Movement disorders 1

P1459 COMPARATIVE ANALYSIS OF USE OF LONG ACTING DOPAMINE AGONISTS IN CURRENT CLINICAL PRACTICE: ONGOING SURVEY ACROSS EUROPE

A. Rizos¹, G. Durner¹, A. Martin¹, B. Kessel², T. Henriksen³, A. Antonini⁴, P. Odin⁵, C. Falup-Pecurariu⁶, P. Martinez-Martin⁷, P. Reddy⁷, Y. Naidu¹⁸, S. Gay¹¹, K. Ray-Chaudhuri¹,¹⁹, EUROPAR ¹King’s College Hospital, London, ²Princess Royal University Hospital, Orpington, UK, ³Bispebjerg Hospital, Copenhagen, Denmark, ⁴IRCCS San Camillo Venice and University of Padua, Venice, Italy, ⁵Klinikum Renkenheide, Bremerhaven, Germany, ⁶University Hospital, Lund, Sweden, ⁷University Hospital, Brasov, Romania, ⁸Carlos III Institute of Health, ⁹Alzheimer Center Reina Sofia Foundation, Madrid, Spain, ¹⁰University Hospital Lewisham, ¹¹St. Thomas’s Hospital, London, UK

Aims: To address comparative tolerability/retention rates (RR) (minimum 6 months use) of longer acting dopamine agonists (DA, rotigotine skin patch (RTG), ropinirole (ROP) and pramipexole (PPX) extended release) in a European real life population base (target=500).

Methods: Retrospective/prospective case note survey of cases initiated on DA using audit based questionnaire.

Results: 143 cases reviewed currently (mean age 67.9yrs (range 42-89), 29.3%≥75yrs age, mean duration of disease 8.9yrs (range 0.6-25yrs)). RTG used in 64 (average dose 9.87mg), ROP XL (n=27, 12.7mg), PPX SR (n=21, 2.5mg) with RR of 89% for RTG, 89% for ROP XL and 100% for PPX SR (numbers on ROP and PPX are currently low). Average maintenance period on RTG is 27 months (max 48) with average period to discontinuation=16 months (max 47), (number on ROP and PPX are yet too low for averaged maintenance data). In old PD (≥75yrs), 12 RTG, 8 ROP XL and 5 PPX SR continue with no intolerance. 15.3% of the 143 evaluated cases report successful tolerability of 2 or more DAs, while 9 cases (6.3%) of impulse control disorders (ICD) are reported, all in cases exposed to immediate release preparations. In 2, ICDS have attenuated when switched to RTG. 17 cases with dysphagia/dribbling tolerated RTG.

Conclusions: This ongoing survey reveals a good tolerability rate of all longer acting DAs particularly in older (≥75yrs) PD including dual agonist use. RTG use is particularly tolerated in those with swallowing difficulties. ICD rates are low and in some, reversal is reported after switching to RTG.

P1460 TWO-YEAR, PLACEBO-CONTROLLED SAFETY AND TOLERABILITY DATA FOR SAFINAMIDE AS ADD-ON TO L-DOPA IN PATIENTS WITH PARKINSON’S DISEASE

C. Meshram¹, R. Borgohain², M. Bhatt³, D. Chirilău⁴, F. Stocchi⁵, V. Lucini⁶, R. Giuliani⁷, R. Anand⁸, for the Study 018 Investigators ¹Brain and Mind Institute, Napoli, ²Nizam’s Institute of Medical Sciences, Hyderabad, ³Jaslok Hospital & Research Centre, Mumbai, India, ⁴Timisoara University of Medicine and Pharmacy, Timiso, Romania, ⁵IRCCS San Raffaele, Rome, ⁶Newron Pharmaceuticals SpA, Bresso, Italy, ⁷APC AG, St Moritz, Switzerland

Objective: To evaluate the long-term safety and tolerability of safinamide as add-on to L-dopa in patients with Parkinson’s disease (PD) and motor fluctuations.

