothing to disclose

EPO2096

Lymphoma T type with cerebral presentation: report of 3 cases

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Background and aims: More than 90% of lymphoma witch cerebral présentation are diffuse and large cell B type, and most of them are restrained to the CNS.
Aims : define et description of T-Lymphoma with cerebral présentation.
Methods: Based on prospective cohorte of primary cérébral lymphoma, between 2011 and 2017, in a tertiary health-care derpartement of neuro-oncology, Pitie-salpétrière hospital in paris, that include 212 case of PCL. We aimed to select T-lymphoma define by histology analysis and double-analyzed with two différents pathologists.
3 cases have been identified (1.4% of all cases of PCL), 1men/2females, aged between 57 and 77 yo. All of them were immunocompetents.
Results: 1 case had caeliaque disease. 2 of them had a typical radiologic presentation, the third had a lymphomatosis cerebri présentation. None of them had ophtalmologic or LCS dissemination. One of them had an extra-cerebral lesion (surrenal gland localization), the others had no extra-neurologic dissemination.
All have been treated with chemotherapy based on methotrexate high dose : 1 patient presented a complete response, one presented partial response and progression that was prevent by second ligne (Ifosfamide Etoposide carboplatine) completed by autologous cell graft. The third one died after partial response. Complete and sustained response was achieved in 2 cases with a mean follow-up of 26 months (12-40 months).
Conclusion: T-lymphoma with cerebral présentation are rare and seems to share the same prognosis and response to standard treatment, as in primitive cerebral B-lymphoma, but more than in B-lymphoma most make investigate an extra-neurological dissemination.
Disclosure: Nothing to disclose

EPO2097

Epithelial-Myoepithelal Cell Carcinoma (EMCC) arising from salivary glands heterotopia in Meckel's cave

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Background and aims: EMCC is a rare malignancy comprising 1% of all salivary gland tumor generally arising from parotid gland. The histological hallmark is the bi-layered epithelial-myoephitelial phenotype.
Methods: A 36-year-old woman presented with subacute right eye ptosis and unreactive mydriasis. A high-dose corticosteroids (CCS) cycle was tempted without significant clinical improvement. After few days, the patient developed right lateral gaze diplopia and trigeminal V2 hypoesthesia.
Methods: Cerebrospinal fluid (CSF) examination, optical coherence tomography (OCT), brain MRI with/without contrast, orbital CT scan with 3D reconstruction, endoscopic endonasal biopsy.
Results: CSF analysis resulted normal. OCT revealed right eye papilledema. Brain MRI showed slightly T2-hyperintense tissue enlarging Meckel's cave and following as a sheet the course of the carotid artery. After gadolinium (Gd) administration, it presented intense and homogenous enhancement. The orbital CT scan confirmed the right superior orbital fissure enlargement. The second MRI (after CCS cycle) showed right eye muscle cone and trigeminal nerve involvement through the oval foramen. Microscopically, the mass was composed of nests of neoplastic cells with central glandular spaces, surrounded by an inner layer of eosinophilic cells immunoreactive with CK17 and CD117 and by multiple outer layers of clear cells positive with smooth muscle actin. Ki67 immunostaining was positive in 20% of the neoplastic cells.

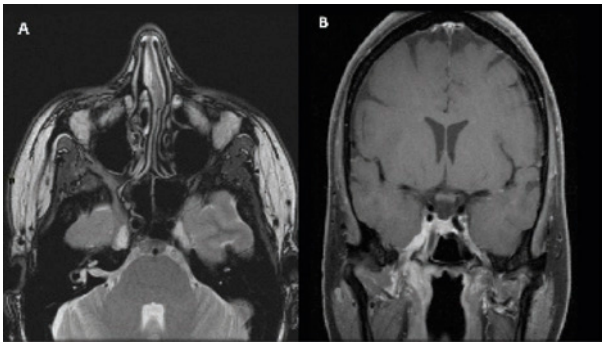

Figure 1. Brain Mri Before (A) And After (B) Gadolinium Administration

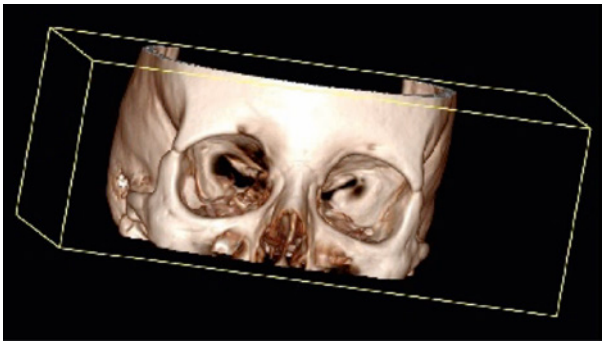
Figure 2. Orbital Ct (3D Reconstruction) Showing Right Superior Orbital Fissure Enlargement

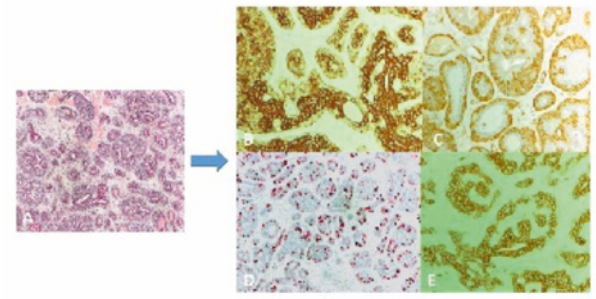
Figure 3. H&E Stain (A) And Immunostaining (B=CK7, C=SMA, D=CD117, E=Ki 67)

Conclusion: Salivary glands heterotropia has been described in various head and neck districts and peripheral organs. On the basis of neuroradiological and clinical features, we described the first case of EMCC originated from salivary gland heterotopia in Meckel's cave.
Disclosure: Nothing to disclose

EPO2098

Multiple sleep latency test and symptoms of paraneoplastic lesion of the limbic system in patients with breast cancer

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Background and aims: Paraneoplastic limbic encephalitis is a rare condition and some difficult to diagnose. The symptoms of paraneoplastic lesions of limbic system occur only in 8% patients with breast cancer, include sleep disorders, anxiety, depression, cognitive impairment, and they are associated with onconeural antibodies. Debut of neurological symptoms of paraneoplastic limbic encephalitis precedes clinical manifestation of breast cancer from 3-5 months to 4 years.
Objective: To detect and analyse the clinical, neurophysiological and neyroimmunological markers paraneoplastic lesions of limbic system in patients with breast cancer.
Methods: 7 women with breast cancer II-IV stages were examined; mean age: 45.28±8.13 years. Detection onkoneural of antibodies in the serum of patients were carried out using Neuronal Antigen Profile EUROLINE (IgG) in vitro by immunoblotting. Was used valid tests and scales: MoCA, HADS, BDI, HDRS. The average time of falling asleep (MSLT) was performed by standard technique on the apparatus firm "Nicolet". Control group: 7 healthy women were matched for age.
Results: Onkoneural antibodies were found in the sera of 100% of patients (anti-Hu-43%; anti-Yo-57%). In patients were revealed high levels of anxiety (BDI: 17.14±9.35; HADS: 12.14±3.53), depression of moderate severity (HDRS:15.14± 5.49) and mild cognitive impairment (MoCA: 21.28±3.14)-memory disorders. Average sleep latency in the group of patients (17.12min) was significantly higher than the average latency in the group of healthy (9.3min) p=0.006012.
Conclusion: Neurophysiological, laboratory and clinical evidences are confirmed paraneoplastic lesions of the limbic system of the brain in pations with breast cancer.
Disclosure: Nothing to disclose

EPO2099

Retracing the steps of melanocytic dissemination: from venous infarctions to cerebral metastases

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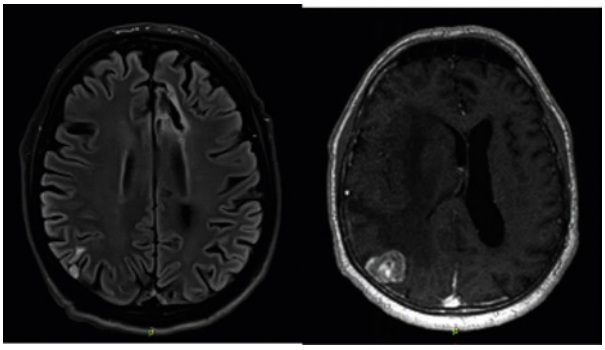
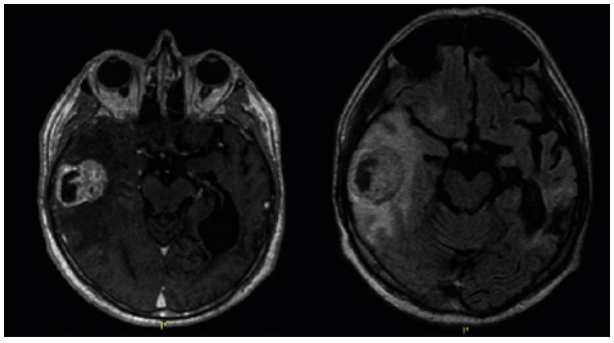
Background and aims: The incidence of brain metastases arising from melanoma is approximately 10% and leptomeningeal metastases occur in 5-7%. Primary central nervous system melanoma is fairly rare, accounting for 1% of all cases of melanoma and 0.07% of brain tumours.
Methods: We report the case of a 65-year-old man presenting with a haemorrhagic venous infarction of the left temporal lobe, conducive to motor aphasia and right-sided hemiparesis. The brain magnetic resonance imaging also revealed peculiar supratentorial cerebral and meningeal lesions suggesting neoplasia or vasculitis. Stigmata of another similar hemorrhage were found in the left frontal lobe. Extensive blood testing and cerebrospinal fluid analysis were unremarkable. The patient declined undergoing brain biopsy at the time. Over the next months the symptoms worsened and progression of lesions with necrosis and surrounding vasogenic oedema was found on computed tomography. A brain biopsy was performed for histological and immunohistochemical assessment.

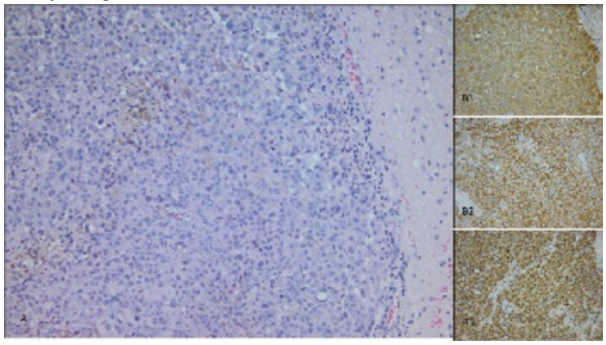


Brain MRI. Axial fluid attenuation inversion recovery-weighted image (left) showing right parietal mass of probable meningeal origin and left-sided frontal lesion bearing stigmata of haemorrhage. Axial T1-weighted image performed 7 months later (right) showing the same right parietal contrast-enhancing mass, larger, with surrounding oedema



Brain MRI. Axial T1-weighted sequence (right) and fluid attenuation inversion recovery-weighted scequence (left) showing a right temporal lesion with an inner necrotic area and surrounding vasogenic oedema

Results: Histopathological and immunohistochemical evaluation were consistent with cerebral metastasis from malignant pigmented melanoma. There were no suspicious primary lesions, but the patient recounts having had a thoracic lump excised some years prior, allegedly benign, unfortunately unavailable for second opinion. The meningeal lesion prompts considering a leptomeningeal metastasis, yet a primary meningeal melanoma, albeit less likely, might also be entertained.



A. Histopatological specimen hematoxylin and eozin stained, 200 times enhanced, showing malignant melanocytic proliferation (left) and immunohistochemical stains 400 times enhanced (right) confirming the melanocytic origin through S100 positivity (B1), HMB45 positivity (B2) and MITF positivity (B3)

Conclusion: The co-existence of cerebral venous infarctions with melanoma is a particular finding and its differential diagnosis will be further discussed. Prompt histopatologic reevaluation of previously excised suspicious lesions should be strongly considered especially if brain biopsy cannot be performed.

Disclosure: Nothing to disclose

EPO2100

Adult ependymoma: experience in our hospital

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Background and aims: Ependymomas are tumors that grow from the ependymal epithelium of the ventricular system; rarely from the brain parenchyma or from other tissues. They represent less tan a 10% of brain tumors and 25% of medullary tumors (60% of intrmedullary ones). We review our experience.

Methods: Retrospective revision of adult ependymoma cases in our hospital from January of year 2012 to May of 2017. We analysed demographic data, location of the tumor, histological type and clinical features.

Results: Forty patients are included, 18 women/22 men, with an average age of 47 years old (from 17-75). There were 20 brain tumors (7 of them of supratentorial location, 13 infratentorial) and 20 medullary (13 in the terminal filum and the rest of them cervicodorsal). 2 of the patients were twins and surgically treated of the same infratentorial tumor type. The most common histological type was classic ependymoma, grade II of the OMS (38% were located in brain, 31% medullary) and the myxopapillary (grade I) represented a 62% of the filum ones. The main symptoms were headache (43%), disbalance (43%) in brain tumors; and pain (58%) in spinal. A fillum ependymoma first symptoms were those of superficial siderosis.

Conclusion: In our series, the number of brain ependymomas is lightly higher than published in medical literature; age and histological types are similar to described. We point out some atypical cases: the presentation in twins and the debut as superficial siderosis of the central nervous system.

Disclosure: Nothing to disclose

Neurorehabilitation

EPO2101

Central hypoventilation syndrome in posterior circulation stroke: a case report.

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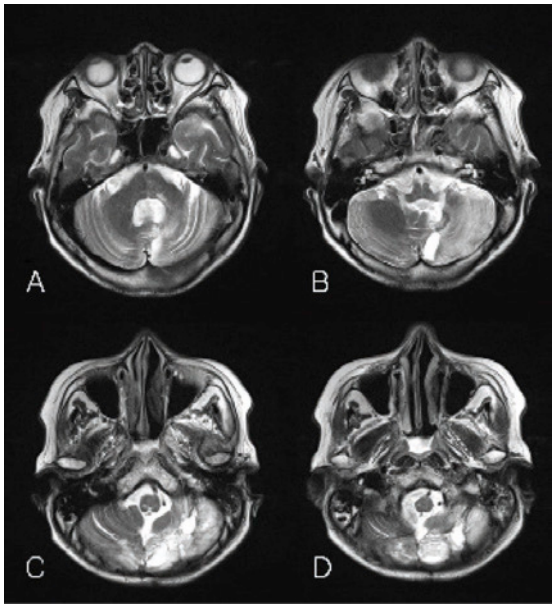
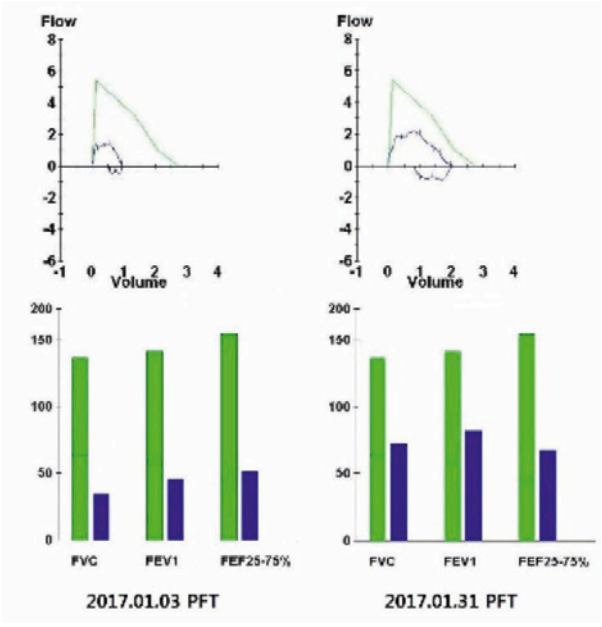
Background and aims: Central hypoventilation syndrome is a rare condition characterized by the failure of automatic breathing, which can result from various central nervous system disorders. Several cases have been reported, most of which resulted in death. We report the case of a patient with central hypoventilation syndrome caused by a posterior circulation stroke, which was improved by respiratory rehabilitation.

Methods: A 59-year-old woman had experienced a hemorrhagic stroke of the bilateral cerebellum, and had suffered from recurrent respiratory distress and aspiration pneumonia since the stroke occurred. The brain MRI showed encephalomalacic changes in bilateral cerebellar hemispheres, the left middle cerebellar peduncle, the left pons, the left anterior, and the right lateral medulla (Fig.1).



The brain MRI showed encephalomalacic changes in both cerebellar hemispheres, left middle cerebellar peduncle, left pons, left anterior and right lateral medulla.

Results: With a portable ventilator applied via tracheostomy, a respiratory rehabilitation program including intercostal muscle strengthening and diaphragmatic breathing exercises proceeded. After 4 weeks of rehabilitation, a pulmonary function test showed improvements in respiratory parameters (Fig.2). Consequently, the portable ventilator was applied for 8 hours only during night time to prevent sudden apnea.



The changes of pulmonary function test. The left showed initial pulmonary function test, and the right showed follow-up pulmonary function test. The results showed improved respiratory parameters after respiratory rehabilitation.

	2017.01.03		2017.01.31	
Spirometry	Pre	%Ref	Pre	%Ref
FVC (Liters)	0.95	35	1.99	73
FEV1 (Liters)	0.82	46	1.65	82
FEV1/FVC (%)	97		83	
FEF25-75% (L/sec)	1.26	51	1.65	67
FEF50% (L/sec)	1.34	42	2.07	65
PEF (L/sec)	1.40	26	2.15	40

The changes of pulmonary function test parameters. After 4 weeks of respiratory rehabilitation, FVC and FEV1 were improved as double.

Conclusion: In this case, the lesions in the pneumotaxic center of the pons and the ventral repiratory group in medulla seem to attribute to reduced chemosensitivity and impaired breathing coordination. There is no consensed diagnostic criteria for central hypoventilation syndrome, and the clinical courses are unpredictable. Several therapeutic options are available, including pharmacological approaches and the use of mechanical ventilators, and diaphragmatic pacemakers. Our case was the first to suggest that respiratory rehabilitation can contribute to favorable outcomes in the treatment of central hypoventilation syndrome.

Disclosure: Nothing to disclose

EPO2103

A preliminary study on the performance of one-leg versus two-leg symptom-limited exercise test in individuals with subacute stroke

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Background and aims: Based on previous studies, healthy individuals have shown to reach higher maximal oxygen consumption and greater workloads in a two-leg maximal cycling exercise test than in a one-leg test. However, for individuals with low aerobic capacity, such as subacute stroke patients, whether the above-mentioned physiological differences between two types of exercise tests still exist is unknown. Therefore, this preliminary study was to investigate physiological performances of one-leg versus two-leg symptom-limited cycling test in individuals with subacute stroke.
Methods: Ten people with subacute ischemic stroke were recruited. A stationary bike (Corival, Lode, Finland) was used to perform one-leg and two-leg symptom-limited exercise tests. Two tests were conducted on separate days within one week. The test order was randomized. Oxygen consumption and heart rate were continuously monitored by a metabolic cart (Metamax 3B system, Cortex, Germany) and data were analyzed breath-by-breath. Peak power (Powerpeak), oxygen consumption (VO2peak), and heart rate (HRpeak) were used for statistical analyses.
Results: Powerpeak, VO2peak, and HRpeak for one-leg versus two-leg tests were 50 vs. 54 watts, 0.617±0.010 mlO2/kg/min vs. 0.651±0.038 mlO2/kg/min, and 119.1±19.7 vs. 117.4±20.3 beats/min, respectively. No statistical significances ($p>0.05$) were found on all physiological responses for one-leg versus two-leg symptom-limited cycling tests.
Conclusion: This pilot study reveals that one-leg and two-leg symptom-limited cycling exercise induce similar physiological responses in individuals with subacute stroke. Future studies recruiting more individuals with subacute stroke are needed to further confirm this finding.
Disclosure: This study is partly supported by a grant from Ministry of Science and Technology, Taiwan (MOST 103-2314-B-037-003-MY3).

EPO2104

The assessment of balance function using the game system "virtual reality"

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[1]Republican Research and Clinical Center of Neurology and Neurosurgery, Neurogical department, Minsk, Belarus, [2]The company [4] iLab, Minsk, Belarus

Background and aims: Balance disorders are common symptoms in patients with diseases of the central nervous system, visual and vestibular analyzers. Assess the condition of balance function (BF) in patients with peripheral vestibular syndrome (PVS) and healthy persons using the game system "Virtual reality" (VR).
Methods: There were investigated 20 healthy persons (mean age 26.22±9.14 years), 10 patients (mean age 29.22±11.04 years) with PVS. There was used the equipment for applications Unity3d with VR "HTC Vive" with optical method of tracking body position. There were designed such parameters as average speed of postural axis (PA), the area of the support contour PA, which were measured in a standing position for 20 s, without using the VR and standing using VR for 20 s. There were calculated the coefficients S and K.
Results: In the group of healthy: 15 S=1.03±0,21; K=0.97±0.29, what characterizes a sustainable BF. 5 S=0.97±0.23, K=0,49±0,41 that reflects of a sustainable BF. In the group of patients with PVS: 5 S=0.77±0.22 and K=0.19±0.19 and reflect latent violations of BF, 2 S=0.91±0.27 K=0.51±0.44, which reflects the phenotypic features of sustainable BF, 3 patients; S=0.90±0.11; K=0.93±0.22 what characterizes a sustainable BF.
Conclusion: The method can be used to reveal disorders and features of the BF in healthy and patients with PVS on the basis of quantitative indicators of the postural movement of the axis in VR that will allow you to develop an individual program of rehabilitation of BF.
Disclosure: Nothing to disclose

EPO2105

Features of the bioelectric motor activity of the cerebral cortex in patients with upper limb motor disorders following a stroke

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Background and aims: The use of non-invasive neurocomputer interfaces based on EEG data in a rehabilitation is a promising strategy for improving the quality of life of patients after a stroke. However, there are still very few studies that have shown the features of EEG in healthy people and in patients with upper limb motor disorders following a stroke.
Methods: 5 healthy subjects and five patients with I63.3 Cerebral infarction due to thrombosis of cerebral arteries (the middle cerebral artery (MCA) infarction) underwent tasks with movements and subsequent movement imagination. The Encephalan-131-03 encephalograph (EEGA-21/26, Russia) with built-in software for data analysis was used for EEG registration. The electrodes were placed according to the scheme of 10-20%.
Results: The alpha-rhythm predominated during the study (8.00-13.00Hz) in healthy subjects. The theta rhythm (4.00-8.00Hz) in zones F3-C3, F4-C4 was registered for movements and the subsequent imaginary movements. While the examination of patients after a stroke has demonstrated beta-1 rhythm to be predominated (13.00-24.00Hz). Also there were theta rhythm (4.00-8.00Hz) in zones F3-C3, F4-C4 and beta-2 rhythm (24.00-35.00Hz) in the zones corresponding to MCA. Similarly, in both groups, alpha rhythm (8.00-13.00Hz) was registered in the P3-PZ-P4 zones during imaginary movements.

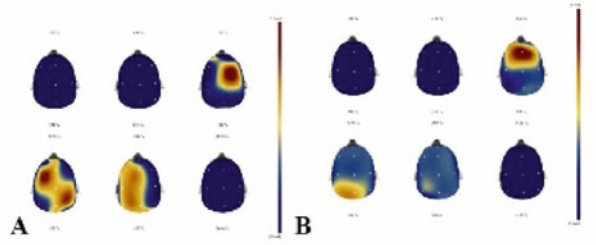

Fig. 1. Topographic mapping of spectral EEG characteristics of a healthy subject
(A) Activity during the execution of the block of tasks of real movements.
(B) Activity during the execution of the block of tasks on the imagination of movements

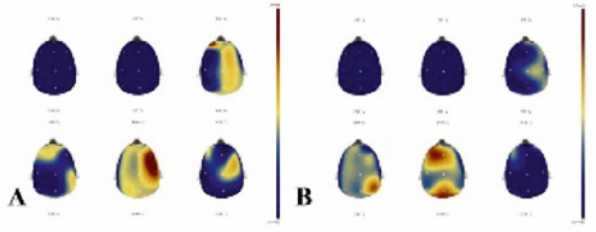

Fig. 2. Topographic mapping of spectral EEG characteristics of the patient after a stroke
(A) Activity during the execution of the block of tasks of real movements.
(B) Activity during the execution of the block of tasks on the imagination of movements

Conclusion: This study confirms the presence of bioelectrical features in patients with upper limb motor disorders following a stroke manifested by differences in the prevailing rhythm, localisation of excitation, the appearance of beta-2 rhythm during motor activity.
Disclosure: Nothing to disclose

EPO2106

Efficacy of training in virtual environment in patients with balance disturbances

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Research center of neurology , Neurorehabilitation, Moscow, Russian Federation

Background and aims: In the recent meta-analysis, it has been shown that the use of VR in combination with conventional therapy and as an alternative technique leads to a more significant recovery. The aim of our research was to study the efficacy of VR training in patients with balance disturbances.
Methods: 25 patients were included in the study, (mean age 67 [49; 72], median Berg balance scale 50 [42, 54]) with static and dynamic balance problems following chronic cardiovascular disease. Main group (n=15), received two weeks (30 min, 5 days\week) of virtual biofeedback training on Kinect based system «Rehabunculus» and conventional therapy. Control group (n=10) received equal time conventional therapy. Evaluation methods: Barg Balance Scale, objective Romberg test on Kinect based system.
Results: The preliminary data showed significant improvement in static and dynamic balance measured with BBS & Romberg test (p>0,05) in the main group. Also is clearly demonstrated improvement of single support phase during forward stepping. 5 patients (33%) increased their ability to walk without cane outdoor. In control group significant changes were observed only in static balance measured with BBS, Romberg test shoved only trend to improvement.
Conclusion: Preliminary data evidence that Rehabunculus VR system can be used for more intensive and effective stationary rehabilitation in combination with conventional therapy than conventional therapy alone.
Disclosure: Nothing to disclose

EPO2107

The impact of stroke severity on the outcome of clinical trials

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Background and aims: Using the results of two identical stroke studies with highly deviating baseline severity the discriminative power of common clinical outcome scales is evaluated in a meta-analytic framework in order to learn for future study designs and to avoid unnecessary loss of test power. Both studies had a prospective, randomized, double-blind, placebo-controlled design.
Methods: Treatment with 30ml Cerebrolysin once daily for three weeks was started 24-72 hours after stroke onset. In addition, patients participated in a standardized rehabilitation program for 21 days that was initiated within 72 hours after stroke onset. For both studies the original analysis data were used for meta-analysis (individual patient data analysis).
Results: Outcome at day 90 shows considerable heterogeneity due to marked ceiling effects in the population with mild baseline severity, while the analysis of early benefit (day 14, day 21) by means of the National Institutes of Health Stroke Scale, which is regarded as most sensitive to early improvements, showed high discriminative power in both study populations despite different baseline severity levels.
Conclusion: These new results strongly support the earlier findings of DeGraba (1999) who highlighted the importance of baseline stroke severity in stroke trials for discriminative power at different selected points in time. Despite heterogeneity of study populations the meta-analysis was able to well demonstrate beneficial effects of Cerebrolysin on motor function and neurological status in early rehabilitation patients after acute ischemic stroke.
Disclosure: Nothing to disclose

EPO2108

Pilot study of visual biofeedback and stabilometric platform use in home therapy of balance impairment in people with Multiple Sclerosis

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Background and aims: Balance impairment in people with multiple sclerosis (MS) is common. Gaming systems (Nintendo, Kinect.) have been tested for home therapy, however, cannot be properly individualised. Therefore a small portable system that includes stabilometric platform with visual biofeedback (Homebalance). Aim of this study is to evaluate the use of portable system for balance training in the home setting.
Methods: Home training was performed daily 20 minutes for 4 weeks The following assessments were performed at baseline and after 4 weeks of the training: Timed 25 foot walk test (T25FW), Timed Up and Go test (TUG), Berg balance test and mini BEST test, MS Walking Scale-12 and Falls Efficacy Scale.
Results: There were enrolled 10 people with MS, mean age 38.4 years (SD 6.7 y), mean disease duration 14.4 years (SD 6.8 y) with EDSS 1.5 to 6,. All participants completed 4 weeks training. Mean T25FW improved from 16.5 to 11.6 sec, TUG improved from 19.5 to 13.5 sec and TUG with a cognitive task improved from 22.3 to 15.2 sec. BEST test changed from 18.4 to 19.6 and Berg test score from 38.8 to 40.2.
Conclusion: Our pilot study showed feasibility of this type of training in group of people with MS. Audiovisual biofeedback helps to control exercise performance at home. Homebalance training was effectively used with people with mild balance and problems as well as with people with severe disability.
Supported by the project Progres Q27/LF1
Disclosure: Nothing to disclose

EPO2109

Clinical effectiveness of Botulinum Toxin (BoTN) injections in patients with sialorrhea and drooling

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Background and aims: Sialorrhea and drooling are common symptoms of many different neurological diseases and can increase the risk of aspiration. It affects the normal chewing mechanism and has a significant negative effect on social function. The objective of this study is to evaluate the effectiveness and safety of Botulinum Toxin A (BotoxR) injections in patients with drooling and sialorrhea and to assess the safety and adverse effects of Botulinum Toxin A (BotoxR) injections in the major salivary glands as there is a lack of NICE guidance.
Methods: We assessed the notes of patients treated with Botulinum Toxin A (BotoxR)* injections for sialorrhea and drooling in the Botox clinic (University Hospitals of Leicester) between 01st July 2015 and 31st December 2015.
Results: In our Botox cohort improvement in the drooling scales (more than 25% improvement) was found in 71% of the patients; no improvement (<25% improvement) in 29% of the patients; which is similar to published data in other studies. 14% of the patients reported mild adverse effects (dry mouth, odd taste).
Conclusion: BoTN injections are a useful option in the symptomatic control of sialorrhea and drooling. The BoNT injections for sialorrhea and drooling improve the quality of life of the patients with mild and infrequent side effects BoNT injections without ultrasound guidance (US) are effective, but the US guidance may improve the safety of the injections, especially in the submandibular salivary glands (Egevad et al.).
Disclosure: Nothing to disclose

EPO2110

The IRCCS Network of Neuroscience and Neurorehabilitation: the Italian platform for care and research about neurodegenerative disorders

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Background and aims: The IRCCS Network of Neuroscience and Neurorehabilitation is mainly focused on the sharing of knowledge, protocols and data, in order to promote the standardization and optimization of patients' clinical-care and therapeutic strategies.
Methods: Involving 24 highly specialized IRCCSs, the Network is providing several improvements to the research on neurodegenerative disorders, allowing:
- the centralization of genetic analyses
- the sharing of analytical and instrumental data
- the sharing of interpretation guidelines for genetic and instrumental data
- the characterization of sub-phenotypes of disease
- the development of standardized protocols
- the creation of a database of genomic variants
- the multidisciplinary evaluation of VoUS (variants of uncertain significance) from genomic analyses

Results: Furthermore, the development of the Network allowed the creation of a multidisciplinary platform for consultation between physicians and telecounseling, in order to improve the medical care of patients. Moreover, the integration of clinical and genomic data lead to a better characterization of patients. This innovative approach lays the foundations for the development of personalized medicine strategies based on a deep characterization of patients. In fact, one of the most innovative aspects of the network was the recording of dynamic data, collected not only at the time of the enrollment, but also in the follow-up evaluations.
Conclusion: It is expected that the collaboration between members of the IRCCS Network will support research programs on neurodegenerative disorders. The platform will support the sharing of genomic, epigenomic, pharmacogenomic data as well as traditional clinical measurements as family history, clinical outcomes and instrumental data.
Disclosure: On behalf of the Genomic and Proteomic Network of the Italian Institutes for Research and Care (IRCCS)

Peripheral nerve disorders

EPO2112

Bifacial weakness with paresthesias: a case associated with Campylobacter jejuni infection and electrophysiologic evidence of axonal loss in facial nerves

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Background and aims: Bifacial weakness with paresthesias (BFP) is a rare variant of Guillain-Barré Syndrome. Patients present with rapidly progressive bilateral facial weakness, distal limb paresthesias, and hyporeflexia, without ataxia, limb weakness or other cranial neuropathies. It is typically a demyelinating neuropathy. Here we report a case of BFP with electrophysiologic evidence of axonal degeneration in facial nerves and Campylobacter jejuni infection.
Methods: Case report
Results: A healthy 39-year-old Native American woman presented with a 10-day history of lower back pain, paresthesias in all limbs, followed by facial diplegia. A week before these symptoms she had fever and myalgia. Examination showed facial diplegia (Figure 1), absent lower extremity reflexes, and otherwise normal neurologic functions. CSF showed albuminocytologic dissociation. Antibody titers to Campylobacter jejuni were elevated. Anti-ganglioside antibodies and other infectious and inflammatory studies were negative. MRI studies of the brain and entire spine were normal. At presentation, facial motor responses were present and blink reflex responses were absent suggesting possible proximal conduction block in the facial nerves. Electromyography showed low amplitude motor unit potentials with reduced recruitment in orbicularis oris. She was treated with IVIG. Electrophysiology studies one week later showed absent facial motor responses, absent blink reflexes, and denervation in orbicularis oris, indicating axonal degeneration. Six months later, she had resolution of paresthesia, and clinical and electrophysiological improvement of bilateral facial neuropathies.

