Movement disorders 3

EP4126

Normal 0 21 Clinical evaluation of neurodegeneration with brain iron accumulation (NBIA) due to MPAN in Hungary

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Introduction: Neurodegeneration with brain iron accumulation is a progressive neurodegenerative disease causing progressing movement disorder. Symptoms may vary greatly. To date, nine genes are associated with different types of NBIA. The factors that influence disease severity and rate of progression are unknown. PANK2 and PLA2G6 gene mutations were most commonly investigated in NBIA patients. Recently the investigation of the C19orf12 gene is also recommended in NBIA patients.

Methods: Eight NBIA patients without PANK2 and PLAG6 gene mutation have been screened for the mutation of the C19orf12 gene encoding the mitochondrial memranprotein associated neurodegeneration (MPAN) by Sanger sequencing.

Results: In a young man a homozygous c.204_21del11 p. Gly69Argfs*10 mutation in the C19orf12 gene have been detected. His symptoms started in his childhood with severe visual impairment which was followed by moderate cerebellar, pyramidal signs and attention deficit. In two patients the c.335 G>A, p.W112X mutation resulted in later onset (at their 30s). One had focal dystonia, while the other had severe and rapidly progressing symptoms such as bulbar signs, spastic palsy, total incontinance, and cognitive decline. He died at the age of 39 years.

Conclusions: In MPAN patients a wide variety of clinical signs can be seen regarding onset, symptoms and case severity even with the same underlying mutation.

Disclosure: Nothing to disclose

EP4127

Huntington’s disease: health policy differences between Italy and France

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Introduction: Huntington’s disease (HD) is a severe condition that burdens patients and family. The study’s objective was to identify differences in the management of HD between Italy and France.

Methods: Euro-HDB is a comprehensive, observational study conducted in several countries in Europe (including Italy and France) to assess the burden of illness of HD. Data were collected on healthcare resource utilization (including home vs. institutional care). Comparisons were made between direct costs and the amount of time caregivers provided care to HD patients.

Results: Patients and caregivers in Italy (124) and in France (176) participated in the study. About half the patients were male (47% in Italy, 51% in France); average age was 54 years (Italy) and 57 years (France). Despite similar patient disability profiles, clear differences were identified. A direct cost ratio of 1:5 (Italy : France), was consistent across most measures. Total direct costs (SD) were evaluated at €6,461 (14,524) in Italy and €30,572 (34,212) in France. Reflecting indirect costs, families in Italy care for patients for an average of 22 hours per day whereas in France they reported 9 hours.

Conclusions: Families in Italy provide more home patient management than in France, where institutionalization is more common. More research is needed to identify how much social and health policy differences contribute to sizeable gaps in direct cost of medical management and indirect costs for patients and families.

Disclosure: Elizabeth Grubb is an employee of Teva Pharmaceuticals.
EP4128

Initial Parkinson’s disease treatment choices and costly health outcomes: a retrospective analysis

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Introduction: Increase understanding of pharmaceutical treatments in newly identified Parkinson’s Disease (PD) patients and associated major and costly outcomes.

Methods: Newly diagnosed US PD patients is from Truven’s MarketScan databases, 1 January 2006 - 31 December 2011. The initial PD prescription (index date) was matched 1-1 with newly diagnosed PD patients not receiving PD pharmacotherapy. Patients had continuous insurance coverage from 12 months prior through 12 months after index date. Logistic regressions examined associations between index PD treatments and subsequent falls and fractures, ER visits, and hospitalizations.

Results: 15,900 patients (3,950 aged ≤64 years, 11,950 aged 65+) met inclusion criteria. Carbidopa/Levodopa (C/L) was most commonly prescribed medication (37% age ≤64; 72% for those 65+). Dopamine agonists (DA) were more common for the younger than older (32% vs. 12%) cohort, as were MAOB inhibitors (13% vs. 4%). For the 65+ group, compared to patients receiving MAOB treatment, Adjusted Odds Ratios (OR) and 95% confidence intervals revealed associations between index PD medications and subsequent falls and fractures, C/L, the OR=1.954 (1.163-3.284) and for DA, the OR=2.091 (1.203-3.635). For ER visits: C/L OR=1.510 (1.142-1.997) and DA OR=1.599 (1.173-2.180). For hospitalizations: C/L OR=1.314 (0.970-1.780) and DA OR=1.311 (0.938-1.832.)