Methods: Study 018 was an 18-month, double-blind, placebo-controlled extension to Study 016, which evaluated 6 months’ treatment with safinamide (50 or 100mg/day) as add-on to L-dopa. Patients continued with existing PD therapies (except MAO-B inhibitors). Safety and tolerability were assessed using adverse events (AEs), laboratory, vital sign, ophthalmological and ECG data.

Results: 544 of the 669 patients in Study 016 entered Study 018; ~80% in all groups completed the extension. Discontinuations due to AEs, serious AEs and deaths over 2 years were similar between placebo and safinamide 50mg/day, and slightly higher with safinamide 100mg/day (Table). The most common newly emergent AEs during Study 018 were PD, dyskinesia and cataract (Figure). There were no clinically relevant differences in other assessments among groups.

Conclusions: This is the first 2-year, prospective, placebo-controlled study in patients with mid-to-late PD. Completion rates were high and no new safety concerns emerged with either dose of safinamide in this extension study.

Study supported by: Newron/Merck Serono S.A. - Geneva

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=222) n (%)</th>
<th>Safinamide 50mg/day (N=223) n (%)</th>
<th>Safinamide 100mg/day (N=224) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuations due</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>to AEs</td>
<td>23 (10.4)</td>
<td>20 (9.0)</td>
<td>30 (13.4)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>37 (16.7)</td>
<td>35 (15.7)</td>
<td>45 (20.1)</td>
</tr>
<tr>
<td>Deaths</td>
<td>8 (3.6)</td>
<td>5 (2.2)</td>
<td>12 (5.4)</td>
</tr>
</tbody>
</table>

[Table]
THE TOPOGRAPHY OF BRAIN DAMAGE IN NON-DEMENTED PATIENTS AT DIFFERENT STAGES OF PARKINSON’S DISEASE

M. Filippi1, F. Agosta1, E. Canu1, T. Stojković2, M. Pievani1, A. Tomić2, L. Sarro1, N. Dragašević2, M. Copetti1, G. Comi4, V.S. Kostić2
1Neuroimaging Research Unit, Institute of Experimental Neurology, Scientific Institute and University HSR, Milan, Italy
2Department of Neurology, School of Medicine, University of Belgrade, Belgrade, Serbia
3Biostatistics Unit, IRCCS-Ospedale Casa Sollievo della Sofferenza, Foggia, Italy
4Department of Neurology, INSPE, Division of Neuroscience, Scientific Institute and University Ospedale San Raffaele, Milan, Italy

Objective: To investigate the patterns of grey matter (GM) loss and white matter (WM) tract damage in patients at different clinical stages of Parkinson’s disease (PD).

Methods: 89 non-demented PD patients and 42 healthy subjects were studied. PD patients were stratified according to the Hoehn and Yahr stage score (17 early, 46 mild, 14 moderate, and 12 severe). GM atrophy was assessed using voxel-based morphometry. Tract-based spatial statistics was used to investigate WM damage.

Results: GM atrophy involving limbic and neocortical areas was detected in patients with early PD and was found to be more severe in more advanced stages. In early PD cases, the picture of WM damage was dominated by cerebellar involvement. In mild PD patients relative to early cases, WM damage involved the brainstem, basal ganglia-thalamo-cortical pathways, olfactory tracts, as well as temporal and frontal WM. The most marked and distributed pattern of WM damage was found in patients with moderate PD compared with mild cases, and included interhemispheric, limbic, and the majority of cortico-cortical association tracts. In severe PD cases, limbic tracts and cerebellar WM showed a greater damage than in moderate cases.

Conclusions: GM and WM abnormalities beyond the nigrostriatal system seem to accumulate with increasing PD severity and are likely to contribute to the more severe dysfunction of motor and non-motor systems known to occur in patients at the later stages of the disease. This study shows the promise of structural and DT MRI techniques to achieve an in vivo staging of PD.