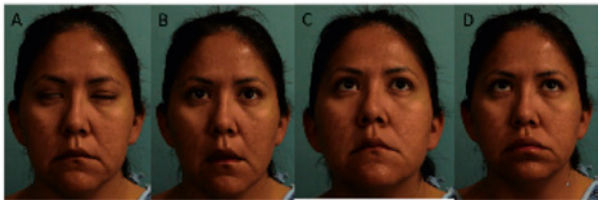

Figure 1: Bilateral lower motor neuron facial nerve weakness. Patient asked to (A) “close eyes”, (B) “smile”, (C) “kiss”, (D) “puff up your cheeks”. The photographs are reproduced with the patient’s permission.

Conclusion: The patient’s clinical presentation is typical of BFP. This is the first report of BFP associated with Campylobacter jejuni infection and electrophysiologic documentation of axonal loss affecting the facial nerves.
Disclosure: Nothing to disclose

EPO2113

Iatrogenic medial antebrachial cutaneous neuropathy – an uncommon complication of a common procedure

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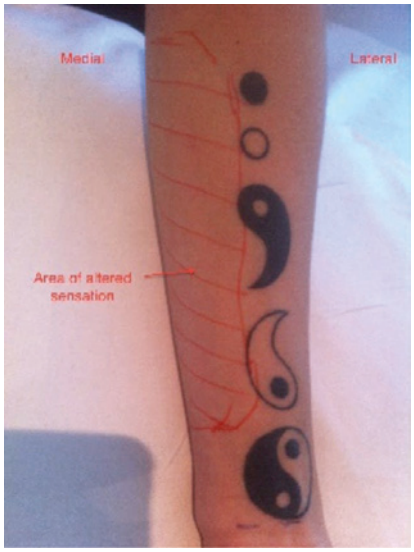
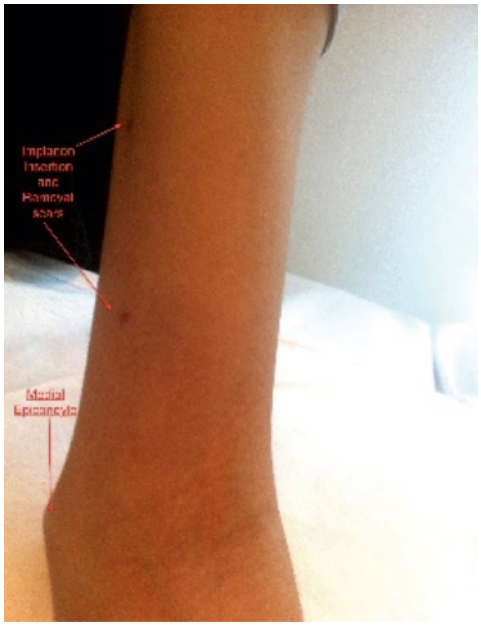
Western Heath, Neurology, Melbourne, Australia

Background and aims: Medial antebrachial cutaneous nerve can be involved in brachial plexopathy especially involving the medial cord but isolated medial antibrachial neuropathy can occur as a complication of ulnar nerve surgery at the elbow or rarely, as in our case, with hormonal contraceptive implant insertion in distal medial arm.
The aim of this case is to highlight an uncommon complication of a comon procedure. We present a case of iatrogenic antebrachial cutaneous neuropathy seconadry to Implanon® insertion.
Methods: We report a case of medial antebrachial cutaneous neuropathy in a 19-year-old female after insertion of an implantable hormonal contraceptive containing etonogestrel (Implanon®). The symptoms started with pain at the site of insertion in the medial arm and left elbow soon after insertion associated with dysaesthsia and reduced sensation in the medial forearm. The implant was removed 4 months later due to ongoing symptoms. Whilst her symptoms have slightly improved, she is left with a reduced/altered sensation in the distribution of left medial antebrachial cutaneous nerve of the forearm.



Picture displaying the approximate area of reduced sensation and dysaesthesia in the distribution of medial ante-brachial cutaneous nerve



Picture showing the scars of Implanon® insertion and removal

Results: The electrophysiological study of the left upper limb were within normal limits except for a reduced left medial antebrachial sensory nerve action potential (SNAP) amplitude–being less than 50% compared to the right indicating an isolated left medial antebrachial cuatenous mononeuropathy.

Conclusion: One needs to be aware of this rarely reported complication of medial antebrachial cutaneous neuropathy due to insertion or removal of hormonal contraceptive implant in the arm. Electrophysiological studies can be useful in the diagnosis. Early recognition and managmement may lead to better outcome.

Disclosure: Nothing to disclose

EPO2114

What may be hidden under the most common forms of polyneuropathy: keep your mind open

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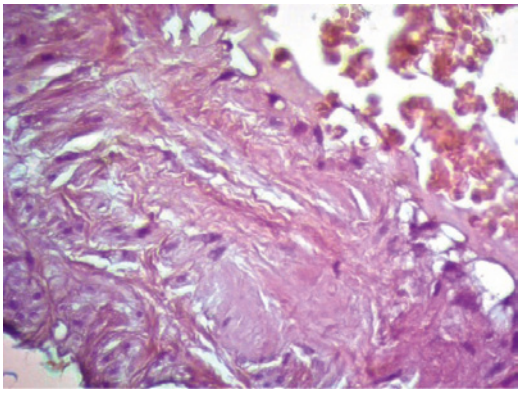
[1]Research Center of Neurology, Moscow, Russian Federation, [2]Ulyanovsk State University, Pathology, Ulyanovsk, Russian Federation

Background and aims: Over the last decade the early diagnostic of TTR-FAP became very important due to an available pathogenic therapy. The challenge of diagnostics is caused by non-specific symptoms of the disease on it's early stage and mimicking for other more common forms of polyneuropathy.

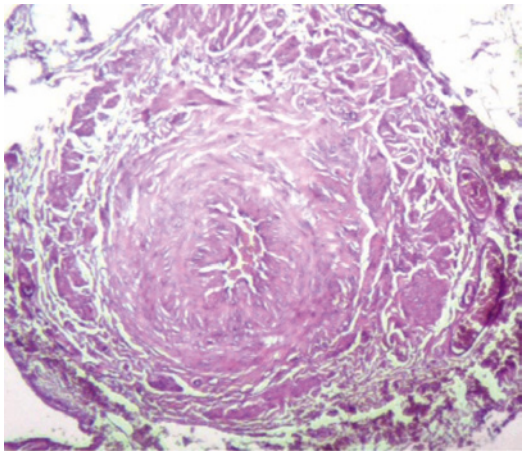
We aimed to report a case of familial amyloid polyneuropathy which was misdiagnosed with toxic polyneuropathy.

Methods: Nerve conduction study and DNA sequencing were performed. A right sural nerve biopsy specimen was obtained for histological investigation.

Results: We observed a 57-year-old caucasian man who complained of a progressive numbness and decreasing of temperature sensation in the feet and hands, which started 6 years ago. Also he presented distal and proximal weakness in the legs, severe fatigue and 10 kg lost within the last year. A history of severe alcohol consumption made the diagnosis of toxic polyneuropathy. Detailed interview revealed problems with urination and diarrhea, which started 6 month ago. There was a positive family history of weakness in the legs. NCS showed signs of sensorimotor axonal and demyelinating polyneuropathy, which fulfilled the electrodiagnostic criteria of probable CIDP. The sural nerve biopsy specimen showed focal edema and very small amyloid deposits in the subperineural tissue. DNA-sequencing of the TTR gene identified a rare c.157T>C (Phe53Leu) mutation, associated with FAP, which is the first case in Russia.



Right sural nerve biopsy, Congo red stain



Right sural nerve biopsy, hematoxylin and eosin stain

Conclusion: "Red flags" of the amyloid polyneuropathy may absent in it's early stage leading to a misdiagnosis. Presented case shows that TTR-FAP is a mimicking disease, requiring complex diagnostics with an obligatory genetic testing.
Disclosure: Nothing to disclose

EPO2116

A case of Facial Onset Sensory and Motor Neuronopathy Syndrome (FOSMN) with familial history of Amyotrophic Lateral Sclerosis (ALS) and sensory symptoms

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Background and aims: FOSMN is a rare neurological syndrome characterised by slowly progressive sensorial disturbs and motor weakness, spreading craniocaudally from the face to the limbs. Only 38 cases were described up to 2016. We report on a case of a 79-year-old man, whose brother died at the age of 57 year of ALS, after 2 years of disease.
Methods: The patient underwent complete neurological examination, brain Magnetic Resonance Imaging (MRI), extensive neurophysiological assessment and muscular biopsy. Information about his brother's neurological history was recollected.
Results: Dysesthesia and burning paraesthesia of the facial area were the initial symptoms, first experienced 20 years ago and slowly spreading to the limbs. Motor involvement came later in the course of the disease. He has no other relevant comorbidity. The last neurological examination showed bulbar involvement and diffused muscular hypotrophy, with spontaneous fasciculations and symmetrical hyporeflexia on all limbs. Brain MRI showed cortical, mesencephalic and pontine atrophy. Neurophysiological assessment confirmed abnormalities in sensory nerve conduction, chronic neurogenic changes with fasciculation but no active denervation, as well as the pathognomonic absence of bilateral blink reflex. The muscle biopsy described typical chronic neurogenic changes. The revision of all available information about his brother was compatible with the clinical diagnosis of ALS: he developed a classical rapidly progressive motorneuron disease, but interestingly also reported hypoesthesia in the right trigeminal region and in the areas innervated by L2-L5 in the right limb.
Conclusion: This is to our knowledge the first description of a case of FOSMN syndrome with familial history of ALS.
Disclosure: Nothing to disclose

EPO2119

Cholesterol level increases in patients with Complex Regional Pain Syndrome

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Background and aims: Based on anecdotal observations, we hypothesized that cholesterol levels increase in patients with Complex Regional Pain Syndrome (CRPS). Our goal was to test this hypothesis, in consecutive patients diagnosed with CRPS in our clinic.

Methods: Serum cholesterol levels (total and LDL) were measured in three patient groups: CRPS in acute phase (< 6 months from start), CRPS in chronic phase (> 6 month from start) and patients with chronic neuropathic pain syndromes, other than CRPS.

Results: Nine patients had CRPS in the acute phase, 33 patients had CRPS in the chronic phase, 24 patients had chronic neuropathic pain, other than CRPS. Patients with chronic CRPS had significantly higher total cholesterol levels as compared with patients with patients with chronic neuropathic pain other than CRPS (p=0.023). A similar trend was observed for LDL cholesterol, but it did not reach the level of significance (p=0.07). The occurrence of abnormally high level of cholesterol (both total and LDL) was significantly higher in the group of chronic CRPS patients, as compared with the patients with chronic neuropathic pain (p=0.04 and 0.01 respectively).There was no difference in gender and age between these groups.

Conclusion: Our results suggest that cholesterol levels increase in the chronic phase of CRPS. However, further data analysis on larger patients, inclusion and follow-up of more patients with acute CRPS is needed to further elucidate this.

Disclosure: Nothing to disclose

EPO2120

Pain and fatigue in PMP22 related neuropathies: comparison of HNPP and CMT type 1A with healthy controls

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Background and aims: Neuropathic pain and fatigue are debilitating symptoms with prominent impact on quality of life. Both of these are recognized in Charcot-Marie-Tooth (CMT) 1A patients; pain is reported as common as 71% of the patients and fatigue rates up to 64%. There are case reports and retrospective studies mentioning pain in hereditary neuropathy with liability to pressure palsies (HNPP). To our best of knowledge, there are no studies investigating fatigue in HNPP patients.

The main purpose of the study is to determine the frequency of the pain and fatigue in HNPP and CMT-1A patients, and establish the type of pain.

Methods: Patients and healthy controls were recruited from social media and Hereditary Neuropathy Foundation. The survey consisted of demographical questions, the duration of fatigue and pain, localization of the pain, disease and medication history, checklist individual strength (CIS), 0-10 numeric pain scale (NPS), ID-Pain, Beck depression inventory and short form-36 questionnaires. The questionnaire was reachable from 24th of May 2015 to 30th June 2017. Only patients with genetically confirmed diagnosis of HNPP or CMT-1A were included. Patient recruitment is demonstrated in figure 1.

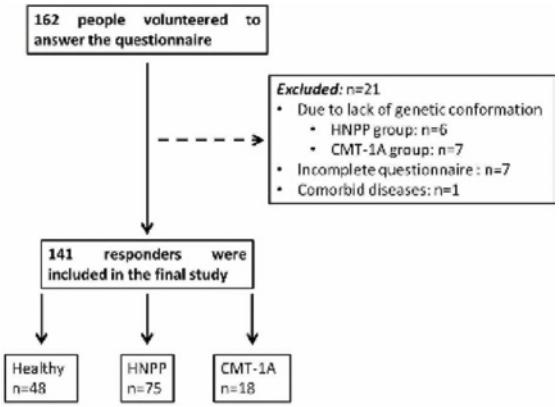

Figure 1

Results: Demographic aspects and detailed findings are summarized in table 1. NPS, total CIS scores and CIS subscales were similar between HNPP and CMT-1A patients and both were significantly higher than healthy controls (p<0.001).

Table 1	N (%)	Age (SD)	Gender (m/f)	Disease duration (SD)	Time to diagnosis (SD)	Pain (n)	Fatigue (n)
Healthy controls	48 (34%)	50.63 (15.22)	13/35	N/A	N/A	39.6% (19)	31.4% (17)
HNPP	75 (53.2%)	42.11 (12.54)	18/57	23.90 (14.34)	15.51 (14.08)	96% (72)	76% (57)
CMT-1A	18 (12.8%)	48.50 (11.59)	4/14	35.89 (17.20)	12.39 (15.47)	94.5% (17)	94.5% (17)
p value		0.105	0.894	0.007	0.476	<0.001	<0.001

Table 1

Conclusion: According to our findings, pain that is mostly neuropathic, and fatigue appear to be major components of HNPP and CMT-1A.
Disclosure: Nothing to disclose

EPO2121

Post bariatric surgery polyneuropathy: gastric banding vs. gastric bypass

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Background and aims: Bariatric Surgery (BS) has gained popularity in order to treat morbid obesity. As post-operative neuropathies (PO-N) are increasingly recognized, our aim was to examine incidence, clinical presentation, and outcomes of PO-N secondary to BS.
Methods: Patients who underwent BS between the years 2012 and 2015 at Parma University were included in this survey, and assessed before (T0) and 1 year after surgery (T1). Baseline characteristics and medical comorbidities, type of surgery, and PO complications were retrieved. Patients with a previous history of peripheral neuropathic disease were excluded from the analysis. If a patient presented with a new onset neurologic symptom including extremity numbness, paresthesia, muscle weakness, the status was considered PO-N+.
Results: Data from 61 patients were retrieved (n=30 Roux-en-Y Gastric bypasses, RYGP; n=31 Gastric banding, GB; 81.0% females). Of them, 7 (11.4%) developed some signs of PO-N, that eventually disappeared at T+24 months. The most common manifestations were paresthesia (n=6) and muscle weakness (n=4), similarly distributed in RYGP (n=4) and GB (n=3) groups. Although PO-N patients exhibited higher SF-36 score at T0 (p=0.018), no significant differences were found regarding BMI (T0, T1), percentual weight loss, serological data (ie vitamin B1, B2, B6, B12: in all cases $p>0.05$).
Conclusion: Neuropathy after BS is usually associated with lower levels of vitamin B1, B2, B12. However, we found no differences in PO-BMI, excess weight loss, and metabolic data levels . Larger data and more extended follow-up are required to validate our results.
Disclosure: Nothing to disclose

EPO2122

NK cells as surrogate marker for predicting efficacy of IVIg in CIDP

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Background and aims: Natural Killer (NK) cells are part of our innate immune system with regulatory and effector functions. Different studies suggest that the treatment with intravenous immunoglobulins (IVIg) has an immunomodulatory effect on NK cells. IVIg is a first-line treatment for various autoimmune diseases in particular in chronic inflammatory demyelinating polyneuropathy (CIDP). The lack of a predictive marker for IVIg responsiveness in CIDP avoids the early preservation of non-responding patients.
Methods: Using semi-quantitative PCR and flow cytometry in the peripheral blood of patients with CIDP, we analysed the effects of IVIg on the NK cell population before treatment initiation and 24h after first dose and correlated the changes with the reponsiveness to IVIg.
Results: IVIg administrations induced a reduction in the expression of several typical NK cell genes. Interestingly, this IVIg-induced reduction of NK cells was reversible four weeks after the IVIg treatment. Flow cytometry data revealed that IVIg reduced the cytotoxic CD56dim NK cell population, while regulatory CD56bright NK cells remained almost unaffected or were even increased. Interestingly, we found that the observed effects on NK cells almost exclusively occurred in CIDP patients who responded to IVIg therapy.
Conclusion: Correlation between the changes in the NK cell population and treatment efficiency suggests a crucial role for NK cells in the immunomodulatory mechanism of IVIg. Further studies are warranted to investigate whether the differences in the NK cell status of patients with CIDP represent a reliable surrogate marker in predicting the outcome of IVIg therapy.
Disclosure: Nothing to disclose

EPO2123

Isolated lesion of the lateral pectoral nerve due to repeated trauma

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Background and aims: The lateral pectoral nerve (LPN) subserves the proximal two thirds of the pectoralis major muscle. It does not contain cutaneous sensory fibers. Clinical findings of lateral pectoral nerve injury include asymmetry of chest wall associated with atrophy and weakness of the pectoralis major muscle. Mononeuropathy of the lateral pectoral nerve occurs less frequently [1,2,3,4]. In this report we present two cases of progressive atrophy and weakness of the clavicular part of pectoralis major muscle innervated by lateral pectoral nerve.
Methods: We present two cases of progressive isolated damage to the lateral branch of the pectoral nerve with marked atrophy of the clavicular portion of the major pectoral muscle.
Results: In our patients, the mechanism of isolated lesions of lateral pectoral nerves have been attributed to repetitive external microtraumas and pressure on the nerve trajectory between the chest and shoulder during sports or occupational activities.
Conclusion: Isolated injury of lateral pectoral nerve is unusual. In the literature there are cases described and attributed to nerve damage as a result of traction injuries, seat belt trauma and as a complication of mastectomy. Our cases were exposed to external forces on the nerve between chest and shoulder while using a tool, or repetitive fists in a certain manner for a long period.
Disclosure: Nothing to disclose

EPO2124

6 minutes walking test as outcome measures in CIDP patients

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disabling disease with monophasic, chronic or relapsing course. CIDP patients frequently complain about fatigue during a relapse or progressive deterioration of their clinical condition, together with sensory and motor symptoms. Moreover, clinical evaluation and clinimetric tests are based on qualitative evaluation or self-administered scale, not so sensitive in capturing minimal variations. Our aim was to find a quantitative measure of clinical improvement and correlate it to those commonly used in clinical practice

Methods: We performed an extensive assessment on 34 CIDP patients before and after therapy (first or second-line) through a large battery of outcome measures both routinely used as modified version of the Inflammatory neuropathy cause and treatment (INCAT) scale, Overall neuropathy limitations Scale (ONLS), Rasch-built overall disability scale (RODS), modified Rankin scale (mRS), Medical research Council (MRC) scale, 10 meters walking test both more rarely used too, as 6 minutes walkin test (6MWT). Response to therapy was evaluated through patients interview and by performing Wilcoxon signed-rank test. Logistic regression model was applied to evaluate the correlation among outcome measuring tools.

Results: We found a significant relationship between total walked meters and ONLS, RODS, mRS and MRC score ($p>0.000$), not with INCAT scale. Mean velocity significantly increased at each time point before and after therapies ($p>0.000$).

Conclusion: Our data suggest that 6 minutes walking test is a useful, reliable, objective scale, letting clinicians able to measure in a quantitative way patient's improvements, and their recovery from fatigue

Disclosure: Nothing to disclose

Monday, 18 June 2018

Cerebrovascular diseases 3

EPO3001

Role of pretreatment blood pressure on outcome of patients with nontraumatic intracerebral Haemorrhage

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Background and aims: Acute intracerebral haemorrhage (ICH) is mostly accompanied by increase in blood pressure (BP). Lowering BP is one of the basic treatment strategies of ICH. Although high BP is suspected to be associated with poor outcome of ICH patients, some results, especially in the very acute stage of ICH, are still controversial.
Aim of our study was to assess the effect of admission BP on 3 months functional outcome and hematoma progression.
Methods: 110 patients with acute nontraumatic ICH were included in the study. The first in hospital measured BP value was evaluated. Primary outcome was 3 months functional outcome classified as good (modified Rankin Scale (mRS) 0-3) and poor (mRS 4-6) and the presence of hematoma enlargement within 24 hours.
Results: A logistic regression was performed. BP above 160 mmHg systolic was associated with poor outcome, OR=4.168 (5% CI 1.135-18.792, p=0.033). There was no association with poor outcome for cut off level of 140 mmHg systolic BP. We did not found any relation between admission BP and hematoma enlargement.
Conclusion: Our data support hypothesis that high BP in the very acute stage of ICH, even if early treated, is associated with poor prognosis. In correspondence with some previous studies, we did not found any association between BP increase and hematoma volume progression. This finding may suggest that early correction of BP prevents the hematoma expansion as well as that the poor outcome of patients with high baseline BP is caused by other factors (e.g. edema or larger baseline hematoma volume).
Disclosure: Nothing to disclose

EPO3002

Influence of platelet indices on response to intravenous thrombolysis in acute ischaemic stroke-preliminary data

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Background and aims: Mean platelet volume (MPV), platelet distribution width (PDW) and platelet-to-large cell ratio (P-LCR) are easy and inexpensive indices reflecting platelet activation that can be derived from routine blood analysis in the emergency setting. In previous studies increased MPV has been associated with a higher risk of myocardial infarction and ischaemic stroke as well as worse prognosis. Alteration in platelet indices may be linked to worse response to IV thrombolysis (IVT). To our knowledge no one has yet addressed this issue. Aim of our study was to assess whether easily available platelet indices can predict response to IVT in patients with acute ischaemic stroke.
Methods: We enrolled 55 patients (mean age 66.96±15.33, range 18-88) with acute ischaemic stroke treated with IVT (Alteplase 0.9 mg/kg) over a period of 24 months. Patients who underwent endovascular treatment were excluded. Mean NIHSS at presentation was 8.16±5.09. Efficacy of IVT was assessed by reduction in NIHSS score at 24 hours and 7 days from treatment.
Results: No correlation was found between MPV, PDW and P-LCR values before IVT and NIHSS reduction at 24 hours. On the contrary, all indices showed a statistically significant negative correlation with NIHSS reduction at 7 days (Pearson's correlation, MPV r=-0.28, p=0.043; PDW r=-0.27, p=0.047; P-LCR r=-0.29, p=0.038). Significance was maintained after controlling for possible confounders. Furthermore, no correlation was found with haemorrhagic transformation.
Conclusion: MPV, PDW and P-LCR may represent useful markers to predict outcome after IVT in acute ischaemic stroke.
Disclosure: Nothing to disclose

EPO3003

Female survivors of first-ever small subcortical stroke have an increased risk of long-term cognitive decline compared to men

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Background and aims: Sex is a significant determinant of functional outcome and survival after stroke. Cognitive aspects of long-term outcome after small subcortical stroke (S3) of lacunar type have been rarely analyzed in the light of sex differences.
Methods: A cohort of small vessel disease (SVD) patients presenting with first-ever S3 has been evaluated 4 years after qualifying event for the presence of depression and cognitive decline (CD).
Results: Study group comprised 136 female and 158 male patients who all underwent neuropsychological assessment and brain MRI. No difference was detected between the groups in regard to age ($p=0.709$) or frequency of vascular risk factors (RF) ($p>0.1$ for all). At baseline, women had more disability compared to men with mean modified Rankin scale (mRS) score 2.6 (1.4 in men, $p<0.0001$). All MRI SVD parameters were more severe in females, including measures of white matter lesions and total number of lacunar infarcts (tLI) ($p<0.0001$ for all). Follow-up data indicated that CD was more frequently detected in women than men (78.7% vs. 51.2%, $p<0.0001$), which was not the case for depression ($p=0.654$). Multivariate regression analysis showed that severity of MRI lesions (HR 1.38, 95%CI 1.17-1.62; $p<0.0001$), CD (HR 1.85, 95%CI 1.06-3.24; $p=0.032$), tLI (HR 0.74, 95%CI 0.59-0.92; $p=0.008$) and mRS (HR 8.35, 95%CI 5.04-13.84; $p<0.0001$) were independently associated with female sex.
Conclusion: On long-term follow-up female sex was associated with more frequent CD after first-ever S3, probably secondary to more severe brain SVD lesions compared to male sex. This finding could not be explained by RF or age differences.
Disclosure: Nothing to disclose

EPO3004

Viral infections as a cause of ischemic stroke

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Background and aims: Viral infections can cause the infective vasculitis with high inflammatory markers and coagulation that can become the risk of ischemic stroke.
Methods: Totally 82 ischemic stroke patients investigated, 45 males, 37 females aged 50 to 70 with anamnesis of herpes simplex ½ and cytomegalovirus infection 3 months previously of stroke. Major risk-factors including atherosclerosis, diabetes mellitus, arterial hypertension, cardiac diseases, smoking have been researched. Stroke severity assessed by NIHSS. Ischemic lesion ascertained on Brain MRI (1.5 Tesla). Blood researched for Antinuclear antibodies (ANA) and Antineutrophil cytoplasm antibodies (ANCA) by enzyme –linked immunosorbent assay (ELISA), coagulation test and serology for Herpes simplex virus (HSV 1/2) and cytomegalovirus was done. Statistics performed by SPSS -14.0. Pearson correlation and Multivariate logistic regression (entered stepwise model) were done.
Results: From 82 stroke patients 42 patients found were for HSV1, 25 patients –for HSV2 and 15 patients –for cytomegalovirus. Blood ANA was elevated in 72% of patients (11.5U± 4.6)and Anti PR 3 (c-ANCA) in 28% of patients (0.96U±0.05). Positive correlation found between blood ANA and ANCA levels with Blood INR in stroke patients ($R=+0.47$ and $R=+0.25$ respectively, $P<0.05$). Multivariate logistic regression revealed the significance of blood high ANA and ANCA in conjunction with smoking for severity of stroke measured by NIHSS ($p<0.01$). There was not significant correlation between ANA and ANCA levels and ischemic lesion size on MRI.
Conclusion: Herpetic infections can cause the infectious vasculites and by increasing the inflammatory reaction might help to the ischemic stroke development.
Disclosure: Nothing to disclose

EPO3005

Accuracy of identification of acute cerebrovascular accidents at pre-hospital setting in Latvia

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Background and aims: To determine diagnostic quality of acute cerebrovascular incidents in pre-hospital setting in Latvia.
Methods: Retrospective descriptive data analysis was performed including data from Emergency Medical Service (EMS) and hospital records from five hospitals in Latvia. All 8969 adult patients, delivered to stroke-ready hospitals by EMS during 2015 with diagnosis of stroke or TIA, respectively I60-64 or G45, according to ICD-10 were included in the study.
Results: Out of 8969 patients 67.2% were female and 32.8%-male. Median age was equal to 73 years. Overall pre-hospital diagnostic accuracy of cerebrovascular accidents was 44.9%. TIA accounted for 37.4% of all pre-hospital diagnoses but the diagnosis of TIA was proved only in 14.4% of delivered patients. Stroke, without specifying between hemorrhagic and ischemic (I64) accounted for 56.7% of all delivered cases and diagnoses were correct more frequently-in 64.0% of cases. Accuracy of diagnosis were associated ($p < 0.001$) with a reason of calling EMS (e.g., paralysis) and patient age. There were no observed associations with EMS team profile, hour of day or day of the week.
Conclusion: In Latvia accuracy of pre-hospital diagnosis of acute cerebrovascular accidents is relatively low. In particulary, the accuracy is low in diagnosis of TIA. It is necessary to increase EMS staff training, with particular emphasis on the diagnosis of TIA, in order to better select the patients who need urgent treatment and further investigation in stroke unit.
Disclosure: Nothing to disclose

