**Movement disorders 1**

**EP1129**

**Positive effects of granulocyte-colony stimulating factor on a rat model of Parkinson’s disease**

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**Introduction:** Granulocyte-colony stimulating factor (G-CSF) is a glycoprotein structured molecule, and releases from monocytes, macrophages, endothelial cells. Previous studies have revealed that it is present in many areas including substantia nigra in central nervous system. This study aims to investigate the effects of G-CSF on rat model of Parkinson’s disease.

**Methods:** Eighteen Sprague-Dawley adult male rats were included in the study and were divided into 3 groups. Rotenone+Dimethyl sulfoxide (DMSO) was stereotactically injected to left substantia nigra compacta and ventral tegmental area of the group 1 and group 2. Only DMSO was applied to the same location of the third group as a sham group. Rotation test was applied to rats after 10 days by administering intraperitoneally apomorphine. Rats having continuous rotation in the same direction 7 times per minute in apomorphine-induced rotation test (AIRT) were considered as PD. Group 1 was administered with 100 microgram/kg G-CSF, and group 2 with isotonic saline for 28 days. Then, apomorphine-induced rotation numbers were recorded for 10 minutes, and malondialdehyde levels in plasma and thyrosine hydroxylase (dopamine degradation product) (THA) measures in brain of the rats were examined.

**Results:** AIRT scores and malondialdehyde levels of the group 1 were lower than the group 2, while THA levels were higher (p< 0.005). There was no significant differences in terms of malondialdehyde and THA levels between the group 1 and 3.

**Conclusions:** G-CSF was detected to have positive effects on rat model of PD. This positive effect may be associated with of G-CSF’s neuroprotective effect.

**Disclosure:** Nothing to disclose

**EP1130**

**Progressive encephalomyelitis with rigidity and myoclonus: a new variant with DPPX antibodies**

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**Introduction:** Progressive encephalomyelitis with rigidity and myoclonus (PERM) is a variant of the Stiff Person Syndrome. Associated antibodies are mainly directed against glutamic acid decarboxylase (GAD), glycine receptors (GlyR), or amphiphysin. Here, we report a distinct variant of PERM comprising marked hyperekplexia, cerebellar ataxia, and trunk stiffness who tested negative for the antibodies hitherto described, but positive for a new antibody directed against the dipeptidyl peptidase-like protein 6 (DPPX or DPP6).

**Methods:** Case series describing the clinical, paraclinical, and serological features of three patients with PERM. A recombinant, cell-based indirect immunofluorescence assay with DPPX-expressing HEK293 cells was used to detect DPPX antibodies in conjunction with mammalian tissues.

**Results:** All patients presented with a distinct syndrome involving hyperekplexia, prominent cerebellar ataxia with marked eye movement disorder, and trunk stiffness of variable intensity. Additional symptoms comprised allodynia, neurogenic pruritus, and gastrointestinal symptoms. Symptoms began insidiously and progressed slowly. An inflammatory CSF profile with mild pleocytosis and intrathecal IgG -synthesis was found in all patients. High DPPX antibody titers were detected in the patient’s serum and CSF, with specific antibody indices suggestive of intrathecal synthesis of DPPX antibodies. Response to immunotherapy was good, but constant and aggressive treatment may be required.

**Conclusions:** These cases highlight the expanding spectrum of both PERM and anti-neuronal antibodies. Testing for DPPX antibodies should be considered in the diagnostic work-up of patients with acquired hyperekplexia, cerebellar ataxia, and stiffness, as such patients might benefit from immunotherapy.

**Disclosure:** C. Probst, I. M. Blöcker, R. Bahtz and L. Komorowski are employees of Euroimmun. W. Stöcker is a board member of Euroimmun
EP1131

Epidemiological genetic study of familial dystonia in Tunisia

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Introduction: Familial dystonia have been described and reflect the genetic origin. No studies have been conducted on this topic in Tunisia. We report on clinical, genealogical and genetic characteristics of primary dystonia in 22 Tunisian families.

Methods: From 2009 to 2013, we conducted an epidemiological genetic study including 84 patients with primary dystonia. A field survey was conducted and 22 families were visited. Family tree, neurological examination, video and blood sample from the index case and all family members were made. A molecular study was performed in 8 families and the results were analyzed.