NON-MOTOR SYMPTOMS AMONG YOUNG-ONSET PARKINSON’S DISEASE PATIENTS

V. Markovic, M. Svetel, T. Stojkovic, A. Tomic, M. Jecmenica Lukic, I. Petrovic, V. Kostic
Clinic for Neurology, School of Medicine, University of Belgrade, Belgrade, Serbia

Background: Patients with young-onset Parkinson’s disease (YOPD) have dystonia more often and are prone to develop motor complications earlier, but cognitive deficits and dementia later. Relationship of age at onset to other non-motor symptoms is less well defined.

Objective: To compare prevalence of different non-motor symptoms in patients with YOPD and late-onset Parkinson’s disease (LOPD).

Methods: We compared 100 patients with YOPD (symptom onset 21-45 yrs) and 100 patients with LOPD (symptom onset after 55 yrs), mean age at onset 40.57±4.945 and 62.19±5.304 respectively. Patients were matched for sex and disease severity based on Hoehn&Yahr stadium and UPDRS part III examination. Data on non-motor symptoms were collected through structured interview.

Results: Levodopa equivalent dose did not differ among YOPD and LOPD patients (649.94±355.759 vs. 611.84±257.803mg/day). YOPD patients experienced hallucinations after significantly longer disease duration than their older counterparts (143.04±69.783 vs. 98.50±54.271 months, p=0.009). Vivid dreams occurred twice as often in LOPD (25%) than in YOPD (12%). There was no difference in the presence of other sleep problems with insomnia in 38% of YOPD and 47% of LOPD patients (p=0.198) and excessive daytime sleepiness in about one fifth of patients in both groups. Autonomic dysfunction was reported more often by LOPD patients (gastrointestinal dysfunction 84% vs. 68% in YOPD; urinary disturbance in 66% vs. 52% in YOPD and sexual dysfunction in 59% vs. 43% YOPD).

Conclusion: Non-motor symptoms are common among YOPD patients and must not be overlooked especially considering their development in the most productive age of life.
P1463

HUNTINGTON’S DISEASE ITALIAN TRIAL IN NEURO-TRANSPLANTATION: UPDATE ON A GROUP OF 15 PATIENTS

E. Ghelli1, A.M. Romoli1, D. Paolini1, C. Mechi1, V. Berti2, M. Paganini1, P. Gallina2, G. Vannelli4, M.T. De Cristofaro2, S. Piacentini1, N. Di Lorenzo3, S. Sorbi1

1Department of Neurological and Psychiatric Sciences, 2Department of Nuclear Medicine, 3Department of Neurosurgery, 4Department of Human Anatomy, AOUC, Florence, Italy

Introduction: Neuroblast transplantation has been recently explored as therapeutic chance in Huntington’s disease (HD). At the University of Florence, we performed, during the last six years, human foetal striatum transplantations (HFST) in 15 patients, according to the surgical and clinical protocol previously reported.

Methods: Standard procedure (Bachoud-Lévy, 2000) was applied to the first six procedures (3 pt.), the remaining grafts were performed by a double approach refinement. 16 HD patients were enrolled in the control group. Patients underwent Unified HD Rating Scale (UHDRS), neuropsychological, psychiatric battery and performed regular MRI and 18F-FDG PET exams.

Results: 15 patients underwent procedures bilaterally, follow-up ranged between six months and five years. Gender ratio of the patients was 5F/10M, mean age was 50 yrs (±7.72), the age at the disease onset was 39 yrs (±8.41), mean duration of illness 12.13 yrs (±4.31), mean CAG repeats 48 (±5.48). Demographic, genetic and clinical features of the control group were comparable to those of the patients. Although the test scores did not show any objective improvement in cognitive and behaviour pattern, a subjective improvement was noted by patients, families and medical staff. Longitudinal 18F-FDG PET analyses showed a significant metabolic improvement in the grafted striatum of treated HD patients (p<0.05), associated with a slight and diffuse increment, or at least stability of metabolic activity in the cortex.