EPO3006

Our experience of using implantable loop recorder devices to specify stroke etiology in Pauls Stradins clinical university hospital, Riga, Latvia from 2014 to 2017

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Background and aims: Identifying atrial fibrillation (AF) is essential as AF-related strokes are associated with an increased risk of disability and death, and they tend to recur when anticoagulation is not implemented.
To evaluate the incidence of AF among cryptogenic stroke survivors using implantable loop recorders.
Methods: Retrospective study included cryptogenic stroke survivors who had implantable loop recorders (ILR) implanted between the years 2014 and 2017. The data was collected from electronic database, medical histories, and via phone. The analysis of data was carried out using IBM SPSS 23.0.
Results: The study included 22 cryptogenic stroke survivors. The patients were aged from 42 to 74 (mean 55.18) years. There were 5 (23%) women and 17 (77%) men. In 7 (31.82%) patients atrial fibrillation was found, time ranges from 2 to 8 months (mean 4.8). Out of all revealed AF patients, 5 (71.4%) were under anticoagulant therapy. Out of all patients, 2 had a recurrent stroke and 1 was diagnosed with AF and did not use any anticoagulants, and the other one has never checked loop recorder data and was not under any anticoagulant therapy.
Conclusion: Among patients with cryptogenic stroke, AF was detected in 31.82% (n=7). These results suggest that the implantable loop recorder is an effective way of finding subclinical AF. Loop recording monitoring is superior to conventional monitoring and may be considered after a cryptogenic stroke for patients who are good candidates for anticoagulation.
Disclosure: Nothing to disclose

EPO3007

Admission neutrophil to lymphocyte ratio as a possible marker for distinguishing between atherothrombotic and cardioembolic ischemic strokes

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Background and aims: Neutrophil to lymphocyte ratio (NLR) is an important measure of systemic inflammation and was shown to predict prognosis and haemorrhagic transformation in ischemic stroke patients. Since a high NLR value was associated with an increased risk of atrial fibrillation occurrence in previous studies, our aim was to assess the utility of admission-NLR in distinguishing between atherothrombotic and cardioembolic strokes.
Methods: We performed a cross-sectional study including 244 patients hospitalized for acute ischemic stroke and treated with intravenous rtPA. Stroke etiology was established according to ASCOD criteria. Atherothrombotic strokes were defined as A1 or A2 and cardioembolic strokes as C1 or C2. Complete blood count was obtained at admission. NLR was calculated as absolute neutrophils count divided by lymphocytes count.
Results: The median age of the patients was 71 years (25-75 IQR 61-79), 52.1% being male. The median NIHSS score at admission was 14 points (25-75 IQR 9-18). According to ASCOD criteria, 17.6% of strokes were classified as A1, 4.09% as A2, 49.18% as C1 and 6.96% as C2. NLR values were significantly higher in patients with cardioembolic strokes compared to patients with atherothrombotic strokes (median NLR value for cardioembolic strokes 2.84 (25-75% IQR 1.88-3.74) versus 2.19 (25%-75% IQR 1.62-2.87) for atherothrombotic strokes, p=0.02).
Conclusion: Neutrophil to lymphocyte ratio could be a valuable tool in differentiating between atherothrombotic and cardioembolic strokes in the emergency department setting. Further studies including larger number of patients are needed to confirm the present results.
Disclosure: Nothing to disclose

EPO3008

Intravenous fibrinolytic therapy in Centenarians

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Background and aims: Early intravenous thrombolysis (IV-rtPA) within 4,5 hours after onset is the standard treatment for ischemic stroke (IS). Currently elderly patients are treated with IV-rtPA safely although benefit may be inferior to younger patients. Experience beyond 100 years is anecdotical.
Methods: Prospective registry (2010-2017) of patients treated with rt-PA in our tertiary university hospital stroke unit (SU). Patients 100 years or older with IS treated with IV-rtPA were selected. Demographic and clinical variables, IS severity as measured by NIHSS, hemorrhagic complications and functional outcome at 3 months (modified Rankin scale, mRS) were registered.
Results: Three patients, all women, of 101, 103 and 104 years, were treated in our SU. All were functionally independent (mRS $\leq$2) and presented with cardioembolic stroke due to atrial fibrillation without previous anticoagulant treatment. Their Chad2vasc2 sacle was$\geq$4 and IS was severe with NIHSS of 15, 21, and 23 respectively. Treatment with IV-rtPA was applied within 4,5 hours of stroke onset, with a median time from the onset of symptoms of 235 minutes (-). Two patients were asymptomatic (mRS $\leq$2) at discharge and at 3 months, while the third had a mRS of 3 at 3 months. No serious hemorrhagic or systemic adverse events were registered. All three were prescribed direct oral anticoagulants at discharge.
Conclusion: In our experience, centenarians with IS treated with IV-rtPA had severe cardioembolic strokes, which were successfully treated without serious adverse events. When functional basal status is good, age per se should not be regarded as a contraindication for IV-rtPA.
Disclosure: Nothing to disclose

EPO3009

The change in antithrombotic medication profile of cardioembolic stroke prevention in Latvia from 2014 to 2016

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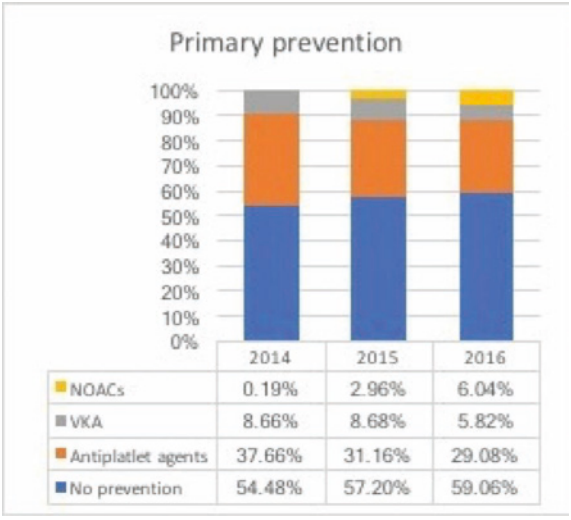
Background and aims: Current studies show that NOACs are non-inferior to VKA in stroke prevention and present fewer bleeding complications. But there are no guidelines that suggest that NOACs should be preferred over VKA for stroke prevention. We wanted to evaluate if the preferred antithrombotic medication has changed over the recent years.

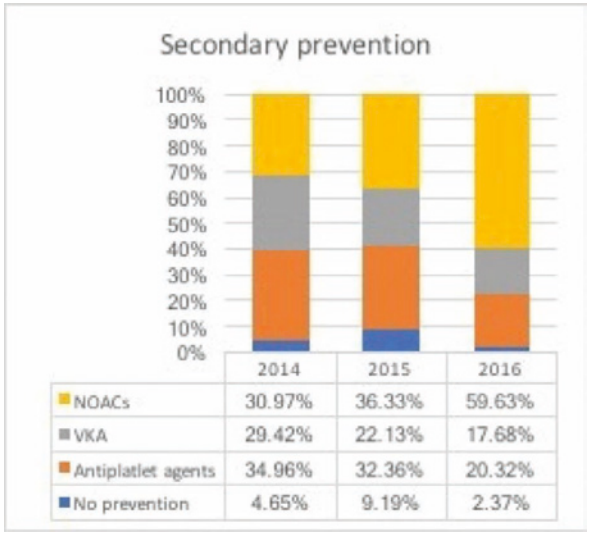
Methods: All cardioembolic stroke patients admitted to P. Stradins Clinical University hospital, Riga, Latvia during 2014-2016 were included in the study. The use of antithrombotic medication was evaluated- before stroke onset, on discharge and one year after discharge.

Results: A total of 1485 patiens were included in the study, 531 in 2014, 507 in 2015 and 447 in 2016. The results are shown in the added charts.



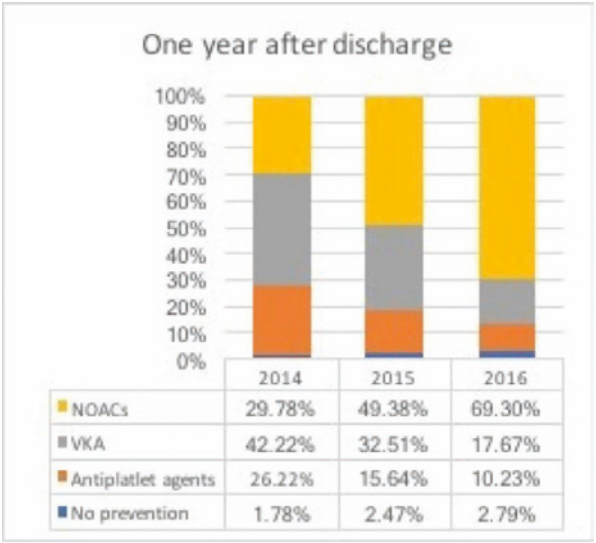
	2014	2015	2016
NOACs	0.19%	2.96%	6.04%
VKA	8.66%	8.68%	5.82%
Antiplatlet agents	37.66%	31.16%	29.08%
No prevention	54.48%	57.20%	59.06%

Primary prevention



	2014	2015	2016
NOACs	30.97%	36.33%	59.63%
VKA	29.42%	22.13%	17.68%
Antiplatlet agents	34.96%	32.36%	20.32%
No prevention	4.65%	9.19%	2.37%

On discharge



	2014	2015	2016
NOACs	29.78%	49.38%	69.30%
VKA	42.22%	32.51%	17.67%
Antiplatlet agents	26.22%	15.64%	10.23%
No prevention	1.78%	2.47%	2.79%

One year after discharge

Conclusion: The preference of NOACs over VKA in secondary stroke prevention is significantly increasing over the years.

Disclosure: Nothing to disclose

EPO3010

Marital status and in-hospital mortality of ischemic stroke

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Background and aims: Social isolation is a factor with important influence on the outcome of ischemic stroke. The aim of this study was to investigate the influence of marital status on in-hospital mortality of ischemic stroke.
Methods: We have analyzed 1591 consecutive patients with ischemic stroke hospitalized at the Clinic of Neurology in Nis, Serbia. Binary logistic regression was performed in order to measure the influence of multiple factors on the stroke in-hospital mortality. This model contains the following independent variables: sex, age, National Institutes of Health Stroke Scale (NIHSS) on admission and marital status (married, divorced, widowed or never married).
Results: It was shown that the model as a whole was statistically significant $\chi 2$ (df=8, N=1591)=480.367, p<.001), and that it successfully discriminates stroke survivors and patients who died during hospitalization. The model explains 37% (r2, Nagelkerke) of the variance in stroke mortality and successfully classifies 77% of cases. The influence of age, NIHSS and marital status were statistically significant. The strongest predictor of stroke mortality was NIHSS on admission (odds ratio 1.165). Our results showed that marriage is a strong independent protective factor for stroke in-hospital mortality, with odds ratio of 0.266 for currently married patients (p=0.001), 0.34 for divorced patients (p=0.027) and 0.33 for widowed patients (p=0.009).
Conclusion: In conclusion, marriage or history of marriage is a protective factor for in-hospital mortality of ischemic stroke.
Disclosure: Nothing to disclose

EPO3011

Evaluation and outcome of triage for patients with transient ischemic attack: a two-year analysis of the TIA Clinic of the University Hospitals Leuven

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Background and aims: Urgent evaluation of transient ischemic attack has shown to lower the risk of recurrent cerebrovascular events. We present the results of the TIA clinic model in UZ Leuven, Belgium, during its first two years (2015-2016).
Methods: We prospectively collected data including the rate of recurrence at 90 days, hospitalization rate, patient characteristics and patient assessment, and compared the results with a historical cohort.
Results: Fifty-six patients were included and compared to 75 historical controls. Ninety-day recurrence rate was 3.6% for TIA Clinic patients (versus 6%, p=0.70). No low-risk TIA clinic patient had a recurrent cerebrovascular event at 90 days follow up, compared to two patients in the high-risk group. The rate of hospital admissions was similar during TIA Clinic period compared to the 2013-2014 period (67.9% vs 72%; p=0.61). There was faster access to MRI scans (p=0,001), more usage of MRI brain scans (p=0.0017) and CT angiography (p=0.0058), less CT whole brain scans (p<0.001), more prescriptions of statin therapies at discharge (p<0.0001) and more follow-up visits (p=0.0085) in comparison to the historical data.
Conclusion: The TIA Clinic model resulted in low rates of recurrent cerebrovascular event at 90 days after TIA. It is a safe and efficacious model for management of low risk TIA patients. The TIA Clinic model improved patient assessment and resulted in equal percentage of recurrence at 90 days.
Disclosure: Nothing to disclose

EPO3012

Non-aneurysmal basal cistern haemorrhage: does initial blood distribution influence presentation and outcome?

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Background and aims: Non-aneurysmal subarachnoid haemorrhage (SAH) is divided into perimesencephalic SAH (PM-SAH), usually a benign entity, and non-perimesencephalic SAH, a heterogeneous group ranging from CT-negative to diffuse SAH (D-SAH), with a wide range of outcomes. The authors evaluated the presentation and outcome of these entities.
Methods: Retrospective review of records of patients admitted between 2008-2016 with angiogram-negative SAH and haemorrhage centered to the perimesencephalic cisterns, classified as PM-SAH and D-SAH according to Rinkje criteria.
Results: Of 283 patients with SAH, no etiology was found in 46 and 23 patients were included, with a mean age of 57 years. PM-SAH was present in 13 patients and D-SAH in 10 patients. On admission, all PM-SAH patients scored <3 on the World Federation of Neurosurgical Societies (WFNS) scale and one patient had focal neurological deficit. In the D-SAH group three patients had a WFNS >3, all of whom had hydrocephalus and one seizures. During the in-hospital stay, vasospasm occurred in one PM-SAH patient and two D-SAH. One PM-SAH patient had new-onset seizures. At discharge, all patients with PM-SAH had <3 in the mRankin scale, while three in D-SAH group scored ≥3, corresponding to the patients with WFNS >3 at admission. Past medical history revealed hypertension in 13 patients (56.5%) and anti-thrombotic use in 5 (27.2%).
Conclusion: In our sample D-SAH has a poorer outcome, which is associated with worse clinical status at admission. The finding of a high number of patients with hypertension and anti-thrombotic therapies suggests an increased risk for these pathologies.
Disclosure: Nothing to disclose

Epilepsy 3

EPO3013

The efficacy of an online learning tool in improving EEG analysis and interpretation skills of neurology registrars, neurologists and technologists

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Background and aims: Web-based, distance learning programs may provide effective electroencephalogram (EEG) training in resource-poor settings. EEGonline is an interactive, web-based, 6-month multi-modality, learning program designed to teach basic principles and clinical application of EEG. This study aimed to determine the effectiveness of EEGonline in improving EEG analysis and interpretation skills.

Methods: Fifty-three participants (19 neurologists, 28 neurology residents and 6 medical technologists) from 13 mostly African countries registered on EEGonline from 19th June to 17th December 2017, were enrolled. Pre- and Post-course multiple-choice question (MCQ) test results and EEGonline user logs were analysed. Differences in pre- and post-test performance were correlated with quantified exposure to various EEGonline learning modalities. Participants' impressions of EEGonline efficacy and usefulness were assessed through Pre- and Post-course perception surveys.

Results: Forty-two participants attempted both pre- and post-course tests. Mean scores were 49.0% and 66.8% respectively (t=7.2156, df=41, p<0.0001) [Figure 1]. Median percentage improvement was 37.8% (Range -35.5 to 262.5) with 77% of participants showing improvement. Post-course test performance was better in participants accessing interactive EEG-activities versus didactic lecture-notes. Further analysis will correlate post-course test performance with overall use of EEGonline and its various learning modalities.

Over eighty percent of post-course survey respondents felt their EEG analysis skills had improved, that EEGonline was a useful learning tool (Figure 2) and should be recommended as part of EEG training curricula.

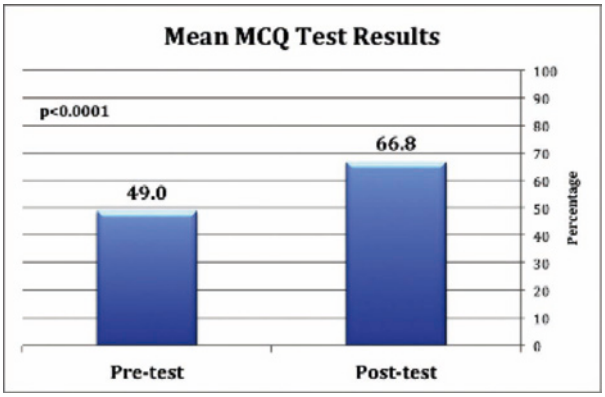

Figure 1

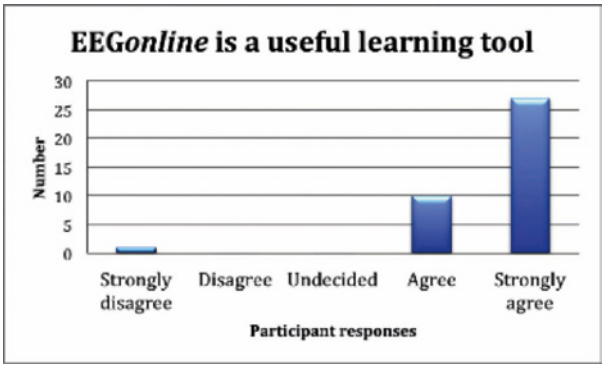

Figure 2

Conclusion: Preliminary results confirm that EEGonline, a web-based, multi-modality learning tool is effective in improving EEG analysis and interpretation skills and may be useful in resource-poor settings

Disclosure: Nothing to disclose

EPO3014

The neuroprotective effect of Hericium erinaceus in the mouse hippocampus after pilocarpine-induced status epilepticus

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Background and aims: Hericium erinaceus (HE), an edible mushroom in Asia, has been used in traditional medicine for treating various diseases. However, roles of HE in epilepsy remain to be investigated. Thus, we evaluated HE-induced neuroprotective effects in the hippocampus after pilocarpine-induced status epilepticus and its underlying mechanisms.
Methods: Male 6-week-old C57BL/6 mice were administered HE crude extracts (60mg/kg, 300mg/kg, p.o.) from 14 days before pilocarpine injection to 6 days after the onset of status epilepticus (SE). At 30 min after atropine methyl nitrate and terbutaline hemisulfate injection (2mg/kg, i.p.), pilocarpine hydrochloride (280mg/kg, i.p.) was treated to induce SE. Seizure stages were determined by Racine scale. At 2 h after SE onset, diazepam (10mg/kg, i.p.) was administrated to terminate seizures. All experimental animals were sacrificed at 1 week post-SE. The neuroprotective effects by HE treatment were determined by cresyl violet and NeuN staining. COX-2 expression and seizure-induced gliosis were analyzed by immunohistochemistry.
Results: Cresyl violet staining and immunohistochemistry to NeuN showed prominent cell death in the pyramidal cell layers of the hippocampal CA1 and CA3 subfields in vehicle-treated group. However, neuronal cell damage in the hippocampal CA1 subregion was significantly reduced by HE treatment (60mg/kg). HE did not affect SE-induced reactive astrocytosis or microglial activation in all groups. Interestingly, HE (60mg/kg) decreased the number of COX-2 expressing cells, which were mostly astrocytes and a few microglia.
Conclusion: Chronic administration of Hericium erinaceus showed neuroprotection against pilocarpine-induced status epilepticus, possibly via COX-2 inhibition in the hippocampus.
Disclosure: Nothing to disclose

EPO3016

Adherence to treatment in epileptic patients attending the emergency department: analysis of causes and associated factors.

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Background and aims: Several studies show that patient non-compliance as a cause of treatment failure in epilepsy. Our purpose was to analyse the causes of poor therapeutic adherence in epileptic patients as well as possible related factors.
Methods: An observational retrospective study was carried out on epileptic patients who were evaluated by the neurologist in the emergency department for seizure recurrence during 2016. We analysed demographic and clinical information on these patients and describe the main causes of lack of adherence.
Results: Of a total of 255 patients included, poor adherence was the main seizure trigger in 13.3% (34 patients). In non-adherent patients the mean age was 41.9 ±18.5 years (mean ±SD), 67.6% were male, 17.6% had a history of drug abuse, 23.5% of excessive alcohol consumption and 32,4% of psychiatric disease. 58.8% of on-adherent patients were receiving monotherapy, 8,8% bitherapy and 14.7% polytherapy. 17.6% had dropped out the treatment. Among the patients with poor adherence, 44,1% were not taking properly their prescribed medication by choice, 42.1% of patients forgot to take medication and 5,9% dropped out because of poor tolerance. Non-adherence was positively and significantly correlated with history of drug abuse ($p=0.018$) and excessive alcohol consumption ($p<0,005$). Differences were not significant in age, gender or history of psychiatric disorder.
Conclusion: In our study, the main cause of lack of adherence was voluntary decision. Poor adherence was significantly associated to history of drug abuse and excessive alcohol consumption. It is important to develop strategies to enhance patient adherence.
Disclosure: Nothing to disclose

EPO3017

Cessation of seizures following endoscopic third ventriculostomy and septostomy

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Background and aims: Chronically increased intracranial pressure is not recognized as a cause for seizures. We report three patients with medically refractory seizures who became seizure-free following their treatment of chronic hydrocephaly via endoscopic third ventriculostomy and septostomy without any antiepileptic medication modifications.
Results: We report a 21-year-old female, a 36-year-old male and a 30-year-old male with medically refractory focal epilepsy. First and second cases had asymmetric triventricular hydrocephaly and third case had an enlarged lateral ventricle with transependymal oedema. None of them were suitable for resective surgery due to multiple epileptogenic foci. First patient has undergone septostomy and third ventriculostomy due to a new onset progressive headache and MRI findings. For second and third patients, operation decision was based mainly on imaging findings and lack of alternative solutions. Preoperative seizure frequencies were 8, 2 and 1 seizures per month, respectively. All patients were seizure free at the follow ups (2 months, 5 months and 7 months respectively). Case 1 and 2 reported rare auras without propagation to seizures.
Conclusion: Refractoriness of the seizures in chronic hydrocephaly patients might emanate from increased pressure leading to relative ischemia and changes in the microenvironment of the tissues that are already under stress. Surgical treatment for chronic obstructive hydrocephaly might aid in seizure control in selected refractory epilepsy patients.
Disclosure: Nothing to disclose

EPO3018

Preliminar study on BDNF regulation by DNA methylation in Mesial Temporal Lobe Epilepsy

R. Ferreira[1], B. Leal[2], J.M.M. Chaves[3], C. Carvalho[2], A. Bettencourt[2], J. Freitas[3], J.E.D.P. Ramalheira[3], J.M.C.F. Lopes[3], A. Martins da Silva[3], P.P. Costa[4], B. Silva[2]
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Background and aims: Brain-derived neurotrophic factor (BDNF) is a neurothrophin associated with a wide range of neurophysiological processes, such as neurogenesis, gliogenesis, synaptogenesis and neuroprotection. BDNF has been described as overexpressed in hippocampus of both animal models and Mesial Temporal Lobe Epilepsy (MTLE) patients. Gene expression may be modulated by DNA methylation of the respective promoter regions. We sought to analyze, the DNA methylation of the BDNF exon I promoter, a region associated with neuronal imbalance.
Methods: DNA methylation levels were evaluated by Quantitative Methylation-Specific PCR (QMSP) in hippocampus and adjacent neocortex of 23 MTLE patients and 10 healthy controls.
Results: No statistically significant differences in DNA methylation levels of BDNF exon I promoter were found between MTLE patients and controls
Conclusion: MTLE has been associated with alterations in the DNA methylation profile. Our preliminary results suggest that these methylation changes do not affect globally the promoter regions but may be gene / promotor region specific. BDNF gene presents a complex structure with multiple promotor regions that allows to fine-tune transcriptional regulation and may be responsible for the variety of BDNF neuronal functions. Different promotor regions have been analysed in experimental and clinical studies with conflicting results. We suggest that to a better comprehension of BDNF dysregulation in MTLE it is necessary a study of DNA methylation of all promoter regions of this gene. This is particularly important as BDNF can orchestrate different cellular processes involved in epiletogenesis.
Disclosure: Supported by a BICE Tecnifar Grant

EPO3019

Cognitive disorders in idiopathic generalized epilepsies

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Background and aims: The aim of our study was to determine whether there is cognitive impairment in patients with IGE, to analyse the cognitive profile of patients with Idiopathic generalized epilepsies (IGE) and compare it with the cognitive profile of patients with temporal lobe epilepsy (TLE).
Methods: A comprehensive battery of neuropsychological tests was used to analyse 27 patients with IGE and 26 patients with TLE, treated and evaluated at the Centre for Epilepsy Clinic of Neurology, Clinical Centre of Serbia, as well as 25 healthy controls. In all patients, the diagnosis of epileptic syndromes was established according to the current criteria of the International League Against Epilepsy. The following cognitive functions were analysed: intelligence, attention, speech, frontal (executive) functions, memory and visuospatial construction skills. The control group was older and had a higher level of education compared to the groups with epilepsy, while did not differ in terms of sex and manipulative dominance. Global cognitive screening (MMSE) was significantly lower in IGE.
Results: The results showed that the patients with IGE had significant global cognitive impairment. It was also found that patients with TLE had significant impairment that was not different compared to the group with IGE. In patients with IGE intelligence, attention, speech and frontal functions were predominantly impaired.
Conclusion: Our study showed that patients with IGE had significant global cognitive decline, but absence of any meaningful difference in the cognitive profile compared to the patients with TLE.
Disclosure: Nothing to disclose

EPO3020

Withdrawal antiepileptic drug: is it safe?

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Background and aims: Epilepsy is a chronic disease of the central nervous system, affects 1% of the population. Patients who are seizure-free, want to continue with antiepileptic drugs (AEDs), despite financial burden, side effects and stigmatisation, due to the risk of seizures. Theobjective of thisstudy; is to estimate the risk of recurrence after withdrawal of AEDsand to determine risk factors in patients who are seizure free on monotherapy.
Methods: Eighty eight patients, who were seizure free for at least 2 years were included in the study. The patients were divided into two groups as relapse or remission status.
Results: Forty-six of the patients were female (52.3%), 42 were males (47.7%) and the mean age was 28.8±12.3. 71 patients (80.7%) were at remission and 17 patients (19.3%) had seizure recurrence after clinical follow-up. Late onset drug initiation age of relapse group was significantly higher than remission group. It was determined that the relapse rates were increased in patients who had pathologic findings in the EEG examination after withdrawal of AEDs.
Conclusion: Well-defined individual risk factors will protect patients from side effects of AEDs, stigmatisation and risk of recurrence.
Disclosure: Nothing to disclose

EPO3021

300 consecutive cases of status epilepticus: a retrospective study

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Background and aims: Status epilepticus (SE) is defined as a condition of abnormally prolonged seizures or as a condition with two or more discrete seizures between which there is incomplete recovery of consciousness. SE a life threatning emergency with significant mortality and morbidity. Reported annual incidence is 9.9-41.0/100.000. If SE continues despite treatment with adequate dosage of first and second-line drugs, it is defined as refractory SE (rSE). Super-refractory status epilepticus (srSE) is rSE that continues or reoccurs 24h after the onset of adequate anaesthetic therapy. Objective of our study was to evaluate clinical data of 300 consecutive cases of SE patients treated in our department of neurology in 2014-2017.
Methods: Medical records of 300 consecutive patients treated for SE in 2014-2017 were reviewed. We colected data on age, sex, pre-existing neurological disorders, aetiology and type of SE, use of antiepileptic drugs before and after admission, clinical course, EEG and outcome.
Results: Out of 300 patients treated for SE, 136 were women. In 248 cases SE was symptomatic (103 acute, 90 remote and 55 progressive), etiology was unknown in 52 cases. 96 cases of rSE and 9 cases of srSE were identified. Further data and statistical analysis of the above mentioned clinical variables will be presented.
Conclusion: According to our data the calculated annual incidence in the area covered by our department is 8.7-14.7/100,000 and the overall mortality of SE is 6.7%. We dicovered underuse of EEG and suboptimal adherence to SE treatment protocol.
Disclosure: Nothing to disclose

EPO3022

Etiology of interictal periodic epileptiform discharges on ambulatory scalp EEG

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Background and aims: Periodic discharges (PEDs) are frequently seen in several acute / subacute structural and metabolic brain disorders. Interictal PEDs in chronic seizure disorders are rare and their occurrence in patients with refractory epilepsy has been associated with cortical dysplasia. We aim to review the etiology of interictal PEDs on ambulatory scalp EEGs of epileptic patients.
Methods: EEG reports from 1991 to 2017 were screened for PEDs and its variants. Clinical records were reviewed and patients were included if they met the following criteria: a diagnosis of epilepsy; evidence of an epileptogenic lesion on imaging or a normal 3T MRI. Inpatient EEGs or EEGs performed in patients with acute cerebral lesions were excluded.
Results: From a total of 18667 EEGs, 40 patients met the selection criteria. Mean age was 40 years (8-81 years) and 60% were female. PEDs were most frequently unilateral (85.0%) and frontotemporal (45.0%). Maximal frequencies ranged from 1 to 4Hz (median 1Hz). The following etiologies were found: hypoxic/ischemic (n=6, 15.0%); unidentified epileptogenic lesion (n=6, 15.0%); hippocampal sclerosis (n=5; 12.5%); malformations of cortical development (n=4; 10.0%), including focal cortical dysplasia (n=3) and periventricular heterotopia (n=1); immune (n=4; 10.0%); infectious (n=2; 5.0%); miscellaneous etiologies (n=7; 17.5%). Three patients had more than one epileptogenic lesion, namely tuberous sclerosis, hypoxic-ischemic encephalopathy and cortical atrophy, coexisting with hippocampal sclerosis in all cases.
Conclusion: Interictal PEDs on ambulatory EEG are rare. In our sample PEDs were unspecific for an etiological diagnosis, in contrast to the documented association in refractory epilepsy.
Disclosure: Nothing to disclose

Headache and pain 2

EPO3023

Pressure pain sensitivity in extracephalic regions after Onabotulinumtoxin: a therapy in Chronic Migraine

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Background and aims: One of the pathophysiological hallmarks of migraine is a lower threshold to pressure pain sensitivity. It has been related not only with the peripheral sensitization when it happens in the cephalic area but also with central sensitization when it occurs in extracephalic regions. Previous data showed changes in the cephalic region after OnabotulinumtoxinA (OnabotA). We aimed to evaluate changes in pressure pain sensitivity in extracephalic regions in patients with Chronic Migraine (CM) after therapy with Onabot A.
Methods: We considered CM patients with indication to be treated with OnabotA (PREEMPT paradigm) according to local guidelines. We evaluated pressure pain thresholds (PPT) in the cervical region, metacarpal and pretibial, taking the mean value out of three determinations, one week before and one month after the first OnabotA injection. We compared the change in PPT in responders and non-responders. We considered responders patients with a reduction of at least 50% in the number of migraine days after OnabotA.
Results: We included 20 patients, 18 of them female, with a mean age of 45.4 years (20-65). The responder rate was 50%. There was no difference in the PPT pre-treatment. The change in the PPT after the treatment in the responders and non-responders group was 0.71 vs. -0.185 in cervical region; 0.988 vs. 0.09 in metacarpus and 1.31 vs. 0.13 in pretibial region.
Conclusion: CM patients responding to a first OnabotA procedure exhibited an increase in PPT in extracephalic regions, which might represent changes in central sensitization.
Disclosure: Nothing to disclose

EPO3024

Long-term adverse effects of Onabotulinumtoxin A: experience in a series of 34 chronic migraine patients

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Background and aims: Efficacy and safety of OnabotulinumtoxinA (OnabotA) in Chronic Migraine (CM) have been established both in controlled trials and real-world data. It has been described local muscle atrophy in cases treated during more than five years. We aimed to evaluate long-term adverse effects of OnabotA in a series of patients.
Methods: CM Patients treated with OnabotA during 10 or more procedures. Treatment was offered to non-responders to topiramate and at least one other oral preventative, according to local guidelines. We prospectively gathered efficacy and adverse effects.
Results: We included 34 patients (29 women) treated during 10–18 procedures. Age at first injection was 41.4±12.6 (16-69) years. In 22 cases (64.7%) dose was increased accordingly to "follow the pain strategy", and in 9 (26.5%) the maximum dose of 195 IU was reached. In 10 patients (29.4%) an adverse effect appeared throughout the observation period; in 9 musculoskeletal pain or stiffness, mainly in occipital location, and in one fronto-temporal atrophy. Pain was initially managed with anesthetic blockades before injection and, in 4 cases was finally necessary to reduce the dose of OnabotA. None of the clinical or demographic variables analyzed, nor the maximum dose of OnabotA used, showed differences when comparing groups of patients with and without adverse effects.
Conclusion: Long-term adverse effects of OnabotA in patients with CM were not rare in our series of patients. Their appearance do not depend on the maximum dose of OnabotA and, generally, they can be avoid with modifications of the procedure.
Disclosure: Nothing to disclose

EPO3025

A sleep study in cluster headache: polysomnography of episodic cluster headache patients and healthy controls

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Background and aims: Cluster headache (CH) is characterized by extremely severe, unilateral attacks of pain and by a high nocturnal attack burden. The primary aim was to compare the macrostructure of sleep in episodic CH (eCH) patients in bout with in remission and secondly to compare eCH patients with controls.
Methods: ECH patients, aged 18-65 years, diagnosed according to the International Classification of Headache Disorders 2nd edition, were admitted for polysomnography at the Danish Center for Sleep Medicine, preferably both in bout and in remission. The macrostructure of sleep including arousals, breathing parameters, limb movements (LMs) and periodic limb movements (PLMs) were compared with 25 age-, sex- and BMI-matched healthy controls.
Results: There were no differences in any of the sleep parameters for patients in bout (n=32) compared with patients in remission (n=25). Only 14 out of 32 patients in bout (43.8%) suffered from attacks during the polysomnography and their attacks were not related to specific sleep stages. Interestingly, eCH patients had longer latency (18.9 vs. 11.7 minutes, $p<0.05$) and lower efficiency (84.4 vs. 86.5, $p<0.05$) and compared with controls, but fewer PLMs (0.67 vs. 1.30 hour-1, $p<0.05$). Finally, the sleep apnea index was similar in both groups (9.63 vs. 7.76 hour-1, $p=0.7674$).
Conclusion: This is the first study that systematically investigates eCH patients with polysomnography in both bout and remission and the largest study comparing eCH patients with controls. The observed sleep disturbances were not associated with the bout but rather seem to be the manifestation of a persisting, underlying pathology.
Disclosure: The study was funded by the Danish Tryg Foundation.