Results: Epidemiological genetic study revealed 9 secondary cases belonging to 3 families. A high rate of consanguinity was noted (40%). Generalized dystonia were observed in 12 cases with phenotypic variability (blepharospasm, generalized dystonia and hemiparkinsonism) in a DYT1 family. Ten had focal dystonia, including 2 torticollis. A mutation in TOR1A gene was noted in 8 cases. Three had dopa-responsive dystonia with GCH1 gene mutation. Whole exome sequencing was performed in 2 patients with cervical dystonia.

Conclusion: Our study is the first to report 22 families with primary dystonia in Tunisia. The high rate of consanguinity in our study suggests autosomal recessive inheritance. The frequency of familial forms motivates a battery of genetic tests to reach a clear diagnosis and adequate management.

Disclosure: Nothing to disclose

EP1132

Corpus callosum damage and motor function in Parkinson’s disease

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Introduction: To investigate corpus callosum (CC) microstructural damage and its relationship with motor impairment in Parkinson’s disease (PD) patients at different disease stages.

Methods: We enrolled 173 PD patients (98:Hoehn and Yahr score [HY]=1-1.5; 37: HY=2-2.5; 29: HY=3-3.5; 9: HY=4-5) and 39 controls (HC). Diffusion tensor (DT) MRI tractography was performed to obtain the CC and its main three partitions: CC-genu, CC-body, and CC-splenium. Mean tract fractional anisotropy (FA) and mean diffusivity (MD) values were measured. Pearson’s correlations were used to explore the relationship between CC DT MRI metrics and UPDRSIII.

Results: All PD patients relative to HC showed decreased FA and increased MD of the whole CC and its partitions. CC microstructural damage was more marked with increasing severity, being only mild in PD with HY=1-1.5 (who showed the greatest damage in the CC-body) and severe (same degree of damage in all partitions) in patients at the later disease stages. UPDRSIII correlated (p< 0.001) with FA of the whole CC (r=−0.399), CC-genu (r=−0.199), CC-body (r=−0.481), and CC-splenium (r=0.270) and MD of the whole CC (r=0.367), CC-body (r=0.438), and CC-splenium (r=0.257).

Conclusions: PD is associated with CC microstructural damage that becomes more significant with disease worsening. In PD, the best predictor of motor functions is the involvement of the CC-body, which includes the transcallosal motor tracts. Assessing CC alterations may improve the understanding of the pathogenetic mechanisms associated with motor impairment in PD.

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EP1133

Intensive rater training to standardize cognitive assessment: a study to assess the effect of rasagiline on mild cognitive impairment in Parkinson’s disease patients

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Introduction: Parkinson’s disease (PD) trials using cognition endpoints are relatively new. Formal rater training is critical to increase success.

Methods: The MODERATO study examines effects of rasagiline on cognition in PD patients. Endpoints include the Montreal Cognitive Assessment (MoCA) and the Scales for Outcomes of Parkinson’s Disease - Cognition (SCOPA-COG). To maximize rater reliability, a training program preceded study start. Raters completed on-line didactic and video training requiring 100% correct and video recorded administrations to mock patients which were reviewed by calibrated expert raters. Errors affecting item scores were labeled “major” and required submission of another video.

Results: 80 raters started training and 71 completed it. 30% were classified as inexperienced (≤ 10 pre-trial administrations) on MoCA, 73% were inexperienced on SCOPA-COG. Using a paired samples t-test there was no significant difference between the MoCA and SCOPA-COG online assessment accuracy (MoCA 90% ± 10.9; SCOPA-COG 93% ± 14.2; p=0.07). There was no difference between experienced and inexperienced raters on MoCA errors (3.71 ± 2.93 and 3.96 ± 2.87, respectively; p=0.74) but experienced SCOPA-COG raters made significantly more errors than inexperienced raters (7.94 ± 3.39 vs. 5.21 ± 2.87; p=.001). Of 71 raters submitting videos, 38 (54%) required re-submission. Of 28 raters providing a second submission, 10 (36%) required further training.

Conclusions: Results support enhanced training designed to maximize reliability, regardless of pre-trial clinical or direct scale experience. Multi-step, multi-modal training can standardize raters to fidelity with scale instructions, minimizing error variance and increasing study power.

Disclosure: ElizaBeth Grubb and Azhar Choudhry are employees of Teva Pharmaceuticales.