Conclusions: The HFST was feasible and safe. The evaluation of the HFST as symptomatic treatment is still under debate, our data showed some improvement in the clinical course.

P1464

COMPARISON OF PERIPAPILLARY RETINAL NERVE FIBER LAYER THICKNESS IN PATIENTS WITH PARKINSON’S DISEASE; CARRIERS AND NON-CARRIERS OF MUTATIONS IN THE LRRK2 OR GBA GENES

T. Gurevich1.2.3, H. Shabtai1.2, E. Naftaliev4, M. Neudorfer5, Y. Balash1.3.6, A. Rosenberg3.7, A. Mirelman1.2.6, A. Bar Shira4, Z. Gan Or1.8, A. Orr-Utregler1.8, A. Kesler1.4.5, N. Giladi1.2.3

1Department of Neurology, 2Movement Disorders Unit, Tel Aviv Sourasky Medical Center, 3Sackler School of Medicine, Tel Aviv University, 4Neurophtalmology Unit, 5Department of Ophthalmology, 6Movement Disorders Unit, Department of Neurology, Tel Aviv Sourasky Medical Center, 7School of Health Professions, Faculty of Medicine, Tel Aviv University, 8Genetic Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Background: Thinning of retinal nerve fibre layer (RNFL) has been shown in Parkinson’s disease (PD). The effect of genetic status on RNFL thickness in PD patients with and without mutations in the LRRK2 or GBA genes has never been reported.

Objective: Quantitative assessment and comparison of RNFL in PD with different genotypes.

Methods: Mean peripapillary RNFL thickness of 9 eyes of 5 PD patients, LRRK2 G2019S mutation carriers (mean H&Y stage 2.4; age 61.8±9.2 years; mean PD duration 7 years) was compared to 13 eyes of PD patients - carriers of GBA mutations (mean H&Y stage 2; age 53.1±3.9; disease duration 6 years), 27 eyes of PD patients without these mutations (PD-Nom) (mean H&Y stage 2; age 55.6±9.7; disease duration 5 years), 27 eyes of healthy controls (age 66.6±11.2). The thickness was acquired using optical coherence tomography (Startus OCT 3) according to fast RNFL protocol. In each eye, average RNFL thickness measurements were obtained in temporal, superior, nasal, and inferior quadrants.

Results: Mean RNFL thickness was reduced in PD-LRRK2 and PD-Nom in comparison to controls (85.6±23.6µm, 89.6±10.2µm vs. 95.3±9.9µm, respectively). In PD-GBA patients, average RNFL thickness was reduced slightly with no significant differences from controls. Age and disease duration had no effect on the RNFL thickness.

Conclusions: Differences in RNFL thickness were found in PD with different genotypes. PD carriers of the LRRK2 G2019S mutation demonstrated the lowest RNFL thickness. Further studies in larger cohorts of patients are needed to confirm these findings.
P1465

VOLUNTARY, SPONTANEOUS, AND REFLEX BLINKING IN PARKINSON’S DISEASE: THE EFFECTS OF MEDICATION AND SUBTHALAMIC NUCLEUS STIMULATION.

M. Bologna, A. Fasano, N. Modugno, A. Berardelli
Sapienza University of Rome, Roma, Italy

Objective: To evaluate the effects of subthalamic nucleus stimulation (STN-DBS) and L-dopa on the kinematics of voluntary, spontaneous and reflex blinking in patients with Parkinson’s disease (PD).

Background: STN-DBS have proved to be an effective therapy in PD patients. However, it is unknown whether STN-DBS alone, or in combination with L-dopa, modify voluntary spontaneous and reflex blinking in PD patients.

Methods: 10 PD patients were studied in four experimental conditions: OFF treatment, STN-DBS ON, STN-DBS plus L-dopa and L-dopa alone. Patients were asked to blink voluntarily as fast as possible; spontaneous blinking was recorded during two 60s rest periods; reflex blinking was evoked by electrical stimulation of the supraorbital nerve. Eyelid movements were recorded with the SMART analyzer motion system.