EPO3026

The effects of combined supplementation of Coenzyme Q10 with L-carnitine on mitochondrial metabolic disorders marker and migraine symptoms among patient with migraine: a parallel clinical trial

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Background and aims: Coenzyme Q10 and L-carnitine supplementation have been reported to favorably affect migraine headache. However, we are aware of no study examining the effect of combined supplementation Coenzyme Q10 with L-carnitine on migraine headache.
Methods: In this randomised, double-blind, and controlled-placebo clinical trial, 56 migraine patients aged 20-40 y participated. Subjects were randomly assigned to either intervention or control groups. Subjects in the intervention group were received 30mg/day Coenzyme Q10 with 500mg/day L-carnitine at the same time for 8-weeks and subject in the control group also were given the placebo tablets for 8-weeks.
Results: Mean ±SD age of study participants in intervention and control groups was 31.7±6.6 and 33.2±6.3 years, respectively. Mean weight and BMI of subjects was 68.5±13.7kg, 25.3±4.5kg/m2 in intervention group and 64.3±10.7kg, 23.6±4.3kg/m2 in control group, respectively. Supplements intake led to a significant reduction in serum levels of lactate (changes from baseline in intervention group: -1.37 vs. 0.82mg/dl in control group, $P=0.001$) and migraine symptoms: severity (changes from baseline in intervention group: -3.45 vs. -0.88 in control group, $P=<0.001$), duration (changes from baseline in intervention group: -8.35 vs. -3.01 in control group, $P=0.006$), frequency (changes from baseline in intervention group: -5.87 vs. -1.43 in control group, $P=<0.001$) and HDR (changes from baseline in intervention group l: -115.82 vs. -39.45 in control group, $P=0.003$) after 8-weeks.
Conclusion: This study provides evidence supporting the beneficial effects of Coenzyme Q10 and L-carnitine supplementation on serum levels of lactate and migraine symptoms.
Disclosure: Isfahan University Of Medical Sceiences

EPO3027

Response to lacosamide in patients with chronic migraine

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Background and aims: Chronic migraine (CM) is a frequent and difficult to manage pathology since patients often require frequent visits and numerous medication adjustments. Sometimes the usual treatments do not work so we should look for new therapeutic alternatives.
Methods: We conducted an experimental study of lacosamide response in a patient with CM. Demographic and clinical characteristics of his disease were collected.
Results: We recruited 27 patients with CM. The average age was 45.52 years. The average time of evolution was 151.96 months (12.66 years). By sex, 77.8% were women and 22.2% were men. The number of monthly crisis was around 20.85 days/month. 85.2% had taken 2 or more preventive treatments. There were 2 (7.4%) dropouts, the cause was abdominal discomfort. There was a decrease in the number of crisis in 74.1%. Of these, 70% decreased the consumption of analgesics. 81.5% responded to a dose of 100mg/every 12 hours. The average duration of treatment was 4.03 months.
Conclusion: In our series, lacosamide has been shown to be effective for the treatment of CM because it can be used as an alternative to conventional treatment that no longer interacts with other medications and without side effects.
Disclosure: Nothing to disclose

EPO3029

Lacosamide treatment in status migrainosus: could it be the solution?

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Background and aims: Status migrainosus (SM) is defined as a migraine lasting longer than 72 hours. A combination therapy seems to be the best option in order to have a synergistic effect. Some antiepileptic drugs have been used in SM such as valproic acid or levetiracetam. Lacosamide as a sodium blocker may also be useful.
Methods: We selected patients with SM refractory to usual acute treatment during 2017. We proposed to them a short hospitalization (3 days) with a protocol based on a combination of standard treatments (corticosteroids, metoclopramide, chlorpromazine and nonsteroidal anti-inflammatory drugs) plus lacosamide. We analyzed the clinical outcome 1 and 3 months after the treatment.
Results: We identified 7 patients (2 men/5 women, mean age 46), with a diagnosis of chronic migraine and most of them also with a diagnosis of medication overuse headache (4/7). All patients were taking preventive treatment including onabotulinumtoxin A in high doses (200 units, PREEMT protocol). Lacosamide total daily doses were 100 mg for 1 patient, 200 mg for 3 and 400 mg for 3 patients. One month after hospitalization, 6 patients had improved their migraine control, with less medication abuse and better response to abortive and preventive treatment. Unfortunately, 3 months later, 5 of them reverted back to their previous situation.
Conclusion: Lacosamide may be useful as an acute treatment for SM in combination with other drugs with a different mechanism of action. In our experience, lacosamide was not effective in the long-term for patients with refractory chronic migraine.
Disclosure: Nothing to disclose

EPO3030

Cognitive performance in familial hemiplegic migraine with ATP1A2 mutation

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Background and aims: Familial hemiplegic migraine (FHM) is an autosomal-dominant form of migraine with aura, characterized by the occurrence of a transient hemiplegia during the aura. Most studies have focused on its genetic features, but less attention has been paid to the cognitive function of these patients.
Here, we report the neuropsychological performance of two Portuguese FHM families with mutations in the ATP1A2 gene that affect sodium-potassium pump function.
Methods: Twelve symptomatic and asymptomatic subjects belonging to the same family performed an extensive neuropsychologic assessment, which focused on attention, memory, language and executive functions. Validated questionnaires were also used to evaluate trait and state of anxiety. Genetic tests were performed in 9 subjects and 7 of them were positive.
Results: Neuropsychologic assessment revealed that 5 patients (3 with and 2 without the genetic mutation) had at least one cognitive test significantly below average when adjusted to age and education. Across the subjects with impairments, deficits in episodic verbal learning and memory domains were the most consistent. All but 1 patient showed high anxiety scores.
Conclusion: Selective cognitive impairments were found in this FHM family in those with and without the ATP1A2 mutation. We are currently performing a cognitive revaluation after 10 years of follow-up to assess the long-term progression; and such preliminary data will also be presented.
Disclosure: Nothing to disclose

EPO3031

Evaluating the impact of migraine on work productivity in Switzerland using self-reported data from the Migraine Buddy (c) application

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Background and aims: The primary purpose of the study was to evaluate the impact of migraine on work productivity (absenteeism). A secondary purpose was to evaluate the prevalence of self-reported indication of anxiety and/or depression across migraine chronicities, along with the impact this has on medication usage for these groups.
Methods: A retrospective, cross-sectional analysis was conducted using self-reported data collected from Migraine BuddyÓ users (90 CM, 775 EM 4-14 and 635 LFEM individuals) in Switzerland. The most recent 28-days period for each user was selected as the observation period from registration date on the app through Dec 31, 2017.
Results: Migraine records were retrieved from 90 CM, 775 EM 4-14 and 635 LFEM individuals. Among users who reported being employed (n=700), an average of 56.49, 33.09 and 15.43 work days missed per year were reported by CM, EM 4-14 and LFEM patients, respectively. On average, individuals in Switzerland reported missing 31.91 work days per year due to migraines. Individuals who declared either ‘anxiety’ or ‘depression’ in ‘symptoms’ or ‘triggers’ at least once during the observation period were steadily increasing in number with increasing migraine days, and consumed more migraine medication per migraine recorded over the 28-days observation period
Conclusion: Migraines have a considerable impact on the lives of affected individuals, with work productivity of employed migraineurs impacted across all chronicities, majorly so for chronic migraineurs. Further, the self-reported incidence of anxiety and/or depression also consistently increases with an increase in migraine days, along with consistently higher medication usage across chronicities.
Disclosure: This study was sponsored by Novartis Pharma Schweiz AG, Basel, Switzerland.

Miscellaneous 2

EPO3032

Optic coherence tomography and optic nerve echography in MS patients

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Background and aims: Optic coherence tomography (OCT) is a surrogate marker of neurodegeneration in patients with multiple sclerosis (MS) and has been correlated with disability and brain atrophy. Ultrasonography can easily assess the optic nerve (ON) and might give comparable results in terms of disability and brain atrophy in MS patients.
Methods: We studied 54 MS patients with OCT and orbit echography. We measured ON diameter and ON area as well as haemodynamic parameters of the ophthalmic artery (OA), central retinal artery (CRA) and posterior ciliary arteries (PCA).
Results: We studied 54 recurring-remitting (RR) MS patients, age: mean 39.7 (SD 10). EDSS: mean 1.7 (SD 1.3). Time from diagnosis (years): 6.4(SD 6.9). Nine patients had suffered an optic neuritis at any time before inclusion in the study. OCT and ON echography values were lower on eyes with optic neuritis (OCT: 83 vs 87.8, ON area echography 9.3 vs 10.5mm2, optic nerve diameter echography 3.06 vs 3.6), although these differences were not statistically meaningful. We did not find any correlation between OCT values and either ON area or diameter, but there was a slight positive correlation between OCT values and PCA velocities (OCT-PCA systolic velocity r=0.247, p=0.046; OCT-PCA diastolic velocity r=0.254, p=0.44). Time from diagnosis showed a negative correlation with OCT (r=-0.483, p=0.001) but not with any ON echography values.
Conclusion: OCT but not ON echography can be used as a marker of disease progression. ON area and diameter were lower after optic neuritis.
Disclosure: This study has received funding from Novartis

EPO3033

Reduced cerebral blood flow in untreated middle-aged patients with grade 1-2 essential arterial hypertension compared to normotensive controls

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Background and aims: Arterial spin labeling (ASL), a prospective noninvasive perfusion sequence, may allow to detect early changes in cerebral blood flow (CBF) in patient with essential arterial hypertension (EAH). The aim of this study was to examine whether the CBF values were reduced in untreated middle-aged patients with uncomplicated grade 1-2 EAH compared to controls.
Methods: 82 middle-aged adults (41 healthy volunteers, mean age 46.2±4.6 years and 41 untreated hypertensive patients, mean age 50.3±6.7 years) were recruited. All subjects underwent brain MRI (MAGNETOM Skyra 3.0T, Siemens AG, Germany). Fazekas scale was used to quantify the amount of white matter hyperintensities (WMH). ASL CBF maps were used to calculate the perfusion defects.
Results: Hypertensive patients with and without WMH had significantly lower CBF compared to controls ($p<0.0001$). WMH were found in 9,7% healthy controls (Fazekas 1) and in 53.7% hypertensive patients (Fazekas 1 in 48.8% and Fazekas 2 in 4.9% patients, $p=0.0005$). CBF in the cortical plate of both frontal lobes of the brain was significantly lower in hypertensive patients compared to controls (37.3±6.7 vs 45.3±3.5ml/100g/min; 38.02±6.2 vs 45.8±3.2ml/100 g/min, $p<0.0001$).
Conclusion: CBF in the cortical plate of the frontal lobe can be used as an early marker of brain damage in patients with EAH.
Disclosure: Nothing to disclose

EPO3034

Are recurrent myelitis a prodromic phase of inflammatory diseases or a distinct inflammatory condition?

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Background and aims: Recurrent myelitis (RM) can be the only neurological manifestation of some patients, thus not allowing the diagnosis of a specific inflammatory condition. We evaluated whether patients with RM show differences in lesion distribution and white matter (WM) tract involvement compared to those with neuromyelitis optica (NMOSD) and relapsing-remitting multiple sclerosis (RRMS).
Methods: Brain WM lesion distribution was obtained from the T2-lesion masks of 17 RM subjects, 20 NMOSD and 20 relapsing-remitting MS age- and disease-duration- matched patients. Lesional volumes (LV) were split among WM tracts of the JHU atlas. Intragroup and intergroup analyses of LV distribution and WM tracts involvement (cut-off >5 lesional voxels) were performed.
Results: RM patients had a selective damage of the motor pathways: superior corona radiata (CR) 18% of LV, middle cerebellar peduncle (MCP) 13%, cortico-spinal tract (CST) 12% (p vs other tracts=0.03). MS and NMOSD patients showed a higher involvement of the optic radiations (OR) and of the CR (p=0.04, p=0.03 respectively than other regions). The intergroup comparison of LV distribution confirmed the preferential involvement of MCP (p=0.007) and CST (p=0.04) in RM vs MS, no difference emerged between RM vs NMOSD. Lesions occurred more frequently in the OR and CR in NMOSD and MS (p=0.03, p=0.02, vs other tracts), while RM patients had a preferential involvement of posterior CR (78.6%, p=0.01 vs other tracts).
Conclusion: RM patients evidenced a preferential involvement of the motor pathway also in the brain, suggesting a different pathogenetic mechanism from other WM diseases.
Disclosure: Nothing to disclose

EPO3035

Charles Bonnet syndrome in a patient with Leber's Hereditary Optic Neuropathy (LHON) and sensorineural hearing loss: a functional MRI study

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Background and aims: Charles Bonnet syndrome (CBS) is characterized by simple or complex visual hallucinations (VH) due to damage along the visual pathways.
Methods: A 60-year-old man was diagnosed with LHON (11778/ND4 mtDNA mutation) after subacute visual loss in left eye (right eye amblyopic). One month later, he experienced VH of a few seconds consisting in "moving red and blue miniature cartoon". One year later VH content changed in colored mosaic (10-15 seconds duration), usually stress-related, and blue and white flashes (2-5 seconds), triggered by unexpected auditory stimuli. Audiometry revealed mild sensorineural hearing loss. Three block design functional MRI paradigms were administrated: 1) random "clap", 2) "checkerboard", and 3) non-random "bip".
Results: 1) "Clap" stimuli evoked simple flashes with bilateral activation of primary and secondary visual cortex, cuneus, precuneus and insula, consistent with previous findings. 2) Neither hallucinations nor visual cortices activation (related with the severe loss of visual acuity) were registered after "checkerboard". 3) Primary and secondary auditory cortex were "bip"-activated, without eliciting VH.
Conclusion: CBS in LHON has been reported only once, possibly triggered by brimonidine. The peculiarity of our case is VH triggered by the auditory stimuli, possibly due to a cross-modal plasticity between visual and auditory networks, probably influenced by sensorineural deficit. Functional alterations of both networks in resting conditions have been demonstrated in LHON patients, even without an auditory deficit. The absence of VH triggered by expected stimuli is consistent with the "expectation suppression theory", based on increased neural activations after surprising but not by predicted events.
Disclosure: Nothing to disclose

EPO3036

Autoimmune encephalitis: clinical, laboratory and imaging data comparison between antibody-positive and antibody-negative patients.

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Background and aims: Autoimmune encephalitis (AE) is an emerging and potentially treatable group of encephalitis. Over the years, new subtypes of AE have been described and linked to specific autoantibodies (Ab). However, according to recently published criteria, Ab detection is not strictly necessary for the diagnosis of AE. In this work we compare two groups of AE patients, with or without detectable Ab, in order to explore their features and clinical course.

Methods: We retrospectively analysed demographic, clinical, CSF, EEG and imaging data of two groups of patients admitted to our department between September 2010 and April 2017. We included 19 patients with AE with definite autoantibody (AE+) and 13 patients discharged with diagnosis of autoantibody-negative AE (AE-), who fulfilled recently published criteria for probable autoantibody-negative AE. In AE+ group, 4 patients had anti-NMDAR-Ab, 8 patients VGKC-Ab, 1 patient anti-GAD-Ab, 3 patients Hashimoto encephalitis, 2 patients anti-Ma-Ab and 1 patient anti-Hu-Ab.

Results: We found no relevant differences between the two groups of patients. Clinical picture was homogenous between AE+ and AE-, as well as MRI features, EEG, CSF data and administered treatments.

	Ab+ (n=19)	Ab- (n=13)
Demographics		
Number	19	13
Male (n, %)	11 (58%)	6 (55%)
Age at onset (yrs; mean, range)	54.6 (15-85)	60.2(17-79)
Clinical features (n, %)		
Psychiatric symptoms	12/19 (63%)	9/13 (69%)
Epilepsy	11/19 (58%)	9/13 (69%)
Fever	6/19 (32%)	2/13 (15%)
Memory impairment	10/19 (53%)	9/13 (69%)
Confusion	15/19 (79%)	13/13 (100%)
Hyponatremia	6/19 (32%)	3/13 (23%)
Autonomic disorders	3/19 (16%)	3/13 (23%)
Movement disorders	5/19 (26%)	5/13 (39%)

Table 1. Demographic data, clinical features and association with neoplasm. N=number; Yrs=years; IQR=interquartile range.

	Ab+ (n=19)	Ab- (n=13)	
Altered EEG	16/18 (89%; 1 N/T)	10/13 (77%)	
General organization	12/18 (75%)	9/13 (90%)	
Epileptiform activity	7/18 (44%)	1/13 (10%)	
Slow abnormalities	9/18 (56%)	5/13 (50%)	
Seizures	6/18 (38%)	1/13 (10%)	
Cerebrospinal fluid	18/19 (1 N/T)	13/13	
Proteins (mg; median, IQR)	42 (34-60)	55 (29-101)	p=0.974*
No. of cells (n; median, IQR)	1 (1-4)	7,5 (1-27)	p=0.061*
IEF pattern 1	8/17 (47%)	8/10 (80%)	
IEF pattern 2 or 3	13/17 (18%)	0/10	
IEF pattern 4	6/17 (35%)	2/10 (20%)	
Magnetic Resonance Imaging			
Altered MRI	14/19 (74%)	7/13 (54%)	
Limbic system	11/14 (79%)	5/7 (71%)	
Basal ganglia	4/14 (29%)	2/7 (29%)	
Contrast enhancement	3/14 (21%)	3/7 (43%)	

*Table 2. N/T=not tested. *=Mann-Whitney two-tail test. IEF (isoelectrofocusing) patterns: 1=no OCBs seen; 2=OCBs in CSF only; 3= identical bands in both serum and CSF with extra bands in CSF; 4=mirror pattern.*

	Ab+ (n=19)	Ab- (n=13)
First line treatment	19/19	12/13
IVIG	8 (42%)	6 (50%)
IV steroid	8 (42%)	6 (50%)
Oral steroid	3 (16%)	0
Second line treatment	12/19	9/12
IVIG	6 (50%)	2 (22%)
IV steroid	5 (42%)	2 (22%)
Oral steroid	1 (8%)	5 (56%)

Table 3. Treatment courses. IVIG = Intravenous immunoglobulins.

Conclusion: Autoantibody detection is not mandatory for the diagnosis of AE. From a clinical point of view, autoantibody-negative AE appears quite similar to autoantibody-positive AE. Therefore, alongside from autoantibody testing, recognition of a clinical syndrome suggesting autoimmune encephalitis is the mainstay for timely diagnosis and treatment.

Disclosure: Nothing to disclose

EPO3037

Oligoclonal bands in cerebrospinal fluid in Guillain-Barré Syndrome

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Background and aims: Oligoclonal bands (OB) are an indicative of activation of humoral immunity. OB in cerebrospinal fluid (CSF) in Guillain-Barré Syndrome (GBS) have been poorly described. We studied the presence of OB in patients with GBS and explored their correlation with neurophysiological studies and clinical findings.
Methods: We selected all patients with diagnosis of GBS by Brighton criteria (level 1 and 2) between 2000 and 2016 in our center. We analyzed the association among the presence of IgG OB in CSF and sex, clinical severity, electrophysiological pattern and response to intravenous immunoglobulins (IVIGs).
Results: 45 patients were studied. Medium age was 57.7 years and 62% were males. Twenty three (51%) meet criteria for acute inflammatory demyelinating polyneuropathy, 18 showed the axonal variant, 14 a mixed pattern and 80% were treated with IVIGs. IgG OB were demonstrated in 28 (62.2%) patients of our sample. 25 of them (89.3%) presented an identical pattern in CSF and serum, only 3 (10.7%) had an extra IgG OB CSF pattern. Presence of OB in CSF was not statistically associated to sex, a concrete neurophysiological pattern, clinical severity or IGIVs response.
Conclusion: Presence of IgG OB in CSF is common in patients with GBS, mostly showing an identical pattern compared to serum suggesting a systemic immune activation with lymphocyte B transmission to the nervous system. Presence of OB did not correlate with neurophysiological findings, clinical severity or treatment response.
Disclosure: Nothing to disclose

EPO3038

AQP4-positive longitudinal extensive transverse myelitis associated with Takayasu arteritis: a case report

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Background and aims: Neuromyelitis optica spectrum disorder (NMOsd) is an aggressive autoimmune condition characterized by optic neuritis and longitudinally extensive transverse myelitis (LETM). In 75% of the cases specific autoantibodies against aquaporine 4 (AQP4) are present. Associations with various systemic autoimmune diseases have been reported (mostly lupus erythematosus or Sjögren syndrome). Takayasu arteritis is a rare vasculitis occurring predominantly in young females of Asian origin causing granulomatous inflammation of large-vessels. The exact pathophysiological mechanisms remain unknown.
Methods: A 40-year-old female laboratory assistant of Korean descent consulted for rapidly progressive paraplegia, urinary retention and belt-shaped waist pain. On the bases of a LETM from C6 to the conus medullaris (Figure 1) and of the presence of anti-AQP4 antibodies NMOsd was diagnosed (Wingerchuk criteria 2015). CT scanning revealed bilateral pulmonary embolism. In addition, mural thickening of the left carotid artery, brachiocephalic trunk, right renal artery, and superior mesenteric artery was found, the latter also showing stenotic and aneurismal lesions (Figure 2). Taken together with elevated inflammatory markers, a diagnosis of Takayasu arteritis was made. The patient was treated by anticoagulation and immunomodulatory agents (corticosteroids, followed by IVIG, and rituximab). After 3 months she returned home, able to walk with a cane.

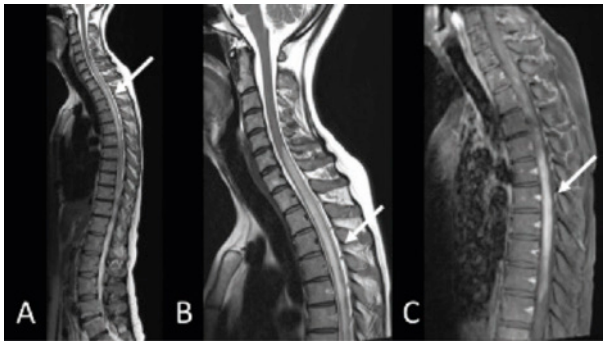

Figure 1 (A) spinal sagittal T2-weighted magnetic resonance image (MRI) demonstrate high signal from C6 to the conus medullaris and (B) cervical sagital T2-weighted MRI demonstrate longitudinal myelitis in the cervical spine. (C) Post gadolinium T1 sequence with heterogeneous contrast enhancement from Th3 to Th8.

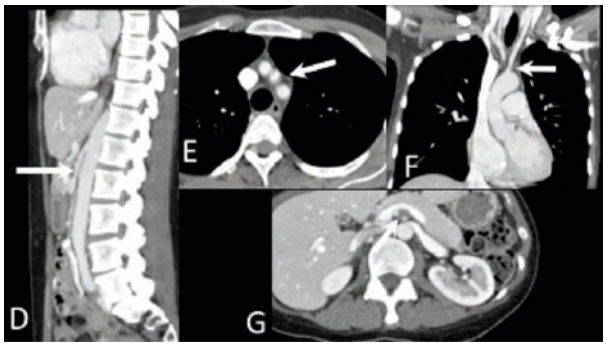

Figure 2 thoracic-abdominal computed tomography shows mural thickening (D) the mesenteric superior artery, (F) brachiocephalic trunk, and (G) right renal artery.