EP1134

Levodopa/carbidopa intestinal infusion complications: the experience of 3 neurology departments in North-West Italy and a case report

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Introduction: Levodopa/carbidopa intestinal infusion represents one of the therapeutic options for advanced Parkinson’s disease (PD) patients with motor fluctuations and dyskinesias unresponsive to other treatments. It relieves symptoms of advanced PD and it improves quality of life. The most common complications of levodopa/carbidopa intestinal infusion are related to the infusion device, especially intestinal tube dislocation, occlusion, kinking or looping. Other complications are peristomal infections, localized peritonitis, pneumo-peritoneum or hemo-peritoneum. Adverse events may be also related to levodopa/carbidopa infusion, such as acute psychosis, weight loss, polyneuropathy.

Case report: From 2007 67 patients underwent levodopa/carbidopa intestinal infusion in our Departments. Among complications, in our experience 5 patients had tube occlusion due to bezoars. We report on a 61 years old patient with advanced PD who started levodopa/carbidopa intestinal infusion in October 2010. Some days later transient obsessive ideation occurred. Three months later agitation, delusions of persecution, hallucinations, false recognition and aggression occurred, alternating with drowsiness and severe brady-akinesia. There were also proteinuria with renal failure and anemia (with a negative gastroscopy). He needed clozapine therapy, transfusion of packed red blood cells and hydration. Subcutaneous continuous infusion of apomorphine was started in association with levodopa/carbidopa intestinal infusion. Patient was discharged after 4 weeks; he presented motor and cognitive improvement.

Conclusion: Also in our experience levodopa/carbidopa intestinal infusion adverse events are similar to those reported in literature.

Disclosure: Nothing to disclose
EP1135

Gastrointestinal dysfunction in PD patients with morning akinesia
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Introduction: It is well established that gastroparesis is common in PD causing delayed gastric emptying of L-dopa with a delayed onset of symptomatic effect. However, little is known about which measures can be used to identify patients that have this problem.

Methods: The AM-IMPAKT study is a Phase IV study designed to assess the effect of apomorphine HCl subcutaneous injection in L-dopa-treated PD patients with morning akinesia. At screening, patient gastrointestinal function was assessed using the SCOPA-Autonomic (SCOPA-AUT) scale and the Gastroparesis Cardinal Symptom Index (GCSI). We present an interim baseline analysis of gastrointestinal function in 50 patients who have completed the study. Patients were categorized according to duration of PD (0-5, 6-10, 11-15 & 15+ years).

Results: In this interim population, mean±SD age was 63.9±11.1 years and duration of levodopa treatment was 49.6±81.6 months. In these patients with delayed time-to-ON, GCSI was variable, although bloating and postprandial fullness subscores were increased. In contrast, baseline SCOPA-AUT total scores ranged from 15.2-16.8, and were driven mainly by GI dysfunction (scores 4.0-5.0) and urinary dysfunction (scores 5.0-6.5). Abnormal SCOPA-AUT total and subscores were already present in patients with PD duration of 0-5 years, and scores were similar to patients with a longer disease duration.

Conclusions: In PD patients with morning akinesia, the SCOPA-AUT appears to be helpful in identifying underlying gastroparesis. Once recognized, the presence of gastroparesis suggests that non-oral drug delivery may be useful to ensure a rapid and reliable ON in patients with morning akinesia.

Disclosure: S. Isaacson reports consulting fees for US WorldMeds LLC

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EP1136

ANDANTE safety review: a placebo controlled, randomized study of rasagiline as an add-on therapy to stable dose of dopamine agonists in early Parkinson’s disease
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Introduction: Dopamine agonists (DA)s are used as initial symptomatic therapy for early PD, escalating dose or addition of levodopa needed over time to maintain symptom control. Increasing DA dose is associated with a higher risk of AEs and addition of levodopa with the emergence of motor complications. Rasagiline is a selective, irreversible MAO-B inhibitor complementing the direct stimulation of dopamine receptors provided by DA monotherapy.

Methods: ANDANTE is a Phase-IV, 18-wk study of PD patients sub-optimally controlled on stable DA dosages (≥6mg/day ropinirole or ≥1.0mg/day pramipexole). Patients were randomized to rasagiline (RAS) 1mg or placebo (PL); DA dosage remained stable throughout; 11 patients required rescue levodopa during the study.