Conclusions: Patients age 65+ tended to be prescribed C/L as initial PD treatment. Those aged ≤64 were more likely to receive DA or MAOB. Among older patients odds of a fall, fracture or other outcome requiring a costly intervention was greater for those prescribed C/L or DA compared to those receiving an MAOB.

Disclosure: ElizaBeth Grubb is an employee of Teva Pharmaceuticals.

EP4129

Regional change in glucose metabolism of essential tremor: FDG-PET study using SPM analysis

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Introduction: There is growing evidence that essential tremor (ET) is a multiple-system disorder. Previous PET studies in ET typically measure the brain oxygen consumption and the cerebral blood flow. We compared ET patients with control subjects to investigate any regional change in cerebral glucose metabolism through SPM analysis of FDG-PET.

Method: We studied 17 patients with ET (17 male, mean age 67.3±4.8 years) and age-sex matched normal subjects. We attempted to measure the severity of tremor symptoms with the score of the Fahn-Tolosa-Marin rating scale (FTM). The evaluation procedure consisted of taking detailed medical history, neurological examinations, laboratory tests, MRI and PET-PET of brain.

Result: The mean age of tremor onset was 57.6±12.9 years and the mean score of FTM is 15.1±4.9 (Part A: 4.5±1.5, Part B : 7.4±2.6, Part C : 3.2±1.1). A brain FDG-PET analysis demonstrated hypometabolism in the medial frontal lobe, medial temporal lobe and precuneus of parietal lobe.

Discussion: Current research provides converging evidence for the role of the cerebellum in ET, although some inconsistencies exist. These discrepancies may depend on the high clinical heterogeneity of ET and on differences among the experimental methods. In our study, there was no significant difference of glucose metabolism in cerebellum. More interesting results were the decreased glucose metabolism in other brain regions that do not mainly participate in motor function. We assumed that abnormal glucose metabolism in these area might be the early marker of non-motor manifestations such as cognitive impairment. However, this assumption requires further studies.

Disclosure: Nothing to disclose
EP4130
Case report: concurrent occurrence of Fragile X syndrome and Fragile X associated tremor ataxia syndrome due to CGG repeat and methylation mosaicism
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Introduction: Fragile X syndrome (FXS) is a genetic disorder resulting from CGG trinucleotide repeat lengths greater than 200 and subsequent methylation of the FMR1 gene on the X chromosome. Fragile X associated tremor/ataxia syndrome (FXTAS) is a recently described syndrome of tremor and ataxia in a relative of a FXS patient with clinical signs not seen in typical FXS patients. This syndrome is typically seen in patients over the age of 50 and is thought to be a result of neuronal toxicity from excess mRNA production due to CGG repeat lengths of 55 to 200.

Results: We present a 34 year old gentleman with a previous diagnosis of FXS presenting with phenotypic features of FXTAS including cerebellar ataxia. Genetic testing with methylation assay revealed that he is a FXS and FXTAS mosaic with methylated CGG repeat lengths of 110 and 540 contributing to FXS and unmethylated CGG repeat lengths of 90 and 600 contributing to cerebellar ataxia and diagnosis of FXTAS.

Conclusions: Despite the close genotypic relationship between FXS and FXTAS there are distinct phenotypic differences attributable to different methylation state. This is the first case to be reported of FXS/FXTAS mosaicism and adds to the increasing understanding of the role played by methylation in determining phenotypic expression of genetic disorders, in particular the importance of methylation mosaicism. We suggest that in a FXS patient presenting with cerebellar ataxia or tremor without an apparent cause, further genetic testing with methylation analysis should be considered in the diagnostic process.

Disclosure: Nothing to disclose

EP4131
Apraxia of eyelid opening: a differential diagnosis of myasthenia
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Background: Apraxia of eyelid opening (AEO) is a non paralytic motor abnormality characterized by difficulty initiating the act of eyelid elevation. We report the case of a woman with AEO who was diagnosed initially as a myasthenia.

Case report: A 50-year-old woman presented fluctuating dropping of the upper eyelid. The diagnosis of myasthenia was initially suspected. There was no history of diplopia, swallowing or respiratory disorders. Ptosis was noted during hospitalization, especially in the late afternoon. The response to Neostigmine (Prostigmine®) was negative. EMG was normal. Anti-acetylcholine receptor and anti-muscle-specific receptor tyrosine kinase (MuSK) antibodies were not detected. Repeated neurological examination revealed difficulty in reopening the eyes after closure of the eyelid, without blepharospasm. The diagnosis of isolated AEO was made. Brain MRI was normal. The patient was treated by botulinum toxin injections with significant improvement.