Results: To our knowledge; this is the first case report of Takayasu arteritis associated with NMOsd.
Conclusion: In patients with NMOsd concurrent Takayasu arteritis should be considered and, as is evidenced by our patient's presentation and the course of her disease, aggressive immune therapy started early.
Disclosure: Nothing to disclose

EPO3039

Retrospective analysis of the sensitivity and specificity of a diagnostic algorithm for autoimmune encephalitis

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Background and aims: The patient with suspected autoimmune encephalitis poses a dilemma: an early initiation of treatment is associated with a more favourable prognosis, but the definitve proof via antibody detection is time-consuming and sometimes impossible. Hence there is an urgent need for diagnostic algorithms acting independently of antibody detection. We aim to retrospectively apply the algorithm published by Graus et al to those patients treated at our departement during a 10-year-period to determine its sensitivity and specificity for the diagnosis of autoimmune encephalitis during the early stages of the disease.
Methods: The medical data of all patients with the diagnosis of "encephalitis" treated at our department between 2007-2017 will be retrospectively analysed. The initial diagnosis will be reevaluated by the author-excluding patients in whom it cannot be classified as either "confirmed" or "possible" -and will serve as a reference against which the diagnosis resulting from the algorithm shall be compared to determine its sensitivity and specificity.
Results: Main target criteria:sensitivity, specificity, negative and positive predictive values of the diagnostic category "possible autoimmune encephalitis" at the time of hospital admission
Subordinate target criteria: sensitivity, specificity, negative and positive predictive values of all other diagnostic categories of the algorithm and of all categories during later stages of the disease.
Conclusion: We expect this study to yield information on the value of the diagnostic algorithm in the early stages of encephalitis. This is significant as a reliable algorithm would enable an early diagnosis and initiation of treatment-thereby improving the patients' chances of recovery.
Disclosure: Nothing to disclose

EPO3040

Autoimmune Encephalitis in central Slovenia

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Background and aims: Autoimmune encephalitis (AE) is nowadays recognized as an important cause of subacute encephalopathies with various accompanying conditions (epilepsies, psychosis) previously diagnosed as idiopathic. Since AE is a relatively new and possibly underdiagnosed entity a study on AE prevalence in Central Slovenia was performed.
Methods: We performed a retrospective analysis of the patients (n=466) admitted to the University Medical Center Ljubljana between 1. 1. 2012 and 31. 12. 2016 which were tested (blood or/and cerebrospinal fluid) for anti-neural antibodies. The subjects with paraneoplastic syndromes other than AE were excluded. We defined seropositive and seronegative AIs (strong suspicion of the diagnosis, positive response to immunotherapy).
Results: We identified 23 patients (12 female, 11 male) with AE, resulting in an estimated incidence of 0.46/100.000. The mean age of patients was 54.9 years (22–79y), with anti-N-methyl-D-aspartate-receptor (anti-NMDAR) encephalitis patients being significantly younger (mean 38y). Six patients (26.1%) were seronegative, half of them had a carcinoma. The majority of seropositive AEs were anti-Ma2 positive (8; 34.8%), followed by anti-NMDAR (5; 21.7%), anti-Yo and anti-Hu (both 2; 8.7%). Malignancy was found in nine (75%) patients with intracellular directed antibodies and in one (20%) patient with cell-surface directed antibodies. The majority improved after immunotherapy; however two patients died due to complications, both having paraneoplastic cerebellar syndromes.
Conclusion: The results are comparable to those in the literature by both the phenomena and the presence of anti-neural antibodies. However, AEs are underdiagnosed in Slovenia and should be included into the differential diagnosis of patients with subacute encephalopathies more often.
Disclosure: Nothing to disclose

EPO3043

The impact of a realistic-simulation course on the self-perception of confidence of healthcare professionals when treating CVA

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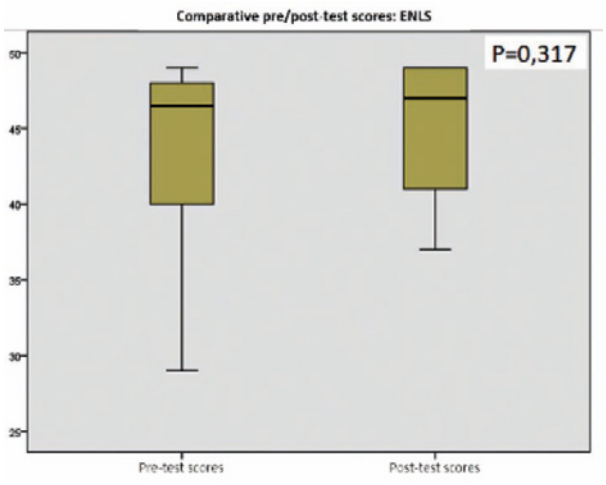
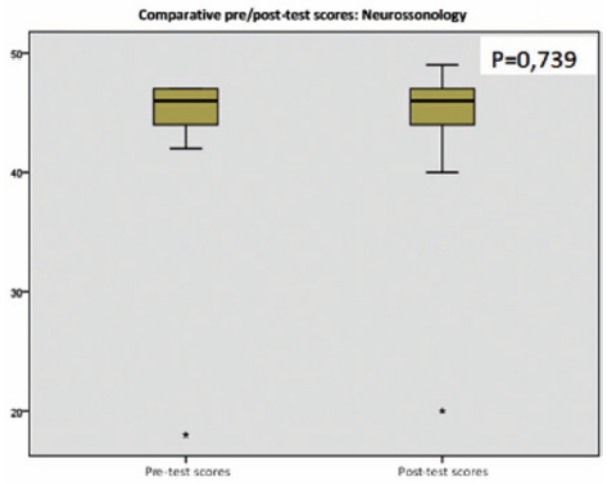
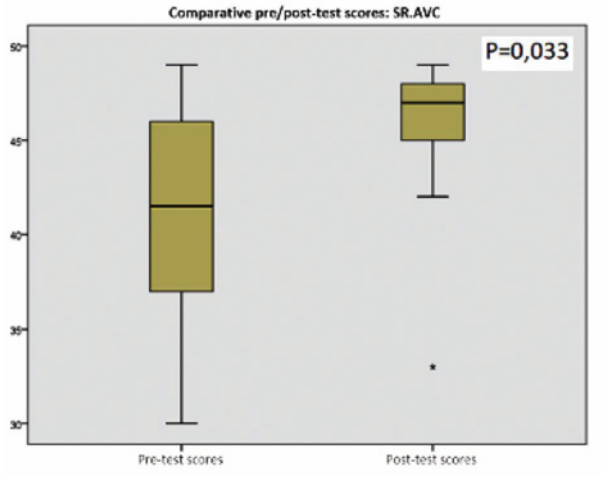
Background and aims: Acute CVA is a neurological emergency which demands quick attention. Simulations are becoming widely used in medical education. However, there is few evidence of its utility on neurocritical care education. We, therefore, aim to assess the impact of a realistic-simulation course on healthcare professionals' self-perception of confidence when treating acute CVA.
Methods: We conducted a three-scenario realistic-simulation course "SR.AVC" to seventeen subjects randomly chosen, during the XI Brazilian CVA Congress. All participants responded pre and post-test questionnaires evaluating the self-perception of confidence on acute CVA care. Other 38 participants, randomly chosen amongst the trainees of ENLS (18) and Neurossonology (20) courses were submitted to the same questionnaires. We evaluated the variations between pre and post-tests results, to assess the change on trainee's self-perception of confidence.
Results: 46 (83.63%) subjects completely answered the questionnaires. ENLS and Neurossonology groups had mainly neurologists (7 and 11) while on SR.AVC® were non-neurologists (11). Friedman's two-way analysis of variance determined that, compared with Neurossonlogy (p=0.739) and ENLS (p=0.317), the change on SR.AVC®'s group was statistically significant (p=0.033). Wilcoxon's signed-rank test, found out that post-test scores statistically higher than pre-tests (p=0.048).







Conclusion: The realistic-simulation course is an effective tool on the training of the skills required for the management of acute CVA. The simulations provided a safe and controlled environment which made possible a significant improvement on trainees' self-perception of confidence, evidenced by a significant variation of scores when comparing pre and post-tests.

Disclosure: Nothing to disclose

Motor neurone diseases; Cognitive neurology/neuropsychology

EPO3044

Fluctuation in behavioral responsiveness in severely brain-injured patients

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Background and aims: To characterize fluctuation in behavioral responsiveness in patients with severe brain injury within a short time period.
Methods: 15 patients (8 females, 9 traumatic, median age: 48 [19-78]; median time since insult:13 [6-59]) were assessed by trained examiners four times with the Coma Recovery-Scale Revised (CRS-R), once a day, twice in the morning, twice in the afternoon, within a 7 days period. A Wilcoxon was used to assess the difference in mean CRS-R total scores between the morning and the afternoon assessments. Descriptive statistics were used to further describe the patient's profiles.
Results: Patients were diagnosed as unresponsive (n=4), minimally conscious minus (MCS-; n=4); minimally conscious plus (MCS+; n=6) or emerged from the MCS (n=1). We did not find a difference between mean CRS-R total scores when the assessments were performed in the morning or in the afternoon. All patients showed variability in CRS-R scores across the 4 assessments, with differences ranging from 0 to 12 (median=2) within morning or afternoon sessions. 53% of the patients (6MCS+; 2MCS-) showed unstable diagnoses across the 4 assessments.
Conclusion: Our data suggest a high heterogeneity in daytime behavioral fluctuation in patients with severe brain-injury. They also support previous literature highlighting the necessity to use multiple assessments within a short time-period in these patients to get a reliable diagnosis. Future studies on a bigger cohort should focus on better characterizing day-time fluctuation within patients.
Disclosure: Nothing to disclose

EPO3045

Metamemory in Mild Cognitive Impairment: relation with progression to Alzheimer's disease

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Background and aims: Mild Cognitive Impairment (MCI) is often used to describe the transitional stage between normal ageing and dementia. Metamemory refers to the subjective knowledge, beliefs and attitudes towards one's own cognitive capacities and tends to decline with the progression of Alzheimer's disease (AD). Our aim was to evaluate the variation of metamemory over time in a population with MCI and determine its relation with progression to dementia.
Methods: Longitudinal study of a cohort of MCI patients who underwent thorough cognitive, functional, psychopathology and subjective memory complaints (SMC) assessment. We analyzed data from the first and final patient's assessment (operationalized as the patients' assessment at conversion or their most recent assessment).
Results: We included 78 participants, 51.3% female, with a mean age of onset of 67.4 years and 6.29 years of education. At follow up (median 3 years), 46.2% converted to dementia; 58.3% were apoE4 carriers and 44.4% had a positive family history of dementia. There were high significant positive correlations between the patients' metamemory and psychopathological symptoms (depression and anxiety); the caregivers' SMC correlated with their general cognitive and functional status. Comparing the first and last assessment, there were no differences between the patient's memory complaints but the caregiver's SMC score was significantly higher at follow up.
Conclusion: Our results suggested that the caregivers' metamemory reflected more accurately the alterations in the patients' cognitive and functional abilities then their own. Furthermore, greater patient memory complains were associated with higher levels of psychopathological symptoms and did not reflect their cognitive performance.
Disclosure: Nothing to disclose

EPO3046

Cerebrospinal fluid biomarkers in patients with mild cognitive impairment

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Background and aims: The usefulness of cerebrospinal fluid (CSF) biomarkers (beta amyloid, total tau and phosphorylated tau) in Alzheimer's disease (AD) is well known, however it remains uncertain in mild cognitive impairment (MCI).
Methods: We studied 105 patients with MCI or subjective memory complaints, 51.4% men, with a mean follow-up of 4.2 years (± SD 2.1). Clinical and functional parameters, CSF levels of beta amyloid-42 (AB42), total tau (TT) and phosphorylated tau (PT) and the progression to dementia were analysed. We studied the sensitivity (S) and specificity (E) of the three biomarkers individually and the combination of the three for the development of any type of dementia and specifically for clinical phenotype of dementia of Alzheimer's type (DAT) (hippocampal memory deficit).
Results: 59.1% developed dementia during follow-up, 38.1% fulfilled clinical criteria of DAT. AB42 CSF levels predicted dementia with a S=65% and E=69%, with S=75.6% and E=65.07% for DAT. For TT, S=39% and E=90% for dementia and S=41% and E=82% for AD. For PT S=52% and E=81% for dementia and S=63% and E=77% for DAT. A combination of the 3 biomarkers, S=63% and E=88% were obtained for dementia and S=73% and E=77% for DAT.
Conclusion: The determination of biomarkers in CSF is useful to predict the progression to dementia, specially AD, but it should not be used individually as a screening test.
Disclosure: Nothing to disclose

EPO3047

Alpha-synuclein in CSF of mild cognitive impairment patients: a preliminary study

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Background and aims: Objectives: To quantificate α-synuclein in cerebrospinal fluid (CSF-AS) in mild cognitive impairment (MCI) patients, and to compare the results of that protein considering the clinical evolution after a 5 years clinical follow-up.
Material and methods: We included 55 MCI patients. After a minimal follow-up of 5 years 22 of them were diagnosed with psychiatric illnesses (CT), 17 developed over time Alzheimer's disease (AD) following NIA-AA criteria (2011) and 16 succumbed to Lewy body disease (LBD) following McKeith criteria (2005). We measured CSF-AS using Covance reagents and Aβ, T-tau and p-tau proteins by means of Fujirebio reagents at inclusion.
Results: The CSF-AS levels were found to be higher in LBD patients in comparison with CT group. In addition, AD patients showed essentially higher CSF-AS than LBD and CT. We excluded the possible relation between CSF-AS and the classical CSF biomarkers, by performing a Spearman correlation test. The alpha-synuclein protein was found to be present in a higher correlation with p-tau protein. But, when we differentiate between the various groups the higher correlation was observed to be predominant with T-tau. However the correlation coefficient has never been 1 with the classical biomarkers.
Conclusion: In this preliminary study, the results suggested that CSF-AS levels were increased in MCI patients who would develop LBD, and specially, in those who would develop AD. Adding alpha synuclein to the classical CSF biomarkers may be worthwhile to predict the evolution of MCI patients. A larger study is guaranteed to confirm these results.
Disclosure: Nothing to disclose

EPO3048

Chromogranin A in the cerebrospinal fluid of patients with Amyotrophic lateral Sclerosis

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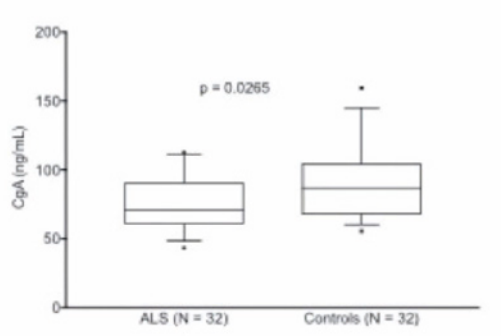
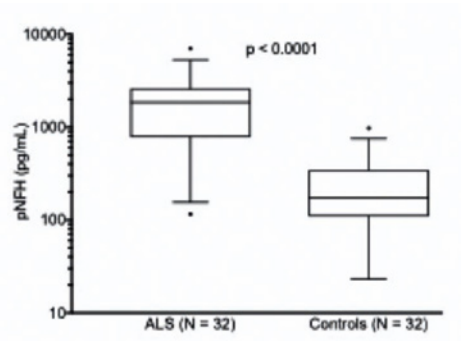
Background and aims: Chromogranin A (CgA), a major constituent of secretory large dense-core vesicles of neuroendocrine cells and neurons, is mainly involved in secretion regulation. Previous preclinical data suggest that CgA could play a role in amyotrophic lateral sclerosis (ALS), and, recently, higher levels of CgA have been reported in the cerebrospinal fluid (CSF) of ALS patients relative to controls.

Methods: We measured CSF levels of CgA and phosphorylated neurofilament heavy chain (pNFH), an established ALS biomarker, in 32 ALS patients (17 (53.1%) males and 15 (46.9%) females; median age, 64.5 y) and 32 disease controls (16 (50%) males and 16 (50%) females; median age, 66.5 y) without degenerative or inflammatory CNS diseases.

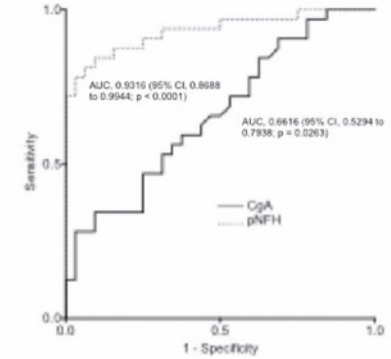
Results: ALS patients displayed slightly lower CSF CgA levels than controls (median, 70.8 ng/mL and 86.7 ng/mL, respectively; Figure 1), with low statistical significance (p=0.0265), wide overlap between patients and controls, and consequent low diagnostic performance (area under the ROC curve (AUC), 0.6616; 95% CI, 0.5294 to 0.7938; p=0.0263; Figure 3). This contrasted with the clear increase in CSF pNFH levels in ALS patients relative to controls (median, 1857.1 pg/mL and 172.9 pg/mL, respectively; p<0.0001; Figure 2), with AUC of 0.9316 (95% CI, 0.8688 to 0.9944; p<0.0001; Figure 3). CgA levels among ALS patients were not associated with any clinical parameters.



CSF CgA levels in ALS patients and disease controls (linear scale). Boxes represent interquartile ranges (25%-75%) with median values, whiskers represent values between 5% and 25% and between 75% and 95%, and points represent outliers. CgA, chromogranin A.



CSF pNFH levels in ALS patients and disease controls (Log-10 scale). Boxes represent interquartile ranges (25%-75%) with median values, whiskers represent values between 5% and 25% and between 75% and 95%, and points represent outliers. pNFH, phosphorylated neurofilament heavy chain.



ROC curves of CgA and pNFH for discrimination between ALS patients and disease controls. CgA, chromogranin A. pNFH, phosphorylated neurofilament heavy chain

Conclusion: Given the considerably lower diagnostic performance in comparison to pNFH and the lack of association with disease parameters, CgA does not appear to be a promising clinical ALS biomarker.
Disclosure: The study was supported by grants from the German Federal Ministry of Education and Research (project FTLDc 01GI1007A, MND-Net 01GI0704), the EU Joint Programme-Neurodegenerative Diseases network PreFrontAls (01ED1512), the Foundation of the state of Baden-Wuerttemberg, the Thierry Latran Foundation, and Boehringer Ingelheim Ulm University BioCenter.

EPO3050

Phrenic nerve motor amplitude predicts function decline in amyotrophic lateral sclerosis

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Background and aims: Phrenic nerve motor amplitude (DiaphrAmpl) has been previously shown to predict hypoventilation and survival in amyotrophic lateral sclerosis (ALS). However, no studies have shown its predictive value in detecting functional decline, which is the aim of our study.
Methods: We prospectively included 39 ALS patients (62.3±10.3 years, 20 males, 18.6±13.1 months from symptom onset, 13 bulbar-onset). Patients were evaluated at baseline and at 2-6 months (mean=3.8±0.9 months) with the functional ALS scale score (ALSFRS), the predicted forced vital capacity (%FVC) and the DiaphrAmpl. The change from baseline on the ALSFRS was analysed with a linear mixed-effects model for repeated measures, taking into account clinical characteristics, DiaphrAmpl and%FVC at baseline.
Results: At baseline, no significant correlations ($p>0.05$) were observed between ALSFRS mean=31.7±4.3), DiaphrAmpl (right/ left mean=0.50±0.16/ 0.56±0.19),) and%FVC (mean=89.7±14.9). We found a significant decline ($p<0.05$) from baseline in ALSFRS (mean=-2.9±2.1),%FVC (mean=-6.9±10.1) and DiaphrAmpl (right mean=-0.06±0.11, left mean=-0.07±0.12). There was no significant difference between DiaphrAmpl (right:-11.1%; left:-12.1%) and%FVC (-7.5%) percentage of change from baseline ($p > 0.05$). When testing the longitudinal effects in functionality, a greater change in ALSFRS was observed if the initial score was higher and the baseline DiaphrAmpl was lower ($p<0.05$); but no influence of baseline%FVC ($p>0.05$).
Conclusion: In addition to its known predictive value in hypoventilation and survival, DiaphrAmpl also relates to longitudinal functional decline and should be considered in clinical trials.
Disclosure: Nothing to disclose

EPO3051

Increased risk of melanoma in c9orf72 expansion carriers

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Background and aims: Some types of cancer have increased prevalence in Amyotrophic Lateral Sclerosis (ALS) patients. There is mounting evidence of an increased risk of ALS in patients who have had melanoma. The inverse relationship has also been suggested.
We aimed to study the hypothesis that c9orf72 expansion is linked to the risk of melanoma development.
Methods: We describe 2 families of interest in which the coexistence of FTLD-ALS spectrum disorders and melanoma are relevant. To investigate a possible link between specific mutations and melanoma, we further compared the risk of melanoma between different pathogenic mutations and between different phenotypes.
Results: We collected information regarding cancer history in 54 patients with c9orf72 expansion or pathogenic mutations of GRN, MAPT and SQSTM1. 29 subjects had c9orf72 expansion, 4 had MAPT mutations, 20 had GRN mutations and 1 had a SQSTM1 mutation. All the 5 patients with melanoma belong to two unrelated families. Four of them have the diagnosis of ALS and one is an assymptomatic carrier.
Melanoma is significantly higher in c9orf72 expansion carriers ($p=0.05$). In our sample, melanoma occurred only in ALS patients, but this did not reach statistical significance ($p=0.155$).
Conclusion: Our study suggests a link between c9orf72 expansion and melanoma. These findings may open a new way to approach and understand ALS and frontotemporal pathophysiology. It also suggests that ALS or FTLD patients with personal or family history of melanoma may be at increased probability of having a c9orf72 expansion, and genetic testing should be considered.
Disclosure: Nothing to disclose

EPO3053

Evaluation of non motor signs in patients with Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a rare neurological condition caused by motor neuron degeneration.Classically, this disease encompasses pure motor signs. Recently, we have seen the emergence of the concept of "ALS-plus" defined by the coexistence of classic motor clinical signs of ALS and atypical neurological signs. Our study aimed to evaluate the frequency of non motor signs (NMS) in patients with ALS and to propose a diagnostic and therapeutic approach.

Methods: A retrospective study was performed, including ALS follow-up patients in the department of Neurology, Razi Hospital between 2002 to 2017. Evaluation focused on the clinical features of motor and NMS in patients with ALS and on results of paraclinical investigations: electroneuromyography (ENMG), electrophysiological study of the autonomic nervous system (ANS) and saccadic eye records.

Results: We included 140 patients. Mean age at diagnosis was 53.8 years. Sex ratio was 1.74. NMS were identified in 63 patients (45%): 19 patients (14.1%) had cognitive impairment, 4 patients (3%) had oculomotor disorders,12 patients (8.5%) had extrapyramidal signs, 32 patients (22.9%) had sensory disturbances and 56 patients (40%) had dysautonomic signs. A statistically significant correlation were present between bulbar onset and NMS (p=0.008). However, there was no significant correlation between age, duration of evolution or use of Riluzole and presence of NMS.

Conclusion: Thi study confirms the high frequency of atypical signs in patients with ALS. An early diagnosis of these manifestations leads to propose an adapted therapeutic management and an improvement of patients' quality of life.

Disclosure: Nothing to disclose

EPO3054

Comprehensive genetic characterisation of an Argentinian cohort with Amyotrophic Lateral Sclerosis

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Background and aims: Recently, the C9orf72 expansion was detected in 2% of sporadic and 1of 3 families in a series of ALS cases from Argentina, but other ALS-causing genes remain unexplored. We aim to characterise a large Argentinian ALS cohort.

Methods: 26 Argentinian patients with a clinical diagnosis of ALS were scrutinised for disease-causing variation by fragment analysis and targeted next-generation sequencing (NGS).

Results: 13 patients harboured 14 potentially pathogenic alterations in the genes SOD1, TARDBP, FUS, UBQLN2, VCP, CHMP2B, SETX, ATXN2 and C9orf72. 8 out of 12 could be confirmed by Sanger, and after genetic analysis, one variant in FUS and one variant on SETX were considered non-pathogenic. There were 5 reported missense mutations: p.G86S and p.D84G in SOD1, p.R155H in VCP, p.N378D in TARDBP, p.497S in UBQLN and 2 C9orf72 expansions. There was one novel alteration in CHMP2B (p.R32Q) in a subject with a family history of ALS, and presented conflicting prediction scores. Segregation could not be studied. Three intermediate ATXN2 repeats were associated to variants in TARDBP, UBQLN and CHMP2B. The total pathogenic mutation rate was of 27%, which accounts for 63% among familial and 12% of sporadic subjects.

Conclusion: Argentinian populations have a similar genetic landscape for ALS as Europeans. NGS is a cost effective screening methods of genetic variation but the gold standard for confirmation is still Sanger sequencing. The next step of this work is to enlarge our cohort and perform ancestry analysis.

Disclosure: Nothing to disclose

EPO3055

A longitudinal Motor Unit Number Index (MUNIX) Estimation study in Frontotemporal Dementia (FTD)

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Background and aims: Motor Unit Number index (MUNIX) is a non-invasive method that that requires minimal electrical stimulation. The technique involves utilizing the surface-recorded compound muscle action potential (CMAP) and electromyographic (EMG) interference pattern to compute the motor unit number index (MUNIX). This is the first ever study applied MUNIX in FTD. The aim was to identify the presence of any neurophysiologic evidence of lower motor neuron system dysfunction across FTD subtypes by applying MUNIX longitudinally to study consecutive patients with FTD. Clinical parameters and MUNIX findings were also compared across FTD subgroups to explore patterns of lower motor neuron system dysfunction in FTD phenotypes.
Methods: We performed longitudinal MUNIX measurements in 6 muscles in a cohort of 39 FTD (22 bvFTD, 9 nfvPPA, 6 FTD-MND and 2 svPPA) patients, 3-monthly, over 21 months period. The right side was chosen for testing and all participants had no clinical evidence of LMN involvement (muscle weakness, wasting of fasiculations).
Results: Of 39 enrolled patients; results varied in different FTD subtypes. All nfvPPA and svPPA: there was no decline in MUNIX values over study period. MUNIX values were below normal at test1 and declined over time in FTD-MND (as expected). MUNIX values were below normal in 3/22 (14%) of bvFTD patients. MUNIX decline in bvFTD was seen in all muscles without concomitant clinical features of LMN involvement (weakness, fasciculations or wasting).
Conclusion: Lower MUNIX values are present in bvFTD patients suggesting lower motor neuron dysfunction without clinical evidence of ALS in some instances.
Keywords: MUNIX, FTD, Longitudinal study.
Disclosure: Nothing to disclose

Movement disorders 4

EPO3056

Alpha-synucleinopathy manifesting as familial atypical parkinsonism with the presence of rare variants of FBXO7 (PARK15) genes and VPS35 (PARK17)

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Background and aims: Three large pedigrees with familial occurence of atypical parkinsonism were found in a small, isolated region of south-eastern Moravia, Czech Republic; our patient belongs to one of these pedigrees.

Methods: Beside the clinical observation and video documentation, a detailed molecular-genetic analysis to confirm or exclude the presence of PARK mutations was done; finally the autopsy was performed, which focused on the pathological changes in the brain.

Results: The patient suffered from an atypical parkinsonism with the phenopetype of progressive supranuclear palsy-parkinsonism. The molecular-genetic analysis revealed the presence of rare variants of genes FBXO7 (PARK 15) and VPS35 (PARK 17). The autopsy finding was the alpha-synucleinopathy (diffuse presence of Lewy bodies and Lewy neurites , Braak stage VI) with some t-inclusions (threads, pretangles) in hippocampus and both occipital lobes.

Conclusion: In our patients, we have documented the joint presence of rare variants of FBXO7 and VPS35 genes. The pathological substrate of this unique and yet unknown familial parkinsonism is diffuse alpha-synucleinopathy.

Disclosure: Supported by AZV 15-32715A (Czech Republic)

EPO3057

Diffusion tensor imaging of olfactory tract in Parkinson's disease

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Background and aims: Olfactory dysfunction is recognized as one of the earliest indicators of developing Parkinson's disease (PD) and one of the major nonmotor symptoms with a significant impact on quality of life. In the present study, we investigated the possible relationships among olfactory impairment and alterations in diffusion tensor imaging (DTI) of olfactory tracts, comparing a cohort of PD patients and a matched control group.

Methods: Olfactory function of each subject was assessed using the Italian Olfactory Identification Test. Motor disability was assessed in all patients using Unified Parkinson's Disease Rating Scale-III part (UPDRS-III) and Hoehn and Yahr rating scale (H&Y). Imaging was performed on a 3T Philips Achieva MR scanner. MRI pre-processing was performed by DTIPrep, DTI reconstruction and fiber tracking by DiffusionToolkit, tractography analyses using TrackVis. The following parameters were used for groupwise comparison: fractional anisotropy (FA), mean diffusivity (MD), tract volume and length.

Results: 17 patients with PD (mean age 64.9±7.6 years, UPDRS III 24.4±11.7, H&Y stage 1.9±0.5) and 9 controls (mean age 60.7±14.2 years) were recruited. Olfactory identification function of all PD patients was decreased. The region of interest analysis of the olfactory tract showed significant FA signal and volume decreases of the PD group when compared with the control group ($P<0.05$). Significant correlations were found between the MD values and the H&Y stage ($r=0.60$, $P<0.01$).

Conclusion: DTI analyses of olfactory structures may be viable as a means of establishing cohorts of subjects with probable pre-clinical PD.

Disclosure: Nothing to disclose

EPO3058

Dopaminergic adverse-events in COMT-naïve patients starting adjunctive therapy with opicapone: the BIPARK-I double-blind experience

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Background and aims: Assess the occurence of dopaminergic adverse-events (AEs) in levodopa-treated COMT-naïve Parkinson's Disease (PD) patients when starting opicapone (OPC) 50mg or entacapone (ENT).
Methods: Double-blind, 14 to 15-week, placebo- and active-controlled study. In the emergence of dopaminergic-AEs during the first 3-weeks, investigators could titrate the levodopa daily-dose. Dopaminergic-AEs were defined as new or worsening post-baseline treatment. This post-hoc analysis investigated the dopaminergic-AEs occurence, namely, dyskinesia, nausea, hallucinations (including delusion, illusion and disturbance-in-attention), vomiting and orthostatic hypotension.
Results: 359 patients were randomized to placebo (PLC, n=121), OPC-50mg (n=116) or ENT (n=122). Cumulatively, patients taking OPC-50mg reported more dopaminergic-AEs (22%) compared to ENT (16%) and PLC (8%). Subjects with dopaminergic-AEs took levodopa≥700mg/day (on average). Cumulatively, by the end of double-blind, cases of dyskinesia, nausea, hallucination, vomiting and orthostatic hypotension were reported, respectively, by 5%, 1%, 2%, 1% and 0% under PLC; 10%, 11%, 1%, 0% and 2% under ENT; and 17%, 3%, 8%, 1% and 1% under OPC-50mg. However, despite no levodopa-adjustment during last 3-months, the actual (by-day) frequency was 2%, 1%, 0%, 0% and 0% under PLC; 3%, 1%, 0%, 0% and 1% under ENT; and 4%, 0%, 0%, 0% and 0% under OPC-50mg, respectively. Under OPC-50mg, dyskinesia presented an earlier onset than hallucinations. Dyskinesia appear to have a later onset under ENT versus OPC-50mg.
Conclusion: There was an apparent treatment-relationship for dopaminergic-AEs with OPC presenting the highest incidence. These observations support an enhanced dopaminergic efficacy of OPC and whilst dyskinesia could be managed by an early follow-up, hallucinations may require a later-stage follow-up.
Disclosure: Nothing to disclose

EPO3060

Are the MDS-UPDRS-based composite scores clinically applicable?

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Background and aims: In the present study we evaluated the feasibility of various composite scores based on the Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS) as potential clinical outcome measures and subsequently determined their minimal clinically important difference threshold values.
Methods: 1113 paired investigations of 452 patients were reviewed implementing three different techniques simultaneously.
Results: Based on the ordinal regression modeling, the MDS-UPDRS II+III, MDS-UPDRS I+II+III, and the total score of MDS-UPDRS are clinically applicable outcome measures. Any improvement greater than 4.9 points or any worsening more than 4.2 points on MDS-UPDRS II+III represent a minimal, yet clinically meaningful change. In reference to MDS-UPDRS I+II+III, the smallest changes considered clinically relevant were 6.7 and 5.2 points for improvement and deterioration, respectively. The thresholds for the total score of MDS-UPDRS were 7.1 points for improvement and 6.3 points for worsening.
Conclusion: Although the developers did not recommend the usage of composite scores, numerous PD-related studies utilize MDS-UPDRS-based composite scores as their outcome measure. The justification for using each Part score independently is based on the clinimetric properties of the scale. However, in the clinical practice and experimental studies, there may be important reasons to combine the outcomes. Utilizing composite scores may generally provide a broader assessment of PD; however, the combination of the domains may weaken the specificity. Employing ordinal regression modeling, we demonstrated that these composite scores including the total score are clinically applicable and responsive to changes.
Disclosure: This study was supported by the Hungarian Brain Research Program (2017-1.2.1-NKP-2017-00002) and OTKA SNN125143 government-based funds. We would thank Jon Marquette for his language editing. The present scientific contribution is also dedicated to the 650th anniversary of the foundation of the University of Pécs, Hungary.