Results: Among 326 patients included in the safety cohort, 204 reported AEs (104RAS vs. 100PL). The most common AEs experienced by patients in any group were dizziness (7.4%RAS vs 6.1%PL), peripheral edema (7.4%RAS vs 4.3%PL), nausea (6.2%RAS vs 4.3%PL), and falls (5.6%RAS vs 1.2%PL). Somnolence, confusion, and hallucinations were not increased. AE severity was similar between rasagiline and placebo treated groups. A total of 13 patients experienced SAEs (4.9%RAS vs. 3.0%PL). No impulse control disorders (ICD) were reported during the study.

Conclusions: In the ANDANTE study, addition of rasagiline to DA monotherapy was safe and well-tolerated. No significant difference in percentage of patients with AEs (64.2%RAS vs. 61.0%PL) or serious AEs (4.9%RAS vs. 3.0%PL) was observed. In early PD patients sub-optimally controlled on DA monotherapy, improvement in motor control by the addition of rasagiline was not accompanied by limiting adverse effects.

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EP1137

Pisa syndrome in Parkinson’s disease: demographic and clinical correlations in an Italian multicenter study


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Idiopathic Pisa syndrome (PS) in Parkinson’s disease (PD) is a rare entity with only sporadic single case descriptions. Therefore, its pathophysiology has been poorly investigated. We performed this multicenter cross-sectional study with the aims to estimate the proportion of patients developing PS in a large cohort of patients with PD and to assess relationships between PS and demographic/clinical variables.

Patients with PD were selected from consecutive outpatients. Age, sex, age at PD onset, UPDRS III and IV, PDQ8, antiparkinsonian therapy and any information on lateral trunk flexion were recorded.

A total of 1631 patients (F:M=679:936) with PD met the eligibility criteria and entered into the study. Mean age and mean duration of parkinsonian motor symptoms were 69 (SD 9.6) and 7.1 (SD 4.9) years, respectively. Mean UPDRS III score was 22.1 (SD 11.2) and Hoehn and Yahr was 2.1 (0.7). The mean daily dose of Levodopa was 424.9 mg (sd 307.3). PS was detected in 150 out of 1631 patients (9.2%). The mean degree of lateral flexion of the trunk was 16.5 (SD 7.7). Concomitant camptocormia was detected in 63 (43.2%) patients with PS.

Patients with PS were significantly older, had longer duration of disease and of treatment with antiparkinsonian drugs than patients without PS; the UPDRS III and IV, H-Y were significantly higher in patients with PS. These results suggest that PS is a frequent and disabling complication in PD in the advanced phase.

Disclosure: Nothing to disclose
EP1138

Self completed non motor symptoms questionnaire (NMSQuest) score used to set up Parkinson’s disease burden in the outpatient clinic

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Introduction: The Non Motor Symptoms Questionnaire (NMSQuest) is a widely used self completed tool to assess NMS in patients with Parkinson’s disease (PD). We had previously recommended a simple grading system using the total NMSQuest score to address the burden of NMS in PD [1]: NMS levels as very mild 0-5, mild 6-12, moderate 13-20 and severe >20.

Methods: We analysed preliminary data from 100 PD patients consecutive completed NMSQuest (mean age 67 years; range 29-92 years), 38 females, disease duration 6 years (range 0.5-49 years). We classified using the NMSQuest total score in four severity levels as NMS burden and correlated with Hoehn and Yahr stages (HY) as motor symptom burden.

Results: In the whole sample, severity of NMS as assessed by NMSQuest levels were very mild (22%), mild (41%), moderate (24%) and severe (13%). 14% of our PD patients in moderate and 7% in severe NMSQuest level were in HY 1 while 16% with moderate and 6% with severe NMSQuest level were in HY 2 showing discordance between NMSQuest levels and HY stage. Furthermore, four patients with drug naive PD at HY 1 and HY 2 had moderate (n=2) and severe (n=1) NMSQuest level whereas only 1 patient had mild NMSQuest level.

Conclusions: This observation further outlines the importance of assessing NMS in PD patients. A substantial proportion of patients, in spite of being in early “motor” stage, had considerable NMS burden prompting the need of specific treatment which would have been otherwise missed.