Discussion: AEO occurs in the absence of ocular motor nerve dysfunction and ocular myopathy. Initiation of eyelid elevation requires activation of the elevator palpebrae superioris (LPS) and the concurrent inhibition of orbicularis oculi activity. AEO is thought to occur with prolonged inhibition of the LPS with or without concurrent clinical or subclinical contraction of the pretarsal portion of the orbicularis oculi. In consequence, a fluctuant ptosis can appear, mainly in idiopathic forms of AEO. Confusion with myasthenia can occurs, as seen in our case.

Conclusion: AEO is an important and often undetected cause of non-paralytic disorder of eyelid motility. It is important to distinguish between these two entities due to therapeutic and prognostic implications.

Disclosure: Nothing to disclose
Structural MRI of the cervical spine in patients with cervical dystonia


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Introduction: We used MRI to investigate, if structural changes of the cervical spine are more frequent in patients with cervical dystonia (CD) compared to healthy controls and which clinical parameters correlate with these abnormalities. Finally, we investigated whether there are clinical parameters which strengthen the indication for an MRI of the cervical spine in those patients.

Methods: We recruited 30 consecutive patients with CD. Three months apart, two identical examinations were performed including a neurological examination and the evaluation of the CD by established rating scales. An MRI of the cervical spine was analyzed by three experienced neuroradiologists with different MRI rating scales. For comparison, 21 age-matched healthy participants were recruited, who underwent the same examinations.

Results: Inter-rater reliability of each MRI rating scale revealed good results. We found no significant differences between both groups regarding structural changes of the cervical spine. Structural changes in patients with CD were associated with several clinical parameters predominantly in segments C3/C4 and C4/C5.

Conclusions: Based on our results, there is no indication for routine MRI of the cervical spine in patients with CD, since degenerative changes are comparable in both groups. An MRI should therefore only be ordered if clinical signs or symptoms of a cervical radiculopathy, excessive pain or spinal cord abnormality are present. If patients with CD are more prone to develop degenerative changes in segments C3/4 and C4/5 – in contrast to non-dystonia patients in whom structural changes are usually found in lower segments – needs to be further investigated.

Disclosure: Nothing to disclose
EP4134
Gait assessment in neurorehabilitation
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Introduction: Gait is often affected in people suffering from neurological disorders. To examine gait impairments or to evaluate interventions aimed at improving gait disorders, effective and efficient measurements are necessary. Therefore, we developed a new device-independent gait assessment (previously evaluated for healthy subjects, n=37) to quantify typical spatiotemporal gait parameters for daily clinical setting.

Methods: Groups of 14 Multiple Sclerosis (MS) and 20 Morbus Parkinson (MP) patients were compared with a healthy (n=17) control group (CG) (Table 1). Gait parameters were measured with participant’s self-paced velocity over a predefined distance (Table 2 and 3). Statistical analyses were conducted by multiple t-tests.

Results: The MS Group showed significant differences in gait velocity (GV) and stride length (SL) compared to CG. There were no significant differences in MP compared with CG.

Conclusions: Analyzing biomechanical outcomes in MS patients, the lower GV is traced back to the shortened SL despite a physiological ST. A possible explanation is a strength deficit in lower extremities which leads to gait instability. Even though, this could not be identified in MP patients. In contrast to typical clinical tests, this new gait assessment enables more differential consideration in patients’ biomechanical system. As a consequence, this allows more detailed and subtle decisions in neurorehabilitation. Additionally, the test is both, reasonably practicable and well-tolerated by patients with neurological diseases. We suggest integrating this new method in already existing assessments. However, more research is required on analyzing greater sample sizes, different neurological disorders and disease severities.

Disclosure: Nothing to disclose

Table 1: Sample characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Numbers [n]</th>
<th>Age [years]</th>
<th>Rating scale [Score]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbus Parkinson (MP)</td>
<td>20</td>
<td>68.1±10.3</td>
<td>UPDRS motor score: 22.4±9.2</td>
</tr>
<tr>
<td>Multiple Sclerosis (MS)</td>
<td>14</td>
<td>53.9±9.1</td>
<td>EDSS: 3.2±1.3</td>
</tr>
<tr>
<td>Control Group (CG)</td>
<td>17</td>
<td>20.8±1.4</td>
<td></td>
</tr>
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</table>