EPO3061

A shoe insole delivering vibratory noise to improve freezing in Parkinson's disease

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Background and aims: The freezing of gait (FOG) is one of the most debilitating symptoms in Parkinson's disease (PD). It is one of the symptoms that does not show a significant improvement with the current treatment. Here, we aim to test the efficacy of a non-invasive treatment, an insole called 'Path Feel', as a device that can improve functional walking ability and FOG via haptic feedback in patients with PD.
Methods: The patients were assessed with the following clinical scales: Unified Parkinson's Disease Rating Scale–part III, Gait and Balance scale, Gait and Falls questionnaire, Activities-Specific Balance Confidence Questionnaire, Fear of Falling Avoidance-Behaviour Questionnaire. Pre-assessment: complation of a diary related to falls and episodes of FOG the week before the first session as well as the week before the second session. Clinical session 1: baseline in 3 conditions: a) OFF medications, b) OFF medications with the insoles, c) ON medications with the insoles. Clinical session 2: after a week of wearing the insoles in 3 conditions: a) OFF medications with the insoles, b) ON medications with the insoles, c) ON medications without the insoles. Self-reporting: completion of the questionnaires after a week without wearing insoles.
Results: The Path Feel insoles appear to be well received by the first patient. The improvement of several scores over the 3 session implies that Path Feel did improve the FOG. Interestingly, there was a coherent improvement of all scores during the 3rd week of the study which was the week following the one with the insoles.
Conclusion: This result suggests that the benefit of the vibratory stimulation on the FOG.
Disclosure: Brain Appeal Charity

EPO3062

Persistence of limb dystonia and myoclonus during sleep in Corticobasal Syndrome: report of three clinical cases.

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Background and aims: Thus far, few studies focused on sleep in Corticobasal Syndrome (CBS), documenting REM sleep behaviour disorder and periodic limb movements. No study evaluated the possible sleep modulation of the motor abnormalities as dystonia or myoclonus in these patients.
Methods: Three patients with clinical diagnosis of CBS underwent a nocturnal polysomnography through an extensive EMG montage. All cases presented with asymmetric parkinsonism and limb dystonia±myoclonus.
Results: All patients showed a severe impairment of sleep architecture and efficiency.
In case 1, PSG revealed the persistence of myoclonic jerks and tonic spasms through all sleep stages, sometimes recurring in a periodic fashion (every 20 seconds). Furthermore, prolonged painful contractions of the left arm, arising both during wakefulness and sleep, were observed.
Regarding case 2, the polysomnographic finding of a tonic activation on distal muscles of the left arm, during NREM sleep, was associated with further periodic phasic increasing of muscular tone. PLMi was increased (35.5/h).
Finally in case 3, PSG disclosed in all sleep stages the persistence of myoclonic jerks and tonic spasms, especially involving the right arm, even if with low voltage amplitude when compared with those recorded during wakefulness.
Conclusion: We documented the persistence during all sleep stages of dystonia and/or myoclonus in patients with CBS. Modulation of central nervous system connectivity occurring during sleep usually leads to disappearance of almost all the abnormal movement associated with basal ganglia dysfunction. In our patients, instead, the persistence of dystonic posture/myoclonus could indicate a cortical generator.
Disclosure: Nothing to disclose

EPO3063

Deletion in the progranulin gene in a patient with classic clinical features of Parkinson's disease

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Background and aims: Mutations in the progranulin gene (GRN) are known causes of familial forms of frontotemporal dementia with autosomal dominant inheritance. Carriers frequently develop parkinsonism, usually with a partial or absent levodopa response. However, parkinsonism at onset is less common and rest tremor is usually absent.
Methods: Case report.
Results: A 51-year-old male presented with right hand rest tremor, mild depression and apathy. He had a family history of dementia with 6 affected relatives over 3 generations. Most notably, the patient's brother had been diagnosed with Alzheimer's disease at the age of 49. On examination, he had pill-rolling rest tremor on the right and re-emergent tremor. He had mild bradykinesia and rigidity, more on the right. Formal neuropsychometry was normal. The patient had a normal brain magnetic resonance imaging scan. 123I-Ioflupane Single-photon emission computed tomography demonstrated reduced uptake, particularly in the left putamen. Motor symptoms responded well to low-dose pramipexole. Over the next two years, his apathy gradually worsened, he developed binge-eating behaviour leading to considerable weight gain and sleep apnoea. Mutations in C9ORF72, MAPT, TARDBP, FUS, APP, PSEN1, PSEN2 were excluded. Both he and his brother were found to carry a novel 64-bp deletion preceded by a single nucleotide change in the GRN gene, predicted to result in p.Gln401LeufsTer50.
Conclusion: We report a patient presenting with classic features of Parkinson's disease who was eventually found to have a GRN mutation. Notable family history should raise suspicion of a genetic cause even in the case of a seemingly benign presentation.
Disclosure: Nothing to disclose

EPO3064

Incidence of mild cognitive impairment and dementia in Parkinson's disease

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Background and aims: Mild cognitive impairment (MCI) is a common feature of Parkinson's disease (PD) even in the early stages of the disease and represents an important risk factor for the development of PD Dementia (PDD). Aim of our study was to evaluate incidence of MCI and the rate of its progression to PDD.
Methods: PD patients fulfilling the Brain Bank criteria who underwent at least two comprehensive neuropsychological evaluations (baseline and follow-up) within 48 months were enrolled in the study. Diagnosis of PD-MCI and PDD was made according to MDS criteria. Person-time incidence rate of PD-MCI and PDD has been estimated.
Results: 139 non-demented PD patients (men 86, mean age 65.9±9.3, mean disease duration 4.0 ±0.4 years, mean follow-up 24.9±10.3 months) were enrolled in the study. At baseline evaluation, 77 (55.4%) were classified as PD-normal cognition (NC) while 62 as PD-MCI. At follow-up among the 77 PD-NC at baseline, 27 developed MCI and 4 PDD. The incidence rate of MCI was 168,2/1000 person-years at risk (pyar) (95%CI 113.5-242.1). Considering the 62 patients with PD-MCI at the baseline, at follow-up 17 developed dementia (PDD). Incidence rate of PDD among patients with MCI at baseline was of 133.0/1000 pyar (95%CI 79.9-208.3) while among PD patients with NC at baseline was 24.9/1000 pyar giving a RR of 5.31 (95%CI 2.00-14.0; p-value 0.0004).
Conclusion: Our study underlined a high incidence rate of MCI in PD patients. Presence of MCI highly increased the risk of dementia in patients with PD.
Disclosure: Nothing to disclose

EPO3065

Dual-site transcranial magnetic stimulation for the treatment of Parkinson's Disease

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Background and aims: Abnormal oscillatory neuronal activity in the subthalamic nucleus (STN) plays an important role in the pathophysiology of motor symptoms in Parkinson disease (PD). Anatomical studies showed that the primary motor (M1) and dorsal premotor cortex (PMd) project directly to different neuronal populations within the STN ("hyperdirect pathway"). We hypothesized that PD motor symptoms can be ameliorated with transcranial magnetic stimulation (TMS) applied to M1 and PMd with the goal to phaselock and desynchronize oscillating STN neurons via the hyperdirect pathway and through induction of long-term depression-like effects comparable to coordinated-reset DBS.
Methods: Asynchronous repetitive TMS to both a premotor area located at 32 mm anterior of M1 and M1 ("associative dual-site rTMS", "ADS-rTMS") was employed at 1 Hz with in 20 PD patients treated in a blinded, placebo-controlled cross-over design using two D-shaped TMS coils. Clinical outcomes were rated based on video-analysis of MDS-UPDRS-III with two certified raters blinded to treatment modality and additional metrics (tapping, tremor analysis).
Results: We found no significant improvement in the MDS-UPDRS-III or secondary motor outcome parameters (finger tapping performance, spectral power of resting or action tremor activity). Variation of the secondary stimulation site outside M1 (to either 50 mm anterior to M1 or to supplementary motor area) did not induce beneficial effects either.
Conclusion: A single session of ADS-rTMS did not produce a clinically meaningful beneficial effect on Parkinsonian motor symptoms. Successful treatment for PD by non-invasive brain stimulation targeting subcortical nuclei may require more detailed physiological information about the individual brain state and stimulation-induced effects.
Disclosure: The project was funded by the CortExplorer program (P1140048) of the Gemeinnützige HERTIE-Stiftung, Grüneburgweg 105, 60323 Frankfurt, Germany.

EPO3066

Defining the bending angle of PD patients suffering from camptocormia

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Background and aims: Camptocormia is a non-fixed forward bending of the trunk which resolves when lying down. Surprisingly there is no agreement how to measure the bending angle. The purpose of this study is to provide the scientific background for a consensus decision.
Methods: Photos of 42 patients with the subjective complaint of forward bending and PD were taken with a lateral view. Three methods of angle measurement were applied by two independent raters: The perpendicular method (PM) measuring the angle between a line connecting spinous process C7 and L5 and a perpendicular line through L5. The malleolus method (MM) assessing the angle between the same C7/L5 line and a line connecting L5 and the lateral malleolus. The fulcrum method (FM) is assessing a line between the fulcrum of the camptocormia and a perpendicular line.
Results: The measured angles differed between the three methods between 33° (PM), 47° (MM) and 55° (FM). The difference of the angle measured between the raters was 10.1° (FM), 2.4° (MM) and 1.7° (PM).
Conclusion: The three methods differ in the measured angles and the inter-rater reliability for the same patient group. FM lacks a precise definition of the fulcrum leading to a low interrater reliability. PM and MM showed a comparable interrater reliability. While MM is orientated in the individual appearance of the forward bending including the hip flexion, PM showed lower angle degrees because of disregarding this aspect. We propose MM as a suitable method to determine the forward bending angle in camptocormia.
Disclosure: Nothing to disclose

EPO3117

Urinary Symptoms and associated clinical features in Parkinson's Disease

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Background and aims: Lower urinary tract symptoms (LUTS) are highly prevalent in patients with idiopathic Parkinson's disease (IPD). Aim of the study was to analyze the prevalence of LUTS and the possible association with patients' age, disease duration, severity and non -motors symptoms.

Methods: 30 IPD patients, 21 men and 9 women without cognitive impairment (MOCA >24) and under 80 years old were enrolled. All patients underwent the unified Parkinson's disease rating scale (UPDRS) motor section part III and Hoehn-Yahr (H&Y) scale,Montreal Cognitive Assessment (MOCA), Hamilton Anxiety Scale (HAM-A), Hamilton Depression Scale (HAM-D), 3- day voiding diary, uroflowmetry and a standardized questionnaire on incontinence (Incontinence-QoL).

Results: All patients investigated complained of overactive bladder symptoms. Urinary incontinence was significantly associated with higher H&Y stages ($p<0.005$) and frequency of nocturia with higher UPDRS scores ($p<0.003$). Old age, longer disease duration and higher H&Y stage were significantly related with reduction in HAM-A scores (mean±SD: 16.3±5.8; $p<0.002$); and also post- void residual volume was related with an increase in HAM-D scores ($p<0.005$). The I-QoL scores (mean± SD: 62.4±26.2) were significantly associated with the MMSE scores (mean±SD: 2.4±0.7; $p<0.01$).

Conclusion: To our knowledge, this is the first study showing a positive correlation between urinary, neuropsychiatric symptoms and QoL.

Our findings, in line with previous studies, suggest that the presence of LUTS in PD patients are strictly related to age, disease duration and the severity of motor impairment.

Disclosure: Nothing to disclose

MS and related disorders 4

EPO3067

Lymphocyte count and Body Mass Index as biomarkers of treatment response in a Multiple Sclerosis Dimethyl-Fumarate-treated cohort

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Background and aims: In dimethyl-fumarate (DMF)-treated relapsing MS (RMS) patients, few data are available about biomarkers of treatment response. We aimed to assess the predictive value of lymphocyte count (LC) and BMI for treatment response in a real life setting of DMF treated patients.
Methods: We collected clinical, demographic and anthropometric data at the beginning (T0) of DMF. LC were assessed at T0 and after 3(T3) and 6(T6) and 12 (T12) months. Relapses within T6 and T12 were considered to evaluate clinical activity; Gadolinium enhancing (Gd+) and new T2 lesions, defined MRI activity at T6 and T12. To correlate LC and BMI with clinical and MRI response, Pearson and Spearman tests were performed. We evaluated using logistic regression models, whether BMI or LC can predict treatment response.
Results: Our cohort of 165 DMF-treated patients was followed up for 15±7 months. The mean BMI at baseline was 24.19±4.48. We observed an inverse correlation between BMI and relapses within T6 (r=-0.31, p=0.001) and T12 (r=-0.32, p=0.019). We also found an inverse correlation between BMI and MRI activity at T12 (r=-0.32 p=0.012). At the multivariate models, predictive factors for GD+ lesions at T12 resulted LC at T3 (p=0.037, OR=1.084, CI=0.997-1) and baseline BMI (p=0.033, OR=0.887, CI=1.032-2.131). Predictive factors for new T2 lesions at T12 were LC at T3 (p=0.005, OR=1.010 CI=0.99-1) and baseline BMI (p=0.026, OR=0.997, CI=0.98-1).
Conclusion: BMI and LC during DMF can be considered early biomarkers of treatment response.
Disclosure: Dr. Paolicelli received honoraria for consultancy and/or speaking from Biogen Idec, Merck-Serono, Almirall, Sanofi-Aventis, TEVA, Novartis and Genzyme. Dr. Manni, Dr. Iaffaldano A, Dr. D'Onghia and Dr. Messina have declared that no competing interests exist. Dr. Iaffaldano P. has served on scientific advisory boards for Biogen Idec and Bayer, and has received funding for travel and/or speaker honoraria from Genzyme, Sanofi-Aventis, Biogen Idec, Teva and Novartis. Prof. Trojano received honoraria for consultancy or speaking from Biogen, SanofiAventis, Merck Serono, Novartis, Genzyme, TEVA, and Bayer-Schering and research grants from Merck Serono, Biogen, and Novartis.

EPO3069

Imaging correlates of EDSS in Multiple Sclerosis

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Background and aims: The Expanded Disability Status Scale(EDSS) is the most widely used neurological disability scale in Multiple Sclerosis(MS), mostly assessing functional systems related to motricity. Its correlation with MRI parameters is still poorly understood.
Objective: To identify which brain MRI volumetric parameters correlate with neurological incapacity as quantified by the EDSS scale.
Methods: 60 consecutive MS patients and 60 healthy controls(HC) were enrolled, matched by sex and age. Neurological impairment in MS patients was determined by the EDSS. All participants underwent 3Tesla-MRI. Volumetric analysis was performed using FreeSurfer software, and the following volumes were obtained:T1 and T2 lesions; total, subcortical and cortical grey matter; white matter; brainstem; cerebellum; corpus callosum; thalamus, pallidum, caudate and putamen.
Results: The volume of all brain structures analysed was lower for MS patients when compared to HC($p<0.05$). There was positive correlation between the EDSS value and the lesional volume in T2($r=0.506$ $p<0.01$) and T1($r=0.438$ $p=0.001$), and negative correlation with brainstem ($r=-0.398$ $p=0.04$), cerebellar ($r=-0.298$ $p=0.024$), pallidum ($r=-0.331$ $p=0.012$) and putaminal ($r=-0.315$ $p=0.017$) volumes. Overall grey matter and white matter volumes did not correlate with EDSS value. In linear regression analysis, the lesional volume in T2 was the only variable with predictive value for EDSS ($r2=0,302$ $p<0.001$).
Conclusion: Neurological disability measured by EDSS correlated mainly with the volume of white matter lesions and brain structures involved in motor control circuits, possibly reflecting the fact that the scale is dominated by gait function.
Disclosure: Nothing to disclose

EPO3070

Permantent lymphopenia and risk of PML in MS patients in real word

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Background and aims: Dimethylfumarate (DMF) is an oral drug for the treatment of RRMS. About6%of patients on DMFhad an absolute lymphocyte count equal to or less than 500/mL in trials. Progressive multifocal leucoencephalopaty (PML)cases have been reported in patients on DMF with moderate and permanent lymphopenia. It seems that durable moderate lymphopenia is a risk factor of PML in patients treated with DMF
Our objetive is to analyse the characteristic of the patients with lymphopenia in a real world MS cohort treated with DMF.
Methods: Retrospective observational study including patients with RRMS on DMF and analyzethe clinical features of those patients, who have presented lymphopenia during at least3months of treatment.
Results: 188patients were studied. 57(30,31%)presented lymphopenia for more than three months.42 (73,7%)were women. The average age was 44,05(23-70), and 17were older than 50 years. The mean time from the start of treatment to the onset of lymphopenia was 8.73months(1-26). The grades of significant lymphopenia : Grade2:20 patients (35,1%); Grade3:24 patients (42,1%); Grade4: 1(1,8%). The rate of lymphocites no recovery was 82,50%.Because of safety reasons, DMF was withdrawn in 33 patients. Of the patients who recovered from lymphopenia, the average recovery time was 10,10months (2-27) after withdrawal.
Conclusion: In the real world analysis ,one third of patients presented lymphopenia and from these patients more than a half had to stop the drug for risk of PML. Moreover, The recovery of the number of lymphocytes was very slow, and must be taken into account for the choice of the next disease modifying drug.
Disclosure: Nothing to disclose

EPO3071

Application of tRNS to improve Multiple Sclerosis Fatigue: a sham-controlled study

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Background and aims: Fatigue is one of the most common, early, and disabling symptom in Multiple Sclerosis (MS). tDCS on Dorso-Lateral Prefrontal Cortex seems to give positive results on MS fatigue. Recently, a new stimulation protocol, transcranial Random Noise Stimulation (tRNS), showed powerful facilitatory effects on motor cortex in healthy subjects and ameliorated pain in MS patients. Here we aimed to explore effects of motor cortex tRNS in MS fatigue.
Methods: 13 MS fatigued patients were enrolled in a blind, sham controlled tRNS study. 7 patients received 1.5 mA, 101-640 Hz tRNS stimulation and 6 patient received sham stimulation, both stimulations applied daily over M1 for 15 minutes, for two consecutive weeks. Outcome measures were Modified Fatigue Impact Scale (MFIS) for fatigue, BICAMS for cognitive impact, Purdue Pegboard for manual dexterity, Timed 25 Foot Walking Test (T25FWT) for fatigability, MSQoL-54 for quality of life.
Results: ANOVA showed statistically significant improvement in MFIS physical subscale in real stimulation group (Real-p=0.004, Sham-p=0.22). SDMT scores improved only in tRNS subjects (p=0.01). MSQoL-54 scores showed a significative improvement only in tRNS patient (REAL-p=0.02, Sham-p=0.5) Patient Global Impression of Perceived Fatigue was significatively reduced in tRNS group (p=0,005).

Table 1 Sample characteristics

	tRNS	SHAM	p-value
Mean Age ± SD	36.7 ± 9.4	47.3 ± 5.3	0.03
Mean age at onset ± SD	24.7 ± 6	34.5 ± 7.5	0.02
Mean age at diagnosis ± SD	29-3 ± 6-3	37.3 ± 5.5	0.03
Mean EDSS ± SD	2-0 ± 1-1	3.1 ± 1.5	0.16
Mean MSSS ± SD	3 ± 3	3.6 ± 2.9)	0.70
Sex (M/F)	2/5	1/5	0.61

Table 1. Demograpnid and clinical features of the real and sham groups

Conclusion: tRNS on primary motor cortex can decrease MS fatigue. If further studies on larger samples validated and strengthened the results obtained so far, the development of stimulation device suitable for self-managed home based treatment should be strongly pursued to optimize management of such disabling symptom in MS.
Disclosure: Nothing to disclose

EPO3072

Immunomodulatory therapy reduces elevated nitric oxide levels in multiple sclerosis patients

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Background and aims: Recent research indicates that apart from reactive oxygen species, reactive nitrogen species, in particular the free radical nitric oxide (NOx) may be a driving factor in multiple sclerosis (MS) pathology. There are reports investigating NOx in cerebrospinal fluid, but the role of serum NOx (sNOx) in MS remains largely unclear. Here, we aimed to investigate sNOx in MS patients compared to healthy donors (HD) and assess its relation to clinical data.

Methods: 214 samples from 29 clinically isolated syndrome (CIS), 109 MS patients and 79 HD were analysed. Among CIS/MS patients 86 (62.3%) received immunomodulatory therapy (interferon-beta n=53, glatiramer acetate n=13, natalizumab n=20). sNOx concentration was quantified spectrophotometrically using the Active Motif® Nitric Oxide Quantitation Kit.

Results: Increased sNOx levels were found in untreated (median 9.1 IQR 7.3-14.2 μM) ($p<0.01$) compared to treated MS patients (median 6.6 IQR 4.9-10.3 μM). In CIS/MS we found higher sNOx in female (median 8.9 IQR 6.1-13.4 μM) compared to male (median 6.6 IQR 4.9-9.1 μM) patients ($p<0.05$). sNOx was unrelated to age, the Expanded Disability Status Scale score, disease duration and age at disease onset.

Conclusion: Increased sNOx levels are present in untreated MS patients, which are reduced to levels of HD under immunomodulatory therapy. Female MS patients seem to be more affected by an imbalanced sNOx status. Future studies are warranted to investigate if serum NOX may serve as a marker to monitor disease activity and treatment efficacy in MS.

Disclosure: Franz Hallwirth received funding from Merck, the Austrian Multiple Sclerosis Research Society and the Austrian Federal Ministry of Science, Research and Economics and was trained within the frame of the PhD Program Molecular Medicine of the Medical University of Graz.

EPO3073

Potential effects of dimethyl fumarate on central cholinergic transmission explored by short latency afferent inhibition in multiple sclerosis

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Background and aims: Dimethylfumarate (DMF) is an oral agent approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). DMF is able to activate the peripheral and centralnuclear factor erythroid-2-related factor (NRF2) pathway and stimulate nicotinic acid HCA2/GPR109A receptors. These pathways are also involved in acetylcholine (Ach) transmission, as shown in vitro. Ach is increasingly recognized to play a role in immunomodulation and neuroprotection.

Aim of this study is to explore the potential effects of DMF on central cholinergic transmission measured by short latency afferent inhibition (SAI) in MS patients.

Methods: In 20 RRMS naïve patients, who started DMF according to clinical practice, we performed SAI at baseline and 6 months after.

Two control groups were provided: I. 20 RRMS naïve patients who started INF-beta (INFg) according to clinical practice; II. 20 healthy subjects (HCg). Disability progression was investigated at baseline and 6 months after by EDSS. Side effects (SE) were also collected.

Results: SAI curves were not different at baseline comparing DMF and INFg at baseline and HSg.

SAI significantly improved after 6 months in DMF group (mean SAI at 20 and 24 ISI pre to post $p=0.010$) while there was no significant effect on SAI in INFg.

EDSS was unchanged comparing baseline and 6 months values; no severe SE were reported

Conclusion: Our study showed that DMF is able to improve SAI in MS patients, providing in vivo evidence of its influence on synaptic transmission. The facilitating action on the central cholinergic system may represent an additional mechanism of action, with potential implications for neuroprotection.

Disclosure: Nothing to disclose

EPO3074

Quantitative EEG differentiate Multiple Sclerosis with and without Cognitive Impairment from healthy controls at the beginning of the disease: preliminary data

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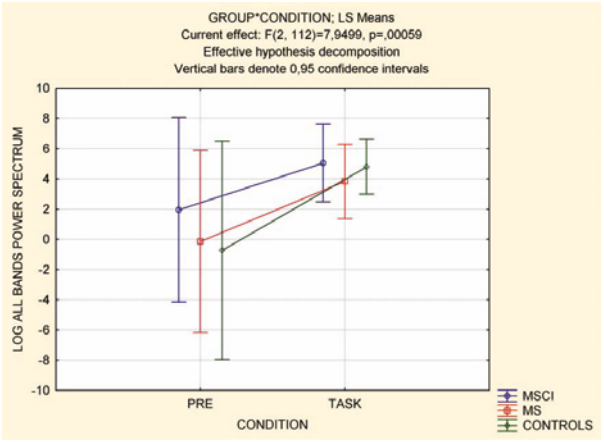
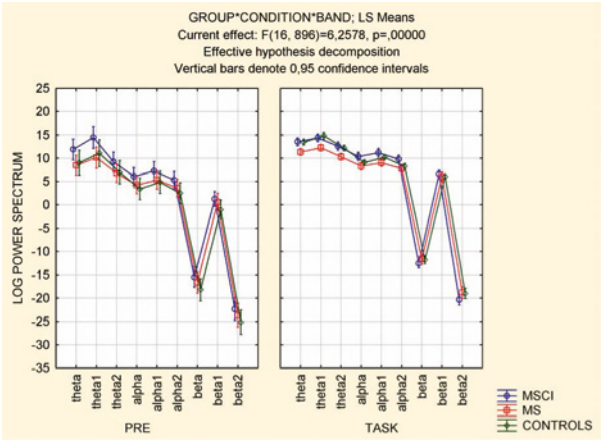
Background and aims: The present study aims to asses possible qEEG differences between newly diagnosed Multiple Sclerosis (MS) patients with or without Cognitive Impairment (CI).

Methods: We enrolled 13 patiens (18-5 years old) treated with first-line drugs for <6 months, and 16 healthy controls. All subjects underwent neuropsychological assessment including BICAMS and BDI. EEG recordings were performed during a cognitive task (computerised "SDMT" subtest of BICAMS) and at rest (5 minutes before and after task). Based on neuropsychological assessment patients were diagnosed as with -MSCI group- or without -MS group- cognitive impairment: only data from MSCI patients matched for sex, age (±5 years) and education to both an MS patient and a healthy control were analysed. Power spectrum analysis (theta, alpha, beta bands and sub-bands) were performed (EEGlab extension for MatLab). Data were log-transformed and analysed through repeated measures ANOVA.

Results: A significant interaction group (MSCI, MS, control) x condition (rest, task) x band (alpha, beta, theta) was observed. Post-hoc analyses showed significant differences between MSCI and both MS and controls in all EEG bands at rest ($p<.05$), whereas MS patients significantly differed from controls only in alpha2 and beta bands ($p<.05$). In task condition MSCI significantly differed from controls in alpha and beta bands, whereas MS in theta band ($p<.05$).





Conclusion: If confirmed in larger series, our results seem to support the hypothesis that qEEG differences exist among MSCI, MS and healthy controls, opening to a new possible neurophysiological hallmark of cognitive impairment in MS patients.

Disclosure: Nothing to disclose

EPO3075

Defective GABAergic transmission is associated with alexithymia in Multiple Sclerosis

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Background and aims: Alexithymia is a multicomponent personality construct characterised by difficulty in identifying feelings or describing them, and an externally oriented thinking. It could affect between 10 and 53% of patients with Multiple Sclerosis (MS). Defective GABAergic transmission and interhemispheric transfer were recently described in the context of alexithymia, but no studies were performed in MS.
Methods: 22 MS patients were classified as alexithymic (n=10) and non-alexithymic (n=12) according to the Toronto Alexithymia Scale score (TAS). Transcranial magnetic stimulation (TMS) was employed to record the interhemispheric inhibition and cortical silent period (CSP). Socio-demographic, clinical and neuropsychological data were obtained. Mann-Whitney and Fisher's exact tests were used for group comparison. Correlation analysis between TAS scores and TMS measures were performed using the Spearman rank correlation coefficient.
Results: In the absence of group difference with regards to clinical, socio-demographic and neuropsychological data, alexithymic patients had significantly shorter CSP duration (mean: 84.34±49.73, median: 91.50, vs. mean: 159.33±76.96, median: 148.50, respectively; p=0.03) than their non-alexithymic counterparts. In addition, TAS scores were significantly inversely correlated with CSP duration (r=-0.59; p=0.004).
Conclusion: This is the first study to address the neurophysiological underpinning of alexithymia in MS patients. In this population, alexithymia might be the result of a defective GABAergic transmission. Further research is needed to confirm the current results.
Disclosure: AC gave expert testimony for CSL Behring, Novartis, received grants from Biogen, Novartis, CSL Behring, GE Neuro, Octapharma, and gave lectures for Genzyme. SSA declares having received travel grants or compensation from Genzyme, Biogen, Novartis and Roche. JPL and MAC: Nothing to disclose

EPO3076

Vaccines and Optic Neuritis: a systematic review

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Background and aims: Vaccinations are often the most effective tool against some diseases known to mankind. Case reports of optic neuritis (ON) following vaccination can lead to distrust in the safety of vaccines, therefore it is important to gather existing knowledge on vaccines and ON in order not to confuse temporal and causal relations.
Methods: This study is a literature review on the role of vaccines regarding the risk of developing ON.
Results: A systematic literature review on the database PubMed.
Conclusion: The summarised results of the studies did not raise sufficient evidence to back up a positive association between ON and vaccination against HBV, HAV, HPV, MMR, influenza, variola, varicella, diphtheria, tetanus, pertussis, anthrax, meningococcal, pneumococcal or typhoid. However, since the identified studies of vaccines and ON were limited, a complete exclusion of correlation cannot be made.
Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 2

EPO3077

Non-invasive evaluation of sudomotor function in patients with Myasthenia Gravis

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Background and aims: Myasthenia Gravis (MG) is an autoimmune disease resulting in most cases from autoantibodies against the acetylcholine receptor (anti-AchR) at the neuromuscular junction. Dysautonomia is not a commonly recognised feature of this disorder although it has been described in several case reports. Electrochemical Skin Conductance (ESC), assessed by Sudoscan®, is a non-invasive method that allows evaluation of sweat gland function. Since sweat glands are innervated by sudomotor, post-ganglionic, cholinergic sympathetic C-fibers, we believe that ESC could be a reliable method for assessing hypothetical autonomic dysfunction in MG patients.
Methods: ESC measurements were prospectively assessed in patients with generalised MG followed at a Neuromuscular Disease Outpatient Clinic and in healthy controls. Patients with Diabetes Mellitus, anticholinergic medication, or electrophysiological findings of peripheral neuropathy were excluded. Data regarding demographic and disease features were collected. For statistic analysis we performed chi-square or Mann-Whitney U-tests for comparison between both groups.
Results: We included 24 patients, mean age of 46.4±10.6 years, female predominance (75%) and mean BMI of 26.5±5.1. Average disease duration was 12.5±8.9 years. Most patients had known serum positivity for anti-AchR (65%). Controls (n=37) were younger (39.6±11.6; p=0,02) with no differences in other baseline characteristics. We found no difference in feet (76.8±7.9 vs 79.7±5.1; p=0,126) and hand (70.7±14.6 vs 70.0±11.9; p=0,83) ESC measurements between both groups. Sudomotor function in MG patients was within the normal range.
Conclusion: Sudomotor function was similar between MG patients and healthy controls.
We found no evidence of autonomic dysfunction in patients with generalised MG as assessed by ESC.
Disclosure: Nothing to disclose

EPO3078

Whole-exome sequencing identifies double trouble in a patient with neuropathic and myopathic symptoms