Disclosure: Nothing to disclose

EP1139

The effect of subthalamic nucleus deep brain stimulation on restless legs syndrome in patients with Parkinson’s disease

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Introduction: Sleep disorders and restless legs syndrome (RLS) are common in Parkinson’s disease (PD) patients. Some of these sleep abnormalities may improve after subthalamic nucleus (STN) deep brain stimulation (DBS). We investigated the effect of STN DBS on RLS in PD patients.

Methods: This study included 59 PD patients (32 male, 54.2%). Patients were detected for RLS before and on the sixth month of the STN DBS according the International Restless Legs Syndrome Study Group criteria and patients fulfilled the four essential criteria accepted as RLS. The severity of clinical symptoms were measured using Unified Parkinson’s Disease Rating Scale (UPDRS) II and III; and dopaminergic treatment dosage calculated as levodopa equivalent dose (LED).

Results: The mean age was 53.93±10.06 and the mean disease duration was 14.09±6.88 years. Thirty-two (54.2%) and 18 (30.5%) patients were noted for having RLS before and after STN DBS. Fourteen patients reported significant improvement of their RLS symptoms (p<0.001), and recently developed RLS was not detected. After STN DBS mean 55.15%; 57.55%; and 50.02% reduction found on UPDRS part II; III scores, and LED respectively.

Conclusions: Our findings indicated that notable improvement of RLS reported by nearly half of PD patients after STN DBS.

Disclosure: Nothing to disclose
EP1140
The study of oxidative status and mitochondria functionality in human neuronal models of pantothenate kinase associated neurodegeneration
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Introduction: Pantothenate Kinase-Associated Neurodegeneration (PKAN) is an early onset autosomal recessive movement disorder, caused by mutations in the Pantothenate Kinase-2 (PANK2) gene that encodes a mitochondrial enzyme involved in Coenzyme A synthesis. The pathology is hallmarked by severe iron accumulation in the brain. Our previous results on patient’s fibroblasts suggested that Pank2 deficiency promotes an increased oxidative status further enhanced by the addition of iron. To clarify the molecular mechanism leading to iron homeostasis dysfunction in more suitable models of disease, we developed and characterized new human neuronal models obtained by patients fibroblast’s direct reprogramming.
Methods: Primary skin fibroblasts from three PKAN patients and three unaffected subjects were infected with lentivirus carrying the three-transcription factors Mash1, Nurr1 and Lmx1a to obtain induced neurons (iNs). They were evaluated for radical oxygen species (ROS), mitochondrial functionality and glutathione measurements by specific fluorescence probes at single cell level. 
Results: The efficiency of fibroblasts reprogramming was around 5%, as identified by the expression of TuJ1, Tyrosine hydroxylase and N-CAM neuronal markers. In basal condition, PKAN iNs showed an increase in ROS level, about 50% higher respect to the iNs from healthy subjects. The reduced form of glutathione resulted decreased by about 15% in PKAN iNs compared to controls. Evaluation of TMRM signal indicated that the mitochondrial membrane potential is not affected in PKAN iNs. 
Conclusions: The data indicated that neurons can be reprogrammed from PKAN fibroblasts. They partially confirmed the results obtained in fibroblasts, indicating an altered oxidative status probably due to iron mishandling.
Disclosure: Nothing to disclose

EP1141
Pallidal deep brain stimulation in the treatment of Huntington’s chorea
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Background: Stereotactic lesions have been occasionally performed in Huntington’s chorea since the dawn of functional stereotactic surgery, however, with modest results. Despite the success of deep brain stimulation (DBS) in surgical treatment of Parkinson’s disease and dystonia, the interest of testing DBS in Huntington’s Disease (HD) has been limited. So far, promising results of pallidal DBS in 7 patients with HD have been reported in the literature.
Objectives: To present the results of pallidal DBS in a patient with HD.
Methods: A 59-year-old woman with HD since 12 years and severe motor symptoms was implanted bilaterally in the Globus pallidus internus. The patient was evaluated at 12 months after surgery.
Results: The effect of DBS was deemed satisfactory concerning the patient’s choreo/dystonic symptoms. The improvement according to the unified Huntington’s disease rating scale was modest, with a score reduction from 92 before surgery to 81 at one year.
Conclusions: The results of pallidal DBS were deemed satisfactory in the patient presented here, confirming previous reports of the role of DBS in HD. However, further randomized studies are needed to ascertain the role of DBS in HD, especially considering the progressive nature of the disease.
Disclosure: Nothing to disclose