Table 2: Descriptive data of MP compared to CG

<table>
<thead>
<tr>
<th>Group</th>
<th>Distance [m]</th>
<th>Gait velocity (GV) [m/s]</th>
<th>Stride length (SL) [m]</th>
<th>Stride time (ST) [s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbus Parkinson (MP)</td>
<td>40.38</td>
<td>1.41±0.04</td>
<td>0.73±0.01</td>
<td>0.53±0.01</td>
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<tr>
<td>Control Group (CG)</td>
<td>40.38</td>
<td>1.48±0.03</td>
<td>0.75±0.01</td>
<td>0.51±0.01</td>
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</tbody>
</table>

Table 3: Descriptive data of MS compared to CG (**p<0.003)

<table>
<thead>
<tr>
<th>Group</th>
<th>Distance [m]</th>
<th>Gait velocity (GV) [m/s]</th>
<th>Stride length (SL) [m]</th>
<th>Stride time (ST) [s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Sclerosis (MS)</td>
<td>18</td>
<td>1.34±0.05**</td>
<td>0.69±0.02**</td>
<td>0.52±0.01</td>
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<tr>
<td>Control Group (CG)</td>
<td>23.17</td>
<td>1.51±0.03</td>
<td>0.77±0.01</td>
<td>0.51±0.01</td>
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</tbody>
</table>

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EP4135

Evaluation of a new device-independent gait assessment in neurorehabilitation

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Introduction: Obtaining feasible parameters from gait assessments is a central issue in clinical reasoning. Beside many-faceted reasons, erroneous therapeutic decisions in neurorehabilitation might be also based on typical clinical tests which only provide few sensitive and objective gait parameters due to practicability. On the other hand, providing objective biomechanical outcomes are associated with high technical, temporal, and financial effort. Therefore, we developed an innovative device-independent gait assessment which allows the quantification of spatiotemporal parameters from overground walking.

Methods: A group of healthy subjects (n=20, age: 22±2.7) were asked to walk at their individual self-paced velocity along a corridor (5 trials, distance: 40.38m). A second group of healthy subjects (n=17, age: 20.8±1.4) performed the test with varying distances (40.38m; 23.17m; 9.41m). Detailed description is shown in Figure 1. Test-retest-reliability and the influence of distance effects were examined. Visual marking and time measurement were validated using video analysis and a pressure plate, respectively (sample rates=100Hz).

Results: Test-retest-reliability showed very high Intraclass Correlation Coefficients (ICC3,1) for distances of 40.38m and 23.17m (Table 1). Concerning validity, the error in time measurement was very low (0.082s±0.047s), as well as the error in visual marking (0.67cm±0.54cm).

Conclusions: It is shown that the gait assessment is a valid and reliable method to easily obtain feasible biomechanical spatiotemporal parameters. Hence, it is a useful tool in neurological diagnostics which might have the potential to provide an advanced basis in order to come to better therapeutic decisions (first results are shown in a second abstract).

Disclosure: Nothing to disclose

EP4136

White matter changes predict cognitive dysfunction in patients with essential tremor

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Introduction: As previous research has not examined changes in white matter related to vascular risk factors and has not sufficiently explained why cognitive deficits occur in patients with essential tremor (ET), the objective of the present study was to evaluate relationships among vascular risk factors, MRI measures of white matter lesions (WMLs), and the rate of decline in the global cognitive functioning of elderly patients with ET.

Methods: We used the Mini-Mental State Examination (MMSE) to assess cognitive decline in patients with ET. The MMSE results of 106 patients were compared with those of 67 age- and sex-matched healthy controls without any vascular risk factors. All participants underwent cranial MRI examinations to exclude other possible causes of cerebellar or extrapyramidal disorders. WMLs were identified via T2-weighted MR scans and then evaluated. We examined correlations of MMSE scores with vascular risk factors, cranial MRI findings, and factors of age, educational level, and sex.

Results: Lower MMSE scores were related to WMLs and age in the patient group (p<0.05), and WMLs independently predicted mental status in this group (Beta value =-0.233, p=0.016).

Conclusions: We found no correlation between MMSE scores and commonly seen vascular risk factors. Cognitive assessments should be part of clinical dialogues with elderly patients with ET, and prospective neuro-imagining studies should be performed when cognitive impairment related to ET is suspected.

Disclosure: Nothing to disclose
EP4137

Frequency of buccopalpebral reflex in Parkinson’s disease

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Introduction: To investigate frequency of BPR according to the stage of Parkinson’s disease and to compare findings age-sex matched control group.