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Background and aims: We present a 39-year-old male patient with progressive proximal weakness, atrophy of thighs, gluteal and parts of the shoulder musculature. By contrast there was hypertrophy of calf deltoid and trapezius muscles. Additional clinical signs included winged scapula, hollow back, Trendelenburg gait, positive Gower sign, funnel chest, decreased muscle reflexes and gynecomastia. Family history was positive as his father showed similar myopathic symptoms, while mother and sister reported unspecific gait disturbance.
Additional pathological findings: While EMG showed myopathic pattern, nerve conduction study was compatible with axonal polyneuropathy. CK and myoglobin were elevated. On MRI thigh musculature showed significant atrophy with volume loss and fatty degeneration.
Methods: To unravel the genetic cause of his disease we performed a next-generation-sequencing (NGS).
Results: NGS detected two (so far unreported) missense mutations in different genes in the index patient: 1., heterozygous mutation within RYR1 (c.1160T>C p. Leu387Pro) compatible with autosomal dominant myopathy (OMIM #180901), and 2., heterozygous mutation within MORC2 (c.311C>T p.Ala104Val) compatible with autosomal dominant axonal polyneuropathy CMT2Z (OMIM #616688) While the father was found to carry the mutation in the RYR1 gene, mother and sister are carriers of the mutation in the MORC2 gene. Thus, the genetic findings are in accordance with the clinical manifestations of the index patient and the affected family members.
Conclusion: Along with comprehensive clinical investigations NGS may help to establish the genetic diagnosis of neuromuscular diseases with even complex clinical constellations.
Disclosure: Nothing to disclose

EPO3079

Progressive respiratory failure: an unusual case of polymyositis

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Background and aims: Polymyositis (PM) is an inflammatory myopathy characterized by progressive weakness, predominantly proximal. Main histological features are fiber size variability, scattered necrotic and regenerating fibers and perivascular and endomysial cellular infiltrates.
Methods: We present a patient, 44 years old, who suffered from breathing shortness. He came to our observation because of elevated CK levels (950 UI), diurnal drowsiness and severe dyspnea. At neurological examination, he had a mild waddling gait and proximal weakness. We performed electromyography (EMG), muscular magnetic resonance (MRI) of diaphragm and upper limbs, muscle biopsy (MB), and pneumological evaluation with spirometry, nocturnal saturimetry and polysomnography.
Results: EMG displayed a myopathic pattern. Muscle MRI pointed out edema of the upper limbs and diaphragmatic muscles; specific sequences showed a severe reduction of the diaphragmatic excursion.Pneumological evaluation evidenced a severe restrictive syndrome, hypercapnia, nocturnal desaturation, high Apnea Hypopnea Index (49.5). MB revealed fiber size variability, scattered necrotic regenerating fibers with perivascular and endomysial cellular infiltrates (inflammatory myopathy). He started Prednisone 75 mg/die and Azathioprine 100 mg/die. 3 months after the patient showed clinical improvement, confirmed by muscle MRI that pointed out a drammatic reduction of the edema, even at the diaphragm.
Conclusion: Hypercapnic respiratory failure due to respiratory muscle involvement as PM presentation is a very rare event and it is described in less than 10% of patients with inflammatory myopathies. In our patient, progressive hypercapnic respiratory failure led to suspect PM that improved after therapy as confirmed by muscle and diaphragmatic MRI, useful tool either for diagnosis or for follow up.
Disclosure: Nothing to disclose

EPO3080

Comparison of thymomatous and non-thymomatous myasthenia gravis on outcome after thymectomy

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Background and aims: To describe the clinical profile and differentiate the clinical features of thymomatous (MGT) and non-thymomatous myasthenia gravis (NTMG) who underwent thymectomy and clinical outcome in a cohort of patients at the Virgen de la Arrixaca University Hospital.
Methods: Demographic information, clinical staging data, surgical and treatment details and patient follow-up data were obtained with a retrospective review of thymectomies performed between 2006-2016.Using the Myastenia Gravis Foundation of America (MGFA) post-intervention status classification, Complete Stable Remission, Pharmacologic Remission and Minimal Manifestatios and Improved were defined as Good Clinical Outcome (GCO) and Unchanged, Worse, Exacerbation or Died of MG as Poor Clinical Outcome (PCO).
Results: In 43 consecutive thymectomies for MG, 11 (25.6%) had pathologic diagnosis of thymoma. Non-thymomatous cases were hyperplasia thymic 21 (48,8%), thymic rests 9 (20,9%) and other findings 2 (4,7%). On univariate analysis, age at diagnosis (MGT 53±20 years vs MGNT 33±24 years), men (54,5% vs 18,8%), findings in mediastinal imaging (100% vs 58,1%), thoracotomy (36,4% vs 9,4%) and time to surgery were statistically significant between two groups. There no was difference at distribution of patients using MGFA Clinical Classification, serological tests or treatment before or a year after thymectomy. MGT was associated with poor clinical outcome a year after surgical intervention (PCO 46,2% vs GCO 16,7% OR 4.286; 95% CI, 1.928-19.796).
Conclusion: The not immediate benefit of thymectomy may be relationated with thymus role in pathogenesis of MG.
Disclosure: Nothing to disclose

EPO3081

Collagen VI encoding genes mutations-phenotypic variability in a cohort of Portuguese patients

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Background and aims: Bethlem myopathy and Ulrich Congenital Muscle Dystrophy are two classical phenotypes associated with mutations of collagen VI encoding genes (COL6A1, COL6A2 and COL6A3). However, a wide range of clinical presentation has been identified.
Methods: Review of clinical cases.
Results: Case 1. A 50-year-old male presented slowly progressive muscle weakness, beginning in childhood. Neurological exam revealed proximal limb muscle weakness (grade 4), contractures of fingers flexors muscles and shortening of the Achilles tendons. His 28-year-old daughter and 19 year-old niece had an analogous but less severe clinical presentation. A heterozygous mutation was found in COL6A1 gene in the three patients.
Case 2. A 29-year-old female presented with muscle weakness in childhood, slowly progressing towards a limb-girdle pattern of muscle weakness (grade 3) and distal muscle contractures. A heterozygous mutation in COL6A1 gene was identified. The same mutation was also identified in her mother.
Case 3. A 55-year-old male presented with muscle weakness begging in childhood, slowly progressive, with proximal lower limb muscle weakness (grade 4), lumbar hyperlordosis and distal muscles contractures. A homozygous mutation in COL6A2 was identified. His consanguineous parents were heterozygous for the same mutation.
Case 4. A 32-year-old male presented in childhood with delayed motor milestones and slowly progressive muscle weakness. Neurological examination identified a proximal muscle weakness (grade 4-), keloid scars and distal contractures. A heterozygous pathogenic mutation in COL6A2 was identified in molecular studies.
Conclusion: The clinical cases presented confirm the significant phenotypic variability in patients with collagen encoding genes mutations.
Disclosure: Nothing to disclose

EPO3082

Polysomnography in patients with Myasthenia Gravis (MG)

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Background and aims: MG is a rare neuromuscular junction autoimmune disorder with a skeletal muscle weakness leading to respiratory failure in 30% cases that is often overlooked and more often revealed while asleep.
Methods: We examined 19 MG patients (18 with generalized MG) without breathing disorder related complaints, 4 men and 15 women, the age was 57 (34;67), min/max 22/85 years old. The research was performed, using polysomnograf Polymate YH-1000C (BMC, China).
Results: We revealed changes in nocturnal saturation in MG patients. Me AHI 5.3 (2.0;12.7), min/max 0.3/22.9; Me ODI 6.1 (3.8;9.4), min/max 1.3/15.7, that indicates increasing of these indexes in comparison with normal indexes. SpO2 min 81%(75;86) min/max 31/90. SpO2 mean 95% (94;96) min/max 93/97–was at the lower level of standard values. Increasing AHI was revealed in 10 patients (52,6%), from them with moderate increase in 4 patients (40%). Increasing ODI–in 14 patients (73.7%), with moderate increase–in 1 patient (7%). Decrease SpO2 mean was revealed in 5 MG patients (26%). Among patients with bulbar dysfunction (12 patients-63%) increase AHI was revealed in most cases–7 patients (58%), with moderate increase–in 4 patients (57%); increase ODI in 4 patients (33%), with moderate increase–in 1 patient (25%); decrease SpO2 mean in 4 MG patients (33%).
Conclusion: When carrying out polysomnagraphy in MG patients without breathing disorder increasing AHI and ODI, while decreasing SpO2 mean was revealed more than at each 2nd patient, that indicates predisposition of MG patients to development respiratory impairment while asleep. More often such changes occur among patients with bulbar dysfunction.
Disclosure: Nothing to disclose

EPO3083

Serum PDGF-BB as a biomarker for the follow-up of late-onset Pompe patients

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Background and aims: Enzymatic replacement therapy stabilizes late onset Pompe disease (LOPD) progression, however is not clear whether earlier treatment could produce better outcome. Decision on starting treatment is based in the presence of muscle weakness, although irreversible fatty infiltration could already be present leading to disability. There are still not validated biomarkers related with the progression of the disease guiding to the start of treatment. We analysed serum concentration of several profibrotic growth factors (GF) in 37 LOPD patients and correlated results with different clinical variables.

Methods: We studied all patients with several motor function tests, spirometry and quantitative muscle MRI (qMRI). GF serum concentrations were analysed using ELISA in blood samples of patients and compared to 48 healthy controls using Mann-Whitney U test. We used Spearman test and ROC curves to study correlation between serum concentration and clinical parameters. Statistical significance was set at $p<0.05$.

Results: We observed significant differences in serum concentration of TGF-beta, PDGF-BB, PDGF-AA and CTGF between patients and controls. PDGF-BB concentration was significantly lower in symptomatic compared to asymptomatic LOPD patients. PDGF-BB was also lower in patients with more than 20% thigh fatty infiltration analysed using qMRI. ROC curves also supported a good correlation between serum PDGF-BB concentration and the presence of symptoms. We did not found significant correlation between serum concentrations and results of muscle function tests.

Conclusion: PDGF-BB serum concentration is a good biomarker candidates that could be useful in order to identify suitable LOPD patients to be treated earlier in their disease's progression.

Disclosure: This study has been funded by Sanofi Genzyme and by Fondos FEDER-ISCIII PI15/01822 to JDM

EPO3084

Pain in patients with Myotonic Dystrophy 1- is there a neuropathic component?

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Background and aims: Myotonic Dystrophy 1 (DM1) is an inherited multisystem disorder caused by a CTG trinucleotide repeat expansion in the Myotonic dystrophy protein kinase gene on chromosome 19. In addition to muscular dystrophy and myotony, some patients develop polyneuropathy. Little is known whether DM1 patients experience pain. We have followed a large group of DM1 patients, and noted that extensive pain was quite common in this group. The occurrence of pain in DM1 and whether a neuropathic component is present, was studied.

Methods: A thorough assessment of pain (localisatien and intensity), psychiatric issues and CTG expansion size, were investigated in 50 DM1 patients. In a subgroup of 20 patients; nerve conduction, quantitative sensory testing and skin biopsy for quantification of intraepidermal nerve fibers were performed. These patients underwent a neurological examination focused on sensory findings, mechanical allodynia or hyperalgesia.

Results: The participants report a large number of pain locations and a high pain intensity with a clear gender difference (more common in women). Preliminary analysis from the subgroup comfirm that neuropathy can be the cause of the reported pain in some of the participants. Exact occurence of neuropathy, and how this relate to the reported and other features of DM1, will be presented.

Conclusion: Pain in DM1 is prevalent. The presence of peripheral neuropathy could be relevant to understand pain in DM1, but more studies are needed to explain the high levels of pain reported.

Disclosure: Nothing to disclose

EPO3086

Mitochondrial multi-organ disorder syndrome score generated from definite mitochondrial disorders

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Background and aims: Mitochondrial disorders(MIDs) frequently present as mitochondrial multi-organ disorder syndrome(MIMODS) already at onset or evolve into MIMODS during the course. This study aimed to find which are the organs/tissues most frequently affected in MIMODS, which are the most frequent abnormalities within an affected organ, if there are typical MIMODS patterns, and to generate a MIMODS-score to assess the diagnostic probability for a MID.
Methods: Retrospective evaluation of clinical, biochemical, and genetic investigations of adult, definite MIDs.
Results: Included were 36 definite MID patients, 19 males, 17 females, aged 29-82y. The diagnosis was based on genetic testing (n=21), on biochemical investigations (n=17), or on both (n=2). The number of organs most frequently affected was four ranging from 1-9. MIMODS was diagnosed in 97% of patients. The organs most frequently affected were the muscle (97%), central nervous system (CNS) (72%), endocrine glands (69%), heart (58%), intestines (55%), and peripheral nerves (50%). The most frequent CNS abnormalities were leucencephalopathy, prolonged visually-evoked potentials and atrophy. The most frequent endocrine abnormalities included thyroid dysfunction, short stature, and diabetes. The most frequent cardiac abnormalities included arrhythmias, systolic dysfunction, and hypertrophic cardiomyopathy. The most frequent MIMODS patterns were encephalomyopathy, encephalo-myo-endocrinopathy, and encepalo-myo-endocrino-cardiopathy. The mean±2SD MIMODS score was 35.97±27.6 (range: 11-71). A MIMODS score >10 was regarded as indicative of a MID.
Conclusion: Adult MIDs manifest as MIMODS in the vast majority of the cases. Organs most frequently affected in MIMODS are the muscle, CNS, endocrine glands, and heart. A MIMODS score >10 suggests a MID.
Disclosure: Nothing to disclose

Neurogenetics 2

EPO3087

Frequency of huntingtin gene intermediate alleles in neurodegenerative diseases

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Background and aims: Even when carriers of Intermediate Alleles (IAs) do not develop HD there are some reported associations between IAs and HD symptoms. The role of IAs in other neurodegenerative disorders has not been fully assessed. Here we searched IAs in different neurodegenerative diseases.
Methods: First we screened expansions of the huntingtin gene in a pool of samples from patients previously diagnosed with AD (n=1053), PD (n=562) and FTD (n=225). We also screened a pool of 342 healthy controls recruited through the Health Community Service (elderly subjects who agreed to participate). Genotyping was performed by means of DNA fragment analysis. Then we computed the relative frequency of IAs in each group and compared frequencies between groups.
Results: We found 3 cases with expansions within the pathological range. These three cases were previously diagnosed with AD. The relative frequency of IAs for each group: 6% (63/1053) in AD, 5.3% in FTD (12/225), 3.3% in PD (19/562) and 2.9% in controls (10/342). The genotype frequency of IA was significantly more frequent among AD patients vs controls (p.=0.027, Yate correction; Odds ratio=2.11). In the FTD cohort, the genotype frequency raised 5.3% but was not significantly different from controls (p=0.16).
Conclusion: The frequency of IAs is higher in AD than in other neurodegenerative diseases and controls. IAs may play a role in the pathogenesis of neurodegenerative diseases, particularly in those presenting with cognitive impairment. More studies are needed to replicate these findings.
Disclosure: Nothing to disclose

EPO3088

"If you hear hooves behind you, don't expect to see a zebra": diagnosis of spinal muscular atrophy type III by whole-exome sequencing

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Background and aims: Spinal Muscular Atrophy (SMA) is an autosomal recessive disease, causing severe progressive muscle weakness due to loss of motor neurons in the spinal cord and the brainstem. Motor neuron degeneration is caused by homozygous absence of SMN1, encoding the "survival of motor neuron" (SMN) protein. The highly homologous SMN2 gene, which differs at only a single position within the coding sequence, can modify SMA disease severity due to its capability of driving low levels of SMN protein expression.
Methods: We developed a computational method for determining SMA (carrier) status in whole-exome sequencing (WES) data, based on statistical analysis of relative read coverage profiles at the nearly identical SMN1 and SMN2 loci.
Results: We identified two siblings, a young boy (10y) and his sister (6y), born to consanguineous Syrian parents, with progressive proximal muscle weakness (with mild elevation of serum creatine kinase levels, ~600U/L) and gait disturbance. WES variant analysis did not yield pathogenic variants in any known myopathy or neuropathy gene. Surprisingly, however, missing read coverage at SMN1 exon 7 was highly indicative for homozygous loss of SMN1. In both patients, multiplex ligation dependent probe amplification (MLPA) confirmed loss of SMN1 and detected four SMN2 copies. Thus, genetic findings were compatible with the diagnosis of juvenile SMA type III (OMIM # 253400).
Conclusion: This case reports underlines the importance of read-depth analyses in clinical WES, also of inherently difficult chromosomal regions (such as the SMN locus), which are commonly excluded from routine analysis.
Disclosure: Nothing to disclose

EPO3089

Jewish MJD patients of Yemenite descent share a recent common ancestor

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Background and aims: Jews arrived to Yemen mostly in the 2nd century, maintaining close communal structures. In 1994, one kindred from Yemen was described as the first Jewish family with Machado-Joseph disease (MJD), a dominant ataxia caused by the expansion of a (CAG)n in ATXN3. MJD is spread worldwide due to an ancient mutation of Asian origin (Joseph lineage). A second de novo expansion arose in a distinct haplotype (Machado lineage); other independent origins are still under study.
Methods: We genotyped 46 MJD patients and relatives, from 6 Israeli Yemenite families, and 100 normal chromosomes, for 28 SNPs spreading 15kb around the (CAG)n, and 8 STRs and one indel in the flanking region. Haplotypes were inferred by segregation; in controls, we used PHASEv2.2 whenever needed.
Results: All Yemenite MJD families shared extended haplotypes, showing no mutation or recombination after a common origin. They differ in 2 SNPs (rs12895357, rs12588287) from the Joseph lineage. Considering the short distances to the (CAG)n (1bp and 396bp, respectively), recombination is unlikely to explain this haplotype. To test for a new mutational origin in this population, we searched for the presence of this Joseph-derived haplotype in Yemenite Jewish controls; the finding of a normal (CAG)32 allele sharing the SNP background with MJD Yemenite patients did not rule out this hypothesis.
Conclusion: Our results pointed to a recent origin/introduction of MJD in the Yemenite population, based on lack of diversity found. To clarify the possibility of third mutational origin for this Joseph-derived lineage, a comparison with MJD haplotypes worldwide is required.
Disclosure: Nothing to disclose

EPO3090

Combined frontotemporal dementia due to C9Orf72 expansion and neurodegeneration with brain iron accumulation in the context of hypoceruloplasminemia

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Background and aims: C9Orf72 expansion is the most common mutation in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Though rare, co-occurrence of second mutations (ATXN2, TDP43, FUS...), influence disease presentation and progression.
Methods: Case report.
Results: 60-year-old male with six-years history of limb and facio-oromandibular movement disorder. He also referred liquid dysphagia in the previous three years, and subtle memory impairment. He had an older sister with symptoms consistent with primary progressive aphasia.
Neurological examination revealed limb and facial chorea, facial and orolingual dystonia, fragmented ocular pursuit, vertical gaze paralysis, dystonic dysarthria and bradylalia, hypomimia and mild limb rigidity. MMSE 30/30.
MRI showed frontotemporal atrophy plus iron deposition in striatum and substantia nigra. Blood tests revealed low serum copper (39) and ceruloplasmin (11.5), normal iron, ferritin and urine copper, and no achantocytosis. Analysis of IT15 and FTL genes showed no alterations.
The patient had 2 missense mutations in CP gene (exon5:c.G929A:p.R310H; and exon16:c.G2684C:p.G895A). These mutations have ExAC frequency <0.001 and Polyphen2 score of 0.8 and 1. During the next two years he developed cognitive and behavioural impairment, worsening of dystonia and dysphagia. He died at 63. Neuropathology showed TDP-43 pathology type B, with p62+ inclusions in cerebellum, and intraneuronal and glial iron deposition in lenticular, hypothalamic nuclei, and substantia nigra. Subsequent C9Orf72 analyses revealed a hexanucleotide expansion.
Conclusion: Extrapiramidal movement disorders have been reported in some patients with C9Orf72 expansion but this is the first case of a co-occurrence of a second mutation explaining this particular phenotype.
Disclosure: Nothing to disclose

EPO3092

Phenotype of three pathogenic variants of CACNA1A gene in Slovak families with episodic ataxia type-2

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Background and aims: Episodic ataxias (EAs) are rare autosomal dominant neurological disorders characterized by recurrent relapses of ataxia lasting minutes to hours. The most common subtype is EA type-2 (EA2) caused by pathogenic variants of calcium voltage-gated channel subunit alpha1 A gene (CACNA1A) on chromosome 19p13.
Methods: We examined three Slovak three-generation families with episodic ataxia. Complex differential diagnosis in each family was performed. Genomic DNA of the family members was extracted from peripheral blood and amplified by polymerase chain reaction. CACNA1A variants were screened by Sanger sequencing.
Results: Genetic analysis with direct sequencing revealed two novel heterozygous variants of CACNA1A-c.5264 G>A (p.Glu1755Gly) and c.889 G>A (p.Gly297Arg) located in highly conserved parts of the gene. Pathogenetic variant c.3832 C>T (p.Arg1278Ter) detected in third family has been already described in few families with epilepsy. We described and compared episodic and interictal signs of 10 affected family members. Acetazolamide was effective in each variant.
Conclusion: We described phenotype of three pathogenetic variants of CACNA1A gene in Slovak families with episodic ataxia type-2. We identified two novel missense variants of the gene.
Disclosure: Nothing to disclose

EPO3093

Clinical exome sequencing in dementias: a preliminary study

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Background and aims: Dementias are clinically and a genetically heterogeneous group of neurodegenerative disorders. Often, dementias with genetic etiology are clinically indistinguishable from non-genetic ones. The aim of this retrospective study was to evaluate the yield of clinical exome sequencing in dementias, potentially associated with monogenic genetic predisposition.
Methods: For this purpose 20 consecutive patients younger than 65 years were studied in the period from January 2014 to December 2017; 13 with the diagnosis of Frontotemporal dementia (FTD), 4 with early-onset Alzheimer disease (EOAD) and 3 with unspecified dementia. In addition to clinical exome sequencing including 32 dementia and 85 neurodegenerative diseases associated genes, C9orf72 (G4C2)4 hexanucleotide expansion was tested in all patients.
Results: We found genetic etiology in 6 patients: 2 mutations in the PSEN1 gene (p.Pro264Ser and p.Phe105Cys) in the EOAD patients, C9orf72 expansion and MAPT (c.1920+16C>T), mutation in the FTD group of patients as well as MAPT (c.1920+16C>T) mutation and likely pathogenic mutation in the TYROBP mutation (p.Asp32Asn) in patients with unspecified diagnosis.
Conclusion: Our preliminary results imply significant diagnostic yield in identifying rare genetic causes of dementia, combining comprehensive clinical exome sequencing and targeted C9orf72 expansion testing.
Disclosure: Nothing to disclose

EPO3094

The C9ORF72 repeat expansion in Greek patients with neurodegenerative disorders

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Background and aims: The C9ORF72 hexanucleotide repeat expansion, an established cause of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), has also been identified in patients with other neurodegenerative disorders. Recent studies from the Neurogenetics Unit, Eginition Hospital have individually investigated the frequency of the C9ORF72-expansion in cohorts of Greek patients with ALS, FTD, and Huntington disease (HD)-like syndromes. The aim of the present report is to update and expand data on the frequency of the expansion in a broader spectrum of neurodegenerative disorders.
Methods: Using molecular biological techniques, including repeat-primed PCR, genetic testing for the C9ORF72 repeat expansion was performed in 549 patients with neurodegenerative disorders (331 ALS, 65 FTD, 44 HD-like, 55 Alzheimer's disease (AD) and 54 with other dementia syndromes) and 321 healthy controls.
Results: In total, 33 patients with ALS (10.0%, 33/331), 14 with positive family history (56.0%, 14/25) and 19 sporadic (6.2%, 19/306), 6 patients with FTD (9.2%, 6/65), 5 with positive family history (27.7%, 5/18) and 1 sporadic (2.1% 1/47), 2 patients with HD-like syndromes (4.5%, 2/44) and 1 patient with AD (1.8%, 1/55) were expansion-positive. Patients with other dementia syndromes and healthy controls tested negative for the expansion.
Conclusion: The frequency of the C9ORF72 repeat expansion in Greek patients with neurodegenerative disorders is high, in line with other European populations. In fact, the frequency of the expansion in Greek familial ALS remains among the highest in Europe. The expansion is also the most common genetic cause of HD-like syndromes in Greece.
Disclosure: Nothing to disclose

EPO3095

Higher relative proportion of Leber's Hereditary Optic Neuropathy in premenarchal and postmenopausal women supports a protective role of estrogens

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Background and aims: Leber's Hereditary Optic Neuropathy (LHON) is caused by mitochondrial DNA mutations, whose overall penetrance is markedly higher in males than females. Accordingly, a protective role of estrogens has been suggested. Here we investigated whether women's reproductive age (menarche, childbearing age, menopause) influences onset of disease.
Methods: Out of 418 LHON patients in our database, 277 were analysed regarding gender, age at onset and genetic mutation; 226 (81.6%) patients were male and 51 (18.4%) female. The distribution of age at onset was analyzed by gender and across three age categories which reflect the three reproductive life stages of women: pre-menarche (≤12 years), childbearing age (13-49 years) and menopause (≥50 years). Mann-Whitney-U –Test was used for statistical analysis of non-parametric samples. A survival analysis with log-rank test was performed.
Results: The mean age at onset was significantly later ($p<0.001$) in female than male patients (37.4 vs. 26.0 years). Remarkably, the proportion of early and late-onset disease was higher in women than in men (15.6% vs. 8.8% and 29.4% vs. 8.8%), while the proportion was lower between 13 and 49 years (54.9% vs. 82.3%). There was no significant difference between groups regarding the causal mutation.
Conclusion: The higher mean age at onset and the higher proportion of females in early and late-onset age groups suggest a preponderance of protective factors or a relative absence of damaging factors in female LHON mutation carriers during childbearing age. These results support a protective effect of estrogens in female LHON patients.
Disclosure: Nothing to disclose

EPO3096

The strange case of vanishing memory after a fall

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Background and aims: Vanishing white matter disease (VWMD) is an inherited leukoencephalopathy caused by a mutation in the EIF2B gene. The disease has a wide phenotypic variation and clinical manifestations usually begin in childhood. We present a case of an adult onset form of the disease.
Results: A 23-year-old male was admitted to our hospital due to a severe traumatic brain injury after a fall. After motor recovery, the patient started complaining of memory loss. Physical examination was unremarkable. Neuropsychological tests revealed a multiple domain cognitive impairment. Brain MRI showed a diffuse white matter lesion. Additional investigation was normal except for the presence of oligoclonal bands in CSF. Main brain inflammatory and genetic disorders with white matter involvement were excluded and no diagnosis was assumed. The patient seemed to have no disease progression for many years. 20 years later he was revaluated due to further deterioration: pyramidal and cerebellar signs were identified, neuropsychological tests revealed a severe cognitive decline and brain MRI showed symmetrical and diffuse white matter lesions. After discussion with a geneticist, the clinical diagnosis of VWMD was warranted and a mutation in the EIF2B gene was identified. Familial genetic counselling was performed.
Conclusion: Although VWMD typically occurs in children this disease should be considered in the differential diagnosis of leukodystrophies in adults. Homozygous mutation of EIF2B5 gene as found in this case is frequently associated with late onset and slow progression. Subjects with this disorder are particularly vulnerable to stressors such as head trauma which may trigger the first symptoms.
Disclosure: Nothing to disclose

EPO3097

Coexisting CACNA1A pathogenic variant and MJD expansion in a single family

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Background and aims: Despite the identification of an increasing number of genes causing dominant spinocerebellar ataxias (SCAs), a significant proportion of cases are still left without a diagnosis. MJD/SCA3 is the most prevalent SCA worldwide. CACNA1A ataxia-causing sequence variants are typically associated with episodic ataxia type 2 and familial hemiplegic migraine, but may also cause a slowly progressive form of cerebellar ataxia.
Methods: Case report of a family with both CACNA1A-associated ataxia and MJD/SCA3.
Results: Two siblings, an 78-year-old man (patient #1) and a 90-year-old woman (patient #2), presented with a slowly progressive cerebellar syndrome, consisting of dysarthria, limb and gait ataxia, starting in their 20s. Family history suggested an autosomal dominant inheritance. Brain MRI showed global cerebellar atrophy. Genetic testing for SCA2, MJD, SCA6, SCA7, SCA10, SCA12, SCA14 and DRPLA was negative.
Patient #3 (son of patient #1) presented at age 26 years with nystagmus, dysarthria, pyramidal signs in the lower limbs and spastic-ataxic gait. His parents were consanguineous. His mother died at age 30 and was said to have had a wide-based gait. Brain MRI depicted mild cerebellar atrophy. A test requested by another neurologist showed an expansion for MJD/SCA3. A NGS panel for AD ataxias subsequently confirmed both patient #1 and #2 (but not patient #3) carried a pathogenic variant in CACNA1A, c.1748G>A (p. Arg583Gln).
Conclusion: Albeit rare, multiple gene mutations responsible for a dominantly-inherited cerebellar ataxia phenotype may coexist in a single family. We highlight the role of NGS in achieving a definite diagnosis in such cases.
Disclosure: Nothing to disclose

Neuro-ophthalmology/neuro-otology

EPO3098

Ocular Vestibular Evoked Myogenic Potentials (oVEMPs): the mid-lateral recording position produces worse responses than the midline position in elderly patients

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Background and aims: oVEMPs are a non-invasive method of evaluating mainly utriculo-ocular pathway function. Initial studies have shown that the optimum recording position is at the midpoint of the inferior orbital ridge, although more recent studies have shown that a more lateral position (between midpoint and lateral canthus) produces larger amplitude responses. However, the latter studies have been done in young individuals (less than 60 years of age).
The aim of this study is to map the oVEMP response and compare between young and elderly individuals.
Methods: Two groups of healthy volunteers (10 each) with no relevant neurotological history were examined: young and elderly (age range 14-50 years and 60-80 years respectively). Stimulation was performed using 500 Hz tone air-conducted auditory stimulation at 120 dB pSPL intensity monaurally with contralateral masking noise. Surface recording was performed from the tonically active inferior oblique muscle with active recording electrodes at five locations along the inferior orbital ridge (medial and lateral canthus, midline and midway between midline and each canthus).
Results: In both groups, the midline recording location for oVEMPs produced optimum and comparable responses with respect to measuring the preceding baseline-to-negative peak amplitude. Significantly smaller amplitudes were recorded from the midlateral position in the elderly, when measuring the negative peak-to-following positive peak, compared to young subjects.
Conclusion: The recent discovery of possible use of the midlateral location is worse in the elderly when measuring offset amplitude. It also demonstrates that optimum recording positions, especially when determined in a young population, do not necessarily apply to all ages.
Disclosure: Nothing to disclose

EPO3099

Features of diagnosis of visual field defects by method of threshold perimetry in Parkinson's disease patients with motor fluctuation

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Background and aims: Visual dysfunction in Parkinson's disease (PD) includes reduced color discrimination, contrast sensitivity, motion perception, etc. The basis of these disorders is retinal dopaminergic system (RDS) insufficiency, which leads to functional and structural retinal disorders. It is well known that glaucomatous-like visual field (VF) defects also often occur in PDpatients. To resolve the disputable question whether these defects are caused by functional or structural changes in the retina, we investigated the VF in different periods of levodopa action.
Aim: To estimate the variability of VF defects in PD patients over "on-off"-periods.
Methods: 24 non-glaucoma PD patients aged 46 to 65 years were examined. Perimetry included 24-2 and 60-4-SITA algorithms for detection of VF defects and determination of sensitivity thresholds in the central and peripheral parts of the retina.
Results: Most often the defect was located in the upper and/or nasal segments (n=18) mainly in the peripheral parts of the retina. In comparison with the on-period the decrease in the generalized photosensitivity within the off-period was more typical for peripheral VF. Within the on-period, we also observed a significant increase in local photosensitivity in those retinal segments where within the off-period the VF defect was revealed (Figure). Peripherally retinal nerve fiber layer thinning was observed more often when VF defects and generalized photosensitivity were unchangeable within "on-off"-periods.