Results: STN-DBS ON increased the peak velocities and amplitudes, for both the closing and opening voluntary blink phases and prolonged the duration of the pause, the neurophysiological marker of switching processes between the closing and opening blink phases. L-dopa had no effects on the kinematics of voluntary blinking and reverted the changes induced by STN-DBS when the two therapies were combined. No significant differences were observed in the four experimental conditions on the kinematics of spontaneous and reflex blinking.

Conclusions: The STN-DBS in PD patients modifies the kinematics of the closing and opening voluntary blink phases and impairs the switching between them. These findings are in line with emerging evidence suggesting a variety of favourable and detrimental effects induced by STN DBS.

P1466

TWO-MINUTE VOCAL TEST AND ACOUSTIC ANALYSIS REVEAL VOICE AND SPEECH DISORDERS IN EARLY UNTREATED PARKINSON’S DISEASE

J. Rusz1,2, R. Cmejla1, H. Ruzickova2, J. Klempt2, V. Majerova2, J. Piamusi2, J. Roth2, E. Ruzicka2
1Czech Technical University in Prague, Faculty of Electrical Engineering, Department of Circuit Theory, 2Charles University in Prague, First Faculty of Medicine, Department of Neurology and Centre of Clinical Neuroscience, Prague, Czech Republic

Background: The disorders of voice and speech in Parkinson’s disease (PD) result from the involvement of several subsystems including respiration, phonation, articulation, and prosody. We have designed a quick vocal test consisting of sustained phonation, diadochokinetic task, and running speech, and assessed its performance in separating PD patients from healthy controls (HC).

Methods: 24 untreated patients with recently diagnosed PD and 22 age-matched HC were tested. In total, 116 vocal recordings were collected and the voice parameters were obtained using 11 measurements designed with the possibility of automatic extraction in a common acoustic environment. Subsequently, a predictive model was built using kernel support vector machine to find the best combination of measurement to differentiate PD from HC subjects.

Results: Significant differences between both groups were found in 10 out of 11 measurements. The best classification performance of 85.02% was reached in a combination of four measures that represent all PD-related speech subsystems, including the ability to maintain sound pressure level, noise-to-harmonics ratio, accuracy of articulation, and melody variations. Reduced melody in running speech appeared essential in characterizing the vocal impairment in PD. In addition, correlations were found between the measures of articulation and phonation, and subscores of bradykinesia and rigidity.

Conclusions: Our designed configuration of acoustic vocal tests can detect abnormalities of speech since the early untreated stages of PD. Thus, these tests can ease the clinical assessment of voice and speech disorders, and serve as measures of clinical progression as well as in the monitoring of treatment effects.
P1467

WEIGHT GAIN IN PATIENTS WITH PARKINSON’S DISEASE AFTER SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION: IMPROVED TASTE SENSATION DRIVING INCREASED APPETITE AS A MECHANISM?

K. Li1, J. Kausar1, R. Mitchell1, H. Pall1,2,3
1Department of Neurosciences, Queen Elizabeth Hospital Birmingham, 2School of Clinical and Experimental Medicine, 3College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

Deep brain stimulation (DBS) in the subthalamic nucleus (STN) is an effective surgical treatment for the disabling motor complications of Parkinson’s disease (PD). A proportion of patients markedly gain weight following STN DBS therapy. The mechanism for this is unknown. Hypotheses include decreased energy expenditure because of a reduction in dyskinesia and alterations of appetite secondary to mood changes. There has been limited data suggesting that olfaction is better in patients with PD who have had DBS compared to those medically treated alone. Given that gustation and olfaction are intertwined such that most of what we taste is actually an olfactory experience, we hypothesise that improved taste sensation may drive appetite and hence weight gain following DBS.

Methods: Amongst patients who have undergone STN DBS in our unit, a random selection was asked whether or not their taste sensation had changed following surgery. Weight at minimum 12 months follow-up was compared to pre-operative weight.