Methods: 115 patients with Parkinson’s disease and 107 control subjects were investigated prospectively. Demographic data and information about Parkinson’s disease were collected for each patient. Unified Parkinson’s disease Rating Scale (UPDRS) was used for staging of Parkinson’s disease and BPR was evaluated.

Results: The mean age in patients with Parkinson’s disease was 69.8±8.6. It was 66.8±8.4 in control subjects. BPR frequency of the control group was 3.7%, while those of were in 13.9%, respectively. This difference was statistically significant (p<0.05). In the analysis of UPDRS sub-groups, activities of daily living sore was 13.3±7.1 in reflex positive group and 9.6±7.7 in reflex negative group. According to the motor score evaluation of BPR positive and negative patients, it was the Motor score was 26.2±13.8 and 19.2±13.0 respectively. These differences were statistically significant (p<0.05).

Conclusions: BPR that mainly was observed in neurodegenerative disease such as Parkinson’s disease may be as result of the removal of cortical inhibition; therefore it should be primitive reflex. Since UPDRS scores were higher in BPR positive groups, BPR frequently seen in more severely affected patients.

Disclosure: Nothing to disclose

EP4138

Do dyskinesias and motor symptoms begin in the same body region in Parkinson’s disease?

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Introduction: In a retrospective work in Parkinson’s disease (PD) we found only a partial relationship between the body site of motor symptoms onset and the body site of levodopa induced dyskinesias (LID) onset (Fabbrini et al, 2009).

Methods: In this study we now investigated this relationship using objective assessment of LID onset. We included 70 PD patients (37 men, mean age 72.1±7.7 years, mean symptoms duration 9.2±5.5 years) who did not have LID and in whom LID onset was objectively observed by the neurologist during a routine follow-up visit.

Results: Motor symptoms (determined retrospectively) started unilaterally in the limbs in 91.4% of the patients and bilaterally in the limbs in 8.6% of the patients. LID (assessed objectively) started unilaterally in the limbs in 25.8% of the patients, bilaterally in the limbs in 7.1% of the patients, in the craniocervical/axial region in 40% of the patients, and in both the craniocervical/axial region and limbs in 27.1% of the patients. Statistical analysis disclosed a borderline significant association between the site of onset of motor symptoms onset and the site of LID onset (p=0.05). The association was highly significant when considering only when considering the subgroup of patients with unilateral onset of motor symptoms and LID (p=0.001).

Conclusions: The association between body site of motor symptom onset and body site of LID onset is clear only in those patients with unilateral onset of both motor symptoms and LID.

Disclosure: Nothing to disclose
Pathological changes in the brain assessed by diffusion tensor MRI and TCS can differentiate Parkinson’s disease patients with dementia

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Introduction: Magnetic resonance diffusion tensor imaging (DTI) and transcranial sonography (TCS) are promising new non-invasive methods for developing neuroimaging biomarkers in Parkinson’s disease (PD).

Aim: To measure the changes in PD patients with dementia (PD-D) using the DTI and TCS methods.

Methods: Fifty-three subjects (33 with PD; 9 demented, 24 non-demented individuals, and 20 age- and gender-matched controls) were studied using a DTI protocol at 1.5T Philips Intera scanner and TCS using Toshiba Aplio XG system. Neuropsychological assessment included Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Parkinson’s Disease-Cognitive Rating Scale (PD-CRS).

Results: DTI identified significantly decreased fractional anisotropy and increased apparent diffusion coefficient (ADC) in corpus callosum (p=0.009 and p=0.0005 respectively) in PD-D patients. Additionally, widespread white matter degeneration with increased total ADC in the anterior regions of the brain (p=0.009), particularly posterior regions (p=0.003), was detected in PD-D. Bilateral mean substantia nigra (SN) area measured with TCS was higher in PD-D versus non-demented patients (0.36±0.05cm² vs. 0.32±0.07cm², p=0.042), while in healthy controls mean SN area was 0.16±0.04cm². Diameter of the third ventricle was wider in PD-D versus non-demented PD patients (9.97±2.10mm vs 7.38±1.71mm, p=0.003), healthy controls - 6.81±1.73mm. PD patients with dilation of III ventricle over 7 mm in 90% of cases had cognitive decline.

Conclusions: These findings suggest that DTI and TCS may be sensitive to cognitive changes in PD and provide additional information in the diagnostics of PD-D patients. The study was supported by the Belarusian Republican Foundation for Fundamental Research (grant#M13-053).

Disclosure: Nothing to disclose