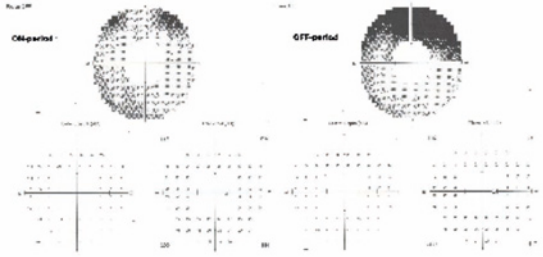

Figure. Variability of the VF defect and generalized photosensitivity in "on-off" periods (Peripheral 60-4 Threshold Test)

Conclusion: Variability of the VF defect and generalized photosensitivity in "on-off"-periods is a distinctive feature of PD patients. Dynamic of sensitivity thresholds reflects changes in functional condition of the retinal cells that is determined by the levodopa level.
Disclosure: Nothing to disclose

EPO3100

Unsteadiness and falls in Kennedy disease: vestibular or somatosensory dysfunction?

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Background and aims: Kennedy disease is an X-linked recessive bulbospinal neuropathy, caused by a CAG expansion in the androgen receptor gene. Falls and unsteadiness in these patients are out of proportion of muscular weakness. Here, we aimed to investigate the cause of this disequilibrum by assessing vestibular, somatosensory, oculomotor and overall balance function.
Methods: Vestibular function was assessed by the video Head Impulse Test and balance was evaluated with static posturography. Sensory nerve function was measured with conventional sural nerve neurography. Finally, saccadic eye movements were quantified by computing the main sequence.
Results: In total, 6 patients were included (age range 40 to 62 yo, CAG repeats 44 to 50). Four patients had normal (0.92±0.08), whereas two patients showed low (0.43±0.11) VOR gains. These two subjects, however, had no corrective saccades, raising the suspicion that the low gain was due to low eye movement velocity without a final retinal error after the completion of the eye movement. Indeed, these two subjects had slow saccades with increased main sequence time constants. Sural SNAPs were markedly low in all patients (2.5±1.5 μV). Posturographic parameters were abnormal in all subjects showing a strong visual dependency as reflected in the computed Romberg quotients.
Conclusion: Our data suggest that postural unsteadiness in Kennedy disease stems mainly from a somatosensory deficit. Vestibular function is spared. Interestingly, some patients exhibit abnormally low velocities in fast eye movements (saccades and high velocity VOR) raising the possibility of an ocular motor neuron degeneration in the brainstem.
Disclosure: Nothing to disclose

EPO3102

The video Head Impulse Test in patients with cerebellar ataxia

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Background and aims: Vestibulo-ocular reflex (VOR) is a reflex that stabilizes the gaze during head motions by compensatory eye movements contrary to the head. The assessment of the VOR by the head impulse test allows to detect paresis of the semicircular canals (peripheral vestibular dysfunction). However, cerebellar impairment can interfere with some dynamic VOR changes during HIT. The aim of the study was to analyze the video Head Impulse Test findings–to assess the VOR and to analyze corrective saccades in patients with cerebellar ataxia and to compare these findings with a group of patients with peripheral vestibulopathy and with healthy controls.
Methods: 45 patients with cerebellar ataxia were examined (11 genetically determined, 34 IDCA), results were compared with 15 patients with peripheral vestibulopathy and 25 healthy persons. Subjects were examined with the video Head Impulse Test, we evaluated gain of VOR and distribution of the corrective saccades. Vestibular reactivity was examined by means of ENG with rotational and caloric testing. Range of impairment in patients with cerebellar ataxia was assessed by SARA.
Results: The video Head Impulse Test, especially the distribution of the corrective saccades helps to distinguish patients with cerebellar impairment from the patients with vestibular impairment and healthy controls. Scattered corrective saccades prevail in patients with cerebellar ataxia (64%), gathered saccades in peripheral vestibulopathy.
Conclusion: The video HIT allows to identify and quantify combined vestibular and cerebellar pathology. VOR gain could serve as a neurophysiological biomarker of the disease and thus help in the diagnostic algorithm.
Disclosure: Nothing to disclose

EPO3103

Paroxysmal positional ocular flutter and square wave oscillations associated with middle cerebellar peduncle demyelination

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Background and aims: Positional ocular flutter (POF) is a rare disorder, with only two cases described in the literature in one patient with degenerative ataxia and one other with Krabbe's disease. However, an underlying focal/strategic lesion has not been identified yet. We present a patient with a right middle cerebellar peduncle demyelinating lesion in association with symptomatic positional ocular flutter, in whom the use of dalfampridine was not effective.
Methods: Review of clinical case.
Results: A 24 year-old woman diagnosed with multiple sclerosis presented with a 3-year history of paroxysmal oscillopsia and nausea when moving to supine position. Brain MRI revealed several demyelinating lesions in the supratentorial region, and one located at the anterior and medial aspect of the right middle cerebellar peduncle. Video-oculography in upright position showed occasional single saccadic pulses and square-wave jerks during fixation. When moving to head hanging position, a ~2 second positional ocular flutter (slow phase velocity 11°/sec) followed by ~30 second square-wave oscillations was consistently precipitated, along with oscillopsia and intense nausea. She was started on dalfampridine, 10mg bid. 180 minutes after first drug intake, positional ocular flutter on head hanging was unchanged. Five days later, dalfampridine–related side effects led to drug discontinuation.
Conclusion: Given POF strictly positional nature, the impairment of the cerebellar saccadic-otolithic network might be one of the underlying mechanisms. Although beneficial in other cerebello-vestibular disorders, dalfampridine does not seem to be effective in POF associated with cerebellar demyelination.
Disclosure: Nothing to disclose

EPO3104

Physiological pituitary hyperplasia: a case report of under-recognised cause of neuroophtalmology disturbances in pregnancy

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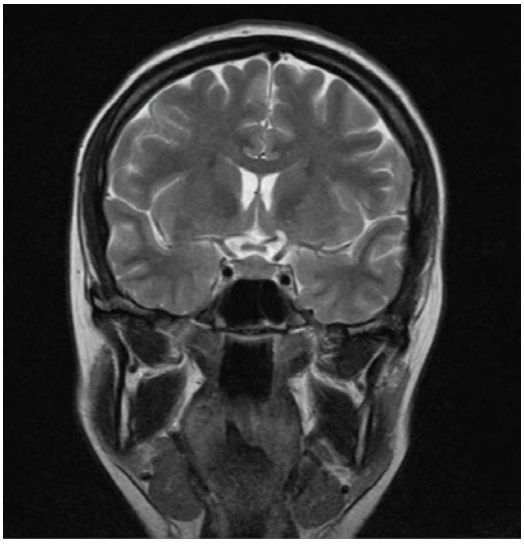
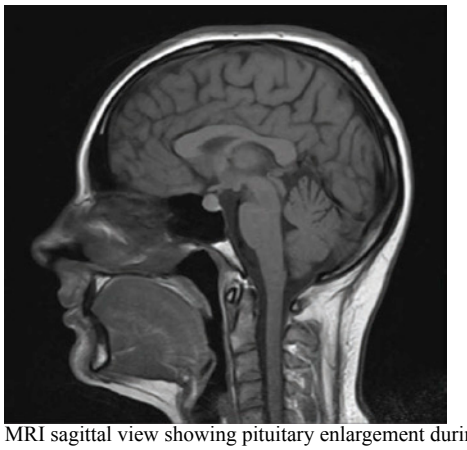
Background and aims: Anterior pituitary undergoes physiological enlargement during normal pregnancy as a result of lactotroph hyperplasia. Compression of the optic chiasm by enlarged pituitary gland often results in visual field defect.
Methods: A 28-year-old female in 37th week of pregnancy was admitted to our hospital due to blurred vision and transient visual loss in the right eye. No other symptoms were present. The past medical history was unremarkable.
Results: Examination revealed normal blood pressure and normal urinalysis. Neurologic examination and funduscopic examination were within normal limits. Best visual acuity was 0.9 in the right eye and 1.0 in the left eye. The visual field demonstrated bitemporal hemianopsia. The MRI of the brain with angiography and venography demonstrated physiological pituitary enlargement with pressure on the optic chiasm resulting in bitemporal hemianopsia. Due to the patient's late pregnancy stage, after the diagnostic workup, she was transferred to the Department of Obstetrics and Gynecology in a different hospital for further observation and treatment.



MRI coronal view showing pituitary enlargement during pregnancy


MRI sagittal view showing pituitary enlargement during pregnancy

Conclusion: Beside of much more serious diseases that may occur during pregnancy and cause visual disturbances (e.g., preeclampsia and eclampsia, posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, stroke and venous sinus thrombosis), to avoid unreasonable diagnostic and therapeutic procedures, neurologists and radiologists should be aware also of possible visual disturbances by physiological pituitary enlargement. The field defects raising from this entity have good prognosis, with recovery occurring one week postpartum

Disclosure: Nothing to disclose

EPO3105

Cervical vestibular evoked myogenic potentials in benign paroxysmal positional vertigo

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Background and aims: Benign paroxysmal positional vertigo (BPPV) is the most frequent cause of vertigo. Vestibular evoked myogenic potentials (VEMPs) generated by activation of the vestibulo-collic pathways can be analyzed easily and can make contributions to the understanding of the pathophysiological mechanisms underlying BPPV. The aim of this study was to evaluate cervical VEMPs (cVEMPs) in patients with BPPV.

Methods: Fifty four patients with BPPV were enrolled in the study. There were 19 men and 35 women with ages ranging from 18 to 65 years (mean age, 52.43±10.59 years). 45 age and sex matched healthy volunteers constituted the control group. P13 and n23 latencies and corrected p13-n23 amplitudes of the cVEMPs were taken into consideration.

Results: cVEMPs were recorded from both sides in all healthy subjects and patients. P13 latencies of the BPPV patients were significantly delayed ($p<0.05$) when compared with the healthy controls. n23 latencies and corrected p13-n23 amplitudes were not significantly affected ($p>0.05$).

Conclusion: Delayed p 13 latencies in patients with BPPV may suggest that BPPV is caused by damage to the otolith organs.

Disclosure: Nothing to disclose

Sleep disorders

EPO3106

Influence of long-term therapy of RLS on patients' quality of life.

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Background and aims: The aim of this study was to assess which initial features of restless legs syndrome (RLS) have the strongest influence of the quality of life (QoL), what kind of improvement is most strongly correlated with change in patients' quality of life and which aspects of patients quality of life are improved most with succesful therapy of RLS.
Methods: We have analyzed data of an outpatient population of RLS subjects. We have compared their initital clinical data (severity of RLS, insomnia, daytime sleepiness and quality of life measured with EQ-5D) with data available after succesful therapy and follow-up
Results: There were 100 RLS patients participating in the study (15 men; mean age 66.4 years; mean course of the disease 15.1 years). Initially there was significant correlation between severity of insomnia and quality of life. Nevertneless, the change in Qol was significantly positively correlated with improvement in severity of RLS. The domains of QoL which improved significantly were everyday activities, pain and anxiety.
Conclusion: Our results suggest that it is disordered sleep that has the strongest influence on patients' quality of life before therapy. Qol improvement is most strongly correlated with total IRLSS score.
Disclosure: Nothing to disclose

EPO3107

Correlation between EEG spectral power and heart rate variability in patients with obstructive sleep apnea

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Background and aims: Seminal studies suggest that patients with obstructive sleep apnea (OSA) have sleep fragmentation and higher risk of autonomic nervous system (ANS) dysfunction. The aim of this study was to correlate EEG spectral power and heart rate variability in patients with OSA and non-OSA subjects.
Methods: Overnight polysomnography with EEG spectral power analysis was performed in 33 consecutive patients (15 female, mean age 48.67 ± 14.08 years). 14 patients had obstructive sleep apnea syndrome (OSAS) whereas 19 were non-OSAS subjects. They all underwent standardized battery of ANS testing, including blood pressure and heart rate response to Valsalva maneuver, deep breathing test and head up tilt table test. In all study subjects heart rate variability (HRV) was determined.
Results: Negative correlation was found between EEG beta power (F4-01) and LF (rs=-0.560, p=0.013) and in non-OSA subjects. In OSA patients, negative correlation was found between EEG beta power (F4-01) and LF/HR (rs=-0.552, p=0.041) and positive correlation was observed between EEG beta power (F4-01) and HFnu (rs=0.552, p=0.042). HRV parameters did not show significant correlation with EEG alpha power, EEG theta power and EEG delta power in any patient group.
Conclusion: The results of this study suggest that cardiovagal dysfunction might be associated with cortical arousal and sleep fragmentation in OSA patients.
Disclosure: Nothing to disclose

EPO3108

Multiple Sclerosis and Obstructive Sleep Apnea: a systematic review and meta analysis

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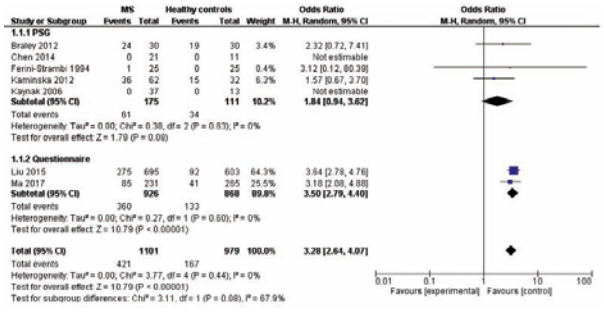
Background and aims: Obstructive Sleep Apnea (OSA) has been frequently reported present in patients with multiple sclerosis (pwMS). The aim of this study was to perform a systematic review and meta-analysis of available scientific evidence on the likelihood of OSA in pwMS.
Methods: A systematic review of the literature (PubMed library, Web of Science library) was performed for studies investigating OSA in pwMS for results up to July 2017. We identified 717 studies, of which 7 studies compared frequency of OSA in pwMS to healthy controls (HC). Polysomnography (PSG) as standard and objective diagnostic instrument was performed in 5 studies, while 2 studies used subjective assessment instruments (1 questionnaire and 1 self-report).
Results: PwMS had a significantly higher frequency of OSA compared to HC [421/1101 patients vs. 167/979 controls; odds ratio (OR) 3.28, 95% confidence interval (CI) 2.64–4.07, p=0.00001] if taking into account both subjective and objective (PSG) diagnostic instruments (Figure 1). No significant difference in frequency of OSA between pwMS and HC [61/175 patients vs. 34/111 controls; odds ratio (OR) 1.84, 95% confidence interval (CI) 0.94–3.62, p=0.08] was observed in PSG studies. Subjective assessment tools of OSA risk revealed a significantly higher frequency of OSA in pwMS vs. HC [360/926 patients vs. 133/868 controls; odds ratio (OR) 3.50, 95% confidence interval (CI) 2.79–4.40, p <0.00001].



Odds ratios (OR) for OSA in pwMS based on data from each individual study and from the pooled analysis. By ''favors control/favors disease'' it is meant that there is an increased likelihood of OSA; thus these data indicate that the likelihood of having PPH is higher in patients with neurological diseases than in healthy controls.

Conclusion: The likelihood of having OSA in pwMS is higher considering both, subjective and objective (PSG) diagnostic instruments. However, PSG study showed no significant difference in OSA frequency.
Disclosure: Nothing to disclose

EPO3109

The role of polysomnography in predicting respiratory failure in a patient with acute ischemic dorsolateral medullary infarction

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Background and aims: Acute unilateral dorsolateral medullary infarction (UDLMI) may cause acute respiratory failure. We assume that subclinical respiratory disturbances may be detected by polysomnography (PSG) in these patients before the onset of overt respiratory failure. We present a patient with UDLMI in whom PSG was recorded before and after transient respiratory failure.
Methods: A 58-year-old man with acute right-sighted UDLMI and concomitant cerebellar infarction was admitted to our stroke unit. PSG, recorded on the third hospital night, revealed periodic breathing (PB) which occurred mainly in non-rapid eye movement sleep (NREM) and consisted of 3-4 breaths of constant amplitude followed by central apnea with oxygen saturation drop from 95% to 80-90% and an arousal.
Results: PB represented 74% of total recording time, apnea-hypopnea index (AHI) was 163/hour (Image 1). A sudden respiratory failure occurred in the evening. He was intubated and transferred to intensive care unit. PSG was repeated 2.5 months after admission when he was weaned from mechanical ventilation support. PB still occurred in the NREM sleep in a different, crescendo-decresendo, pattern consisting of 10-12 breaths followed by central apnea with mild saturation drop to 89-90%. PB represented 54% of total recording time, AHI was 63/hour (Image 2).

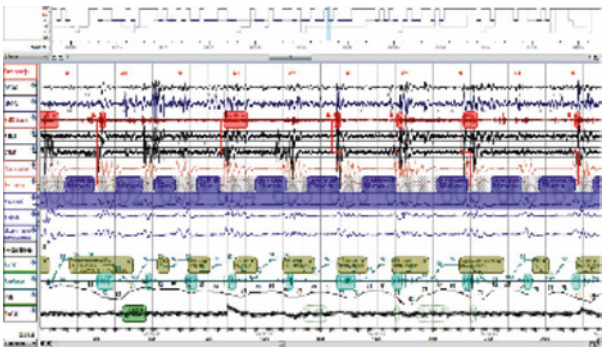

Image 1.

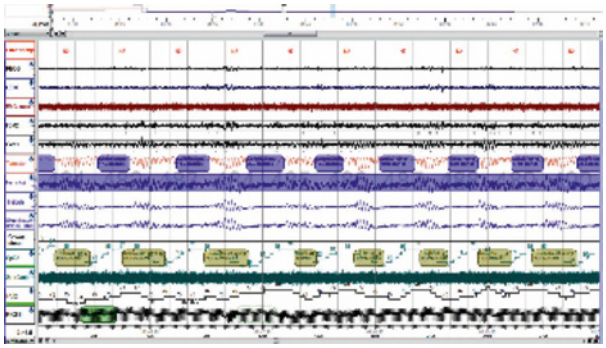

Image 2.

Conclusion: Our case report shows that PSG can detect subclinical breathing disturbances in patients with UDLMI before the onset of overt respiratory failure and after respiratory failure resolution. PSG could therefore be used as a screening tool for detecting patients at risk, for timely introduction of non-invasive ventilation and for long-term clinical monitoring.
Disclosure: Nothing to disclose

EPO3110

Treatment with safinamide in patiens with restless legs syndrome

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Background and aims: Restless legs syndrome (RLS) is a common sensorimotor disorder characterized by an urge to move, and associated with uncomfortable sensations in the legs. Refractory RLS is characterized by unresponsiveness to dopamine agonists (DA) or alpha-2-delta ligands (A2DL) due to inadequate efficacy, augmentation, or adverse effects.
Methods: Safinamide was used in patients with refractory RLS after previous treatment with at least one of the following: DA or A2DL. Restless Legs Syndrome Rating Scale (RLSRS) was used for measuring outcomes. This scale was administered at visit 1 (enrollment) and at visit 3 (3 months after inclusion). Visit 2 was planned 4 weeks after enrollment in order to assess whether the dose of 50 mg once a day of safinamide was effective.
Results: 5 patients were included with a range of ages between 52 and 71 years old. Three of the patients were female and 2 were males. All of them had been previously treated with at least 2 different groups of drugs (DA+clonazepam: 2/5, DA+clonazepam+A2DL: 3/5). In 2 of them DA had been stopped because of adverse events. Range of RLSRS score was between 14 and 28. Mean reduction in RLSRS was 11 points with a greater effect in those patients with a milder disease. Safinamide was well tolerated by all patients.
Conclusion: Safinamide seems to be effective and well tolerated in patients with refractory RLS. Treatment with safinamide could be more effective when used as early treatment. Safinamide is well tolerated when adverse events to DA appear.
Disclosure: Nothing to disclose

EPO3111

Sleep disorders: a key symptom in multiple neurological disorders

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Background and aims: In many neuroimmunological disorders disturbance of sleep and wakefulness play a keyrole. Sleep complaints are often underrepresented in neurological medical history. The aim was to summarise different case reports to emphasise the importance of sleep history in the context of neurological disorders.
Methods: Analysis of case records.
Results: A 69-year-old male reported about strange behaviors during sleep. During these behaviors he fell of the bed twice. He was amnestic for the nocturnal behavior. Sleep was not refreshing. During the day he suffered from involuntary sleep attacks. A few months later he also developed gait instability and ocular motor disturbance as well as chorea like movement disorder. He was diagnosed with Anti-IgLON5 disease. A 33-year-old suffered from excessive daytime sleepiness for more than 1.5 years and from hypnagogic hallucination, sleep paralysis and automatic behavior. Cataplexies were not present. Polysomnography revealed the diagnosis of narcolepsy. He was finally diagnosed with Ma2 Antibody encephalitis associated with germ cell tumor. Insomnia was the first symptom a 51-year-old man suffered from. Insomnia occurred 2 years before muscular symptoms like myalgia, cramps and fasciculations. He was diagnosed with Caspr2 antibody positive Morvans syndrome.
Conclusion: Sleep symptoms play a central role in different neuro immunological disorders. As demonstrated, disturbance of sleep and wakefulness can precede the full blown disorder. Beside parasomnias, disturbance of sleep initiation and maintenance should not be dismissed. Taking a precise sleep history could offer a useful instrument to detect autoantibody mediated neuroimmunological diseases in an early stage of disease.
Disclosure: Nothing to disclose

EPO3112

Atypical clinical and serological presentation of two patients with anti-IgLON5-antibodies-a case series

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Background and aims: The anti-IgLON5-disease is an antibody-related neurodegenerative disorder with a characteristic sleep disorder. Here we report two novel cases of anti-IgLON5-syndrome with atypical clinical and serological presentation.
Methods: Diagnostic workup in case-1 included peripheral nerve conduction, evoked potentials, cerebral/spinal MRI and whole body 18F-FDG-PET as well as HLA-analysis and two nights of video polysomnography (V-PSG). In case-2 cerebral MRI, 123J-FP-CIT, 18F-Fallypride, HLA-analysis, cognitive testing, L-DOPA test and two nights of V-PSG were performed. Laboratory testing of blood and CSF included screening for vasculitis, paraneoplastic, antineuronal, antiganglioside, myositis, and thyroid antibodies in both cases.
Results: Case-1 presented with lower motor neuron syndrome without a sleep disorder. Anti-IgLON5-antibodies were detected in serum and CSF with a predominant IgG4 subtype and lower levels of IgG1. HLA analysis revealed DQB1*05:01, but missed DRB*10:01. Treatment with i.v.immunoglobulins leaded to clinical improvement. Case-2 presented with PSP-symptoms, insomnia and day time sleepiness over 8 years. Anti-IgLON5-antibodies were found only in serum (predominant IgG4). HLA-analysis revealed DRB1*03:14 and DQB1*02:05. Cerbral MRI demonstrated a distinct mesencaphal atrophy,123J-FP-CIT showed an attenuation in the striatum, 18F-Fallypride was negative. V-PSG revealed reduced sleep efficacy, a mild sleep apnea syndrome, but no parasomnia.
Conclusion: We present two novel anti-IgLON5 patients that miss the HLA DRB1*10:01 haplotype and have atypical clinical phenotypes. Case-1 has anti-IgLON5-antibodies in serum and CSF and the lower motor neuron syndrome may represent a novel phenotype in the anti-IgLON5 spectrum responding to immunotherapy. In contrast, the clinical relevance of anti-IgLON5-antibodies only in serum of case-2 needs further investigations.
Disclosure: Nothing to disclose

EPO3113

Clinical presentation of obstructive sleep apnoea without oxygen desaturation

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Background and aims: In a subgroup of obstructive sleep apnoea (OSA) patients, respiratory events are associated with arousals without oxygen desaturation. It is not known if this phenotype has a different clinical presentation.
Methods: We analysed 364 polysomnographies (PSG) with >30min of REM sleep and either RDI≥15 or RDI≥10 and clinical suspicion of OSA. Non-desaturating (ND) phenotype was defined as oxygen desaturation index (ODI) <5 and desaturating (D) as ODI≥5. REM-predominant OSA was defined as RDI-REM/RDI- NREM>2. We analysed a subgroup of 32 ND patients and 31 controls (matched for age, sex, and RDI) with self-reported symptom questionnaires. Comparisons between groups used Mann-Whitney, Chi-squared, or Fisher exact test.
Results: 83 patients were ND. Mean age (57.7±14.0 vs. 46.7±15.7) and BMI (29.0±4.7 vs. 26.7±4.0) were higher in group D. Group ND had more women (47% vs. 31%). RDI was significantly higher in group D (30.5±16.9 vs. 15.9±14.8). 62% D had higher RDI during REM, compared to 47% ND (p=0,016). This difference increased in moderate severity OSA, with 36% REM-predominant OSA in group D and 10% in ND (p=0.002). Symptoms were similar between groups, but more ND patients rated symptoms as frequent or persistent (43% vs. 13%; p=0.01).
Conclusion: The ND phenotype is less common. This group is younger, has lower BMI, and less severe OSA. Events in REM sleep are more frequent in the D group, possibly because of different underlying mechanisms. The ND group had more frequent symptoms, supporting the importance of arousals in OSA physiopathology and the need for complete PSG in selected patients.
Disclosure: Nothing to disclose

EPO3114

Lack of intracortical facilitation to paired-pulse TMS in patients with "idiopathic RBD": a preclinical marker of synucleinopathy?

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Background and aims: Transcranial magnetic stimulation (TMS) provides several measures of motor cortex excitability in vivo, even subclinically. TMS changes, namely a reduced intracortical inhibition and facilitation, have been reported in Parkinson's disease, even in its early stage. REM sleep behavior disorder (RBD) often precedes the onset of synucleinopathies, although very few TMS studies have been carried out so far.
Methods: 60 patients with idiopathic RBD (median age 62.0 years, range 57.0-72.0; median disease duration: 3 years, range 1-4) and six age-matched healthy subjects (median age 62.0 years, range 56.0-65.0) underwent single- and paired-pulse TMS. Resting motor threshold, cortical silent period, latency and amplitude of motor evoked potentials, central motor conduction time, short-latency intracortical inhibition, and intracortical facilitation (ICF) were recorded through a figure-of-eight coil from the right first dorsal interosseus muscle. All participants were right-handed and drug-free. A screening for cognitive status, depressive symptoms, and diurnal sleepiness was also performed.
Results: Neurological examination was normal and no cognitive deficit, depression, or excessive sleepiness were detected in all participants. Compared to controls, patients exhibited a significant loss of ICF (median 0.6, range 0.1-1.1 vs. 1.4, range 1.4-1.8; p<0.05). The other TMS measures did not differ between the groups.
Conclusion: This finding suggests a subclinical electrocortical dysfunction in patients with RBD, raising the possibility that impaired ICF might precede the onset of an overt extrapyramidal syndrome. Such an impairment may result from an excitatory/inhibitory imbalance within intracortical motor circuits. RBD confirms to be a potential determinant of future neurodegeneration also at the TMS level.
Disclosure: This study was partially supported by a grant of the Italian Ministry of Health ("Ricerca Corrente").

EPO3115

Sleep disorders in children with cerebral palsy

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Background and aims: Children with cerebral palsy (CP) are considered to be a population at risk for sleep disorders (SD). SD can lead to important medical problems that affect the child and family and influence their quality of life. The aim of this study was to asses SD in children with CP.
Methods: The study included 50 children (28 boys) with CP aged 2 to 6 years (mean 5y 2m StDev 11 mo) and 50 healthy children (26 boys) aged 2 to 6 years (mean 4y 10 mo StDev 10 mo). SD were assessed using the Sleep Disturbance Scale for Children.
Results: SD was statistically significantly higher in patients with CP compared with the control group. 18 children (36%) from study group had an abnormal total sleep score, compared to 3 children (6%) in the control group ($p<0.05$). The most frequent sleep troubles in the study group were: disorders of excessive somnolence (28%), sleep breathing disorders (24%) and difficulties in initiating and maintaining sleep (20%).
Conclusion: SD are more common in children with CP than in the control group; excessive somnolence, sleep breathing disorders and difficulties in initiating and maintaining sleep being the most frequent disturbances. Thus, to avoid the negative impact of SD in CP children, SD screening should be a routine clinical practice for these children. At the same time Sleep Disturbance Scale for Children is an easy method for early identifying and early management of SD and a better outcome can be expected.
Disclosure: Nothing to disclose

EPO3116

Longitudinal assessment of sleep disturbances after traumatic brain injury: a one-year prospective study

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Background and aims: Sleep disturbances are common after traumatic brain injury (TBI). There are few longitudinal studies that assess patients with sleep disorders after TBI over time. The aim: the assessment of sleep disturbances at 1 year after TBI.
Methods: Prospective study on 57 patients (71.92% males, mean age 43.37±27.39 years). We used a standardised questionnaire which included demographics, sleep quality questions, sleep duration assessment, Center for Epidemiologic Studies Depression Scale (CES-D), The Galveston Orientation and Amnesia Test, Hamilton Anxiety and Depression Scale (HADS), Athens Insomnia Scale, Fatigue Symptom Inventory (FSI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale, and Toronto Hospital Alertness Test (THAT).
Results: At baseline, TBI was mild in 21 cases (36.84%), moderate in 27 cases (47.36%), and severe in 9 cases (15.78%). The mean sleep time/24 hours was 7.9±1.9 hours during week days and 8.6±2.1 hours during weekends. Excessive daytime sleepiness (ESS≥10) was reported at baseline by 19 patients (33%), while at 1 year it was reported by 15 patients (26.31%). Insomnia was found in 23 cases (40.35%) at baseline and in 17 cases (29.82%) at 1 year. There were no correlations between EDS and insomnia with GCS, topography or severity of TBI. Fatigue was reported by 34 patients (59.64%) at baseline and by 39 patients (68.42%) at 1-year follow-up.
Conclusion: Sleep disturbances have a high prevalence at 1-year follow-up after TBI.
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