Results: 21 of 105 patients were randomly selected. All 21 gained weight. 13 (62%) gained >3kg and 8 (38%) ≤3kg. All those who gained >3kg had in fact gained >10kg and all reported an improvement in taste sensation not reported by the others.

Conclusion: Although the number of patients is small, the difference in taste improvement in the group gaining >3kg weight compared with controls (13/13 versus 0/8) is striking. We thus propose that improvement in the taste of food may be a driver to increased appetite and hence weight gain following STN DBS.

P1468

THE PROFILE OF CSF NEURODEGENERATIVE MARKERS IN DIFFERENT PHENOTYPES OF PARKINSON’S DISEASE

H. Přikrylová Vranová1, J. Mareš1, P. Hluštík1, M. Nevrý1, D. Stejska1, J. Zapletalová1, R. Obereignerů1, P. Kaňovský1
1Department of Neurology, 2Department of Biochemistry, 3Department of Medical Biophysics, Faculty of Medicine and Dentistry, Palacky University in Olomouc, and University Hospital Olomouc, 4Department of Psychology, Philosophical Faculty, Palacky University in Olomouc, Olomouc, Czech Republic

Background and objective: The clinical manifestation of Parkinson’s disease (PD) is very heterogeneous, which inspired many attempts to divide PD patients into clinical subgroups. This could lead to a better recognition of pathogenesis, improving targeted treatment and prognosis in PD patients. The aim of the present study was to obtain CSF samples in PD patients and to search for a relationship between neurodegenerative CSF markers (tau protein, beta-amyloid 1-42 and index tau/beta) and the clinical subtypes.

Methods: PD patients were divided into three subgroups - early disease onset (EDO), tremor-dominant PD (TD) and non-tremor dominant PD (NT) according to previously published classification. Neurodegenerative markers in the CSF were assessed in these three groups of patients suffering from PD (EDO-17, TD-15, NT-16 patients) and in a control group (CG) of 19 patients suffering from non-degenerative neurological diseases.

Results: The NT-PD patients were found to have significantly higher levels of CSF tau protein and index tau/beta than the control subjects and also than other parkinsonian subgroups.

Conclusion: In the context of more rapid clinical progression and more pronounced neuropathological changes in the NT-PD patient group, our results corroborate the opinion that CSF level of tau protein may be regarded as a potential laboratory marker of the presence and severity of neurodegeneration.
P1469

NEUROPSYCHOLOGICAL PROFILE IN ATYPICAL PARKINSONIAN SYNDROMES

K. Farnikova¹, P. Kanovsky², J. Prasko³, R. Obereigneru¹
¹Department of Neurology, ²Department of Psychiatry, Palacky University Medical School, University Hospital, Olomouc, ³Department of Psychology, Palacky University, Philosophical Faculty, Olomouc, Czech Republic

Objectives: The aim of this study was to investigate psychological and psychiatric characteristics of atypical parkinsonian syndromes (PDD, DLBD, PSP, CBS).

Background: Psychological and psychiatric disturbances are one of the core features of atypical parkinsonian syndromes.

Methods: 45 consecutive patients who fulfilled the criteria of "clinically possible" or "clinically probable" PDD, DLBD, PSP or CBS underwent detailed neurological, psychological and psychiatric examination with focus on the fluctuations in attention and cognition, visual hallucinations, anxiety, apathy, depression and obsessive-compulsive behaviour and the presence of possible language or speech disorders.

Results: In the PDD/DLBD group all patients exhibited disturbances in attention, dysexecutive syndrome and the impairment of visuospatial functioning. Memory impairment tends to be mild. Depression, anxiety or apathy was less common. Visual hallucinations were present in 100% patients of DLBD group and in 60% PDD group. Behavioural disorders were common in both PSP/CBS groups. CBS patients showed more expressed visuospatial impairment, aphasia and apraxia, while in the PSP group were cognition disorder and dysexecutive syndrome present. Memory complaints were usually mild. There were no patients with hallucinations or compulsive-obsessive disorder.

Conclusions: The results of this study suggest that not only motor signs but neuropsychological and neuropsychiatric features as well reflected an underlying neuropathological process in atypical parkinsonian syndromes; therefore they may be a useful tool in the differential diagnosis of individual "parkinsonism-dementia" syndromes.

P1470

A NOVEL BIOMARKER, ACONITASE 2, FOR HUNTINGTON'S DISEASE

C.-M. Chen, Y.-R. Wu
Neurology, Chang Gung Memorial Hospital, Taipei, Taiwan R.O.C.

Objectives: To investigate the proteome profile in the striatum of the Hdh(CAG)150 knock-in mice modelling an early human Huntington’s disease (HD) stage to reveal the potential therapeutic targets and biomarkers.

Background: HD is caused by an unstable CAG trinucleotide repeat expansion encoding a polyglutamine tract in the huntingtin protein. As yet, there is no valid biomarker and effective treatments for HD.

Methods: We used two-dimensional electrophoresis (2-DE) and mass spectrometry analysis (MS) to analyze the proteome profiles in the striatum of the Hdh(CAG)150 knock-in mice at 16 months of age. We then examined if the results can be also seen in another HD mouse model and HD patients’ peripheral blood.

Results: We identified eight differentially-expressed proteins that are involved in metabolic/mitochondrial pathways, oxidative stress response, and cytoskeleton regulation. Among them, reduction of aconitase 2 (Aco2) level and activity was validated in both Hdh(CAG)150 and the transgenic HD mice (R6/2) using western blot analysis and enzyme assay, respectively. Decreased Aco2 activity was found in the peripheral blood mononuclear cells (PBMC) of both HD patients and pre-symptomatic HD mutation carriers, while the decreased Aco2 protein level in PBMC was only present in HD patients. Aco2 activity correlated significantly with motor score, independence scale and functional capacity of the Unified Huntington’s Disease Rating Scale as well as disease duration.

Conclusions: Our study provides a novel effective biomarker to assess the disease status of HD patients and pre-symptomatic HD mutation carriers, and probably to test the efficacy of the future therapeutic strategies.
P1471
HIGH PREVALENCE AND REDUCED PENETRANCE OF LRRK2 G2019S MUTATION IN PARKINSON'S DISEASE PATIENTS FROM CANTABRIA
J. Infante, M. Sierra, I. González-Aramburu, P. Sánchez-Juan, J. Berciano, O. Combarros
Neurology, University Hospital Marqués de Valdecilla, Santander, Spain

Introduction: The frequency and penetrance of LRRK2 G2019S mutation varies considerably in different Parkinson’s disease (PD) populations, this information being essential both for clinical purposes and genetic counselling.

Objective: To estimate the prevalence and penetrance of the G2019S mutation of the LRRK2 gene in a small region in Northern Spain (Cantabria).

Methods: We tested 355 consecutive patients with PD attended as outpatients at the Neurology department of the University Hospital Marqués de Valdecilla, in Santander, for the G2019S mutation. Taqman probes were used for genotyping. 183 family members of G2019S carriers were also investigated for G2019S mutation and disease status. The gene penetrance was estimated in terms of cumulative age-specific incidence of PD by the Kaplan-Meier method. Proband subjects were excluded from the analysis. In order to increase the sample size for penetrance estimation we considered as putative carriers both parents of G2019S homozygous carriers and one proband parent for each family when reliable information about both parents was available.

Results: 32 PD patients (9%) carried the G2019S mutation (44% sporadic, 56% familial). Penetrance estimation of the G2019S mutation was 3% at 50 years, 13% at 60 years, 30% at 70 years and 52% at 80 years.

Conclusion: The frequency of the G2019S mutation of the LRRK2 gene in PD patients from Cantabria is among the highest reported so far after North African Arabs and Ashkenazi Jewish. At the age of 70 just one out of 3 G2019S mutation carriers manifests motor symptoms of PD.

P1472
COST ANALYSIS OF DEEP BRAIN STIMULATION, APO MORPHINE INFUSION PUMPS AND CONTINUOUS DUODENAL LEVODOPA-CARBIDOPA INFUSION IN PATIENTS WITH ADVANCED PARKINSON'S DISEASE IN SPAIN: SCOPE STUDY
F. Valldeoriola1, J. Puig-Junoy2, R. Puig-Peiró2,3, P. González4, Workgroup of the SCOPE Study
1Neurology Services; Movement Disorders Unit, Hospital Clinic i Provincial, 2Centre de Recerca en Economia i Salut, Pompeu Fabra University, Barcelona, Spain, 3Office of Health Economics, London, UK, 4Health Economics & Reimbursement Dept, Medtronic Iberica SA, Madrid, Spain

Introduction: Three therapeutic options exist for Advanced Parkinson’s Disease (APD): Deep Brain Stimulation (DBS), Continuous Duodenal Levodopa-Carbidopa Infusion (CDLCI) and Continuous Subcutaneous Infusion of Apomorphine (CSIA). This is the first economic analysis to compare the costs of the three therapies, offering payers and physicians useful information to support the decision making in APD.

Methods: Healthcare resources consumption associated with each therapy was elicited with a Healthcare Resources Questionnaire (HRQ) that was completed by a panel of 11 APD experts. A micro-costing approach was used. The average total cost (Euro-Spain 2010) was obtained for each of the therapies for a 5-year period.

Results: Mean cumulative cost per patient was €88,014±2,580, €141,393±9,945 and €233,986±10,552, respectively for DBS, CSIA and CDLCI (p<0.0001), over the 5-year period. Starting from year two, DBS is associated with lowest cumulative costs compared with CDLCI and CSIA. The yearly average cost of DBS was €17,603, compared to €46,797 (p=0.001) for CDLCI and €28,279 for CSIA (p=0.008). For DBS, the initial investment (32.2% of the total 5-year costs) was offset by decreases in antiparkinsonian pharmacological treatment and follow-up costs. CDLCI and CSIA required a constant use of drugs, which represented 95% of their total cost over five years.

Conclusions: The initial investment for DBS is compensated by the reduction in the consumption of other healthcare resources by patients over the years. For every patient yearly treated with CDLCI, two patients could be treated with DBS (€29,194 saved) and for every patient treated with CSIA, €10,676 could be saved.
P1473

A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED, CROSSOVER PILOT STUDY OF THE SAFETY AND SHORT-TERM ANTISIALORRHEIC EFFICACY OF MULTIPLE DOSES OF INTRA-ORAL TROPICAMIDE FILMS IN PARKINSON’S DISEASE

S. Perez-Lloret1, G. Nano2, D. Katzman3, A. Carrosella2, E. Gamzu3, M. Merello2
1University Paul Sabatier, Toulouse, France, 2FLENI, Buenos Aires, Argentina, 3NeuroHealing, Boston, MA, USA

Background: Sialorrhea is a common non-motor symptom in Parkinson’s Disease (PD). Short-acting antimuscarinic, such as tropicamide, may reduce saliva secretion without the side effects associated with long-acting antimuscarinics.

Objective: To explore the anti-sialorrhea effect of single doses of tropicamide administered in a slow dissolving, muco-adhesive, intra-oral thin film.

Methods: 19 PD patients who complained of sialorrhea received 3 doses (0.3, 1, 3mg) of tropicamide and placebo delivered in a muco-adhesive film, in random order, separated by at least 7 days. A 10-cm visual analogue scale (VAS) was used to measure the patients’ subjective assessment of saliva levels, at baseline and at 15, 30, 45, 90 and 120min after treatment administration. For the last 7 patients, saliva volume was measured at baseline and 75min after treatment by weighing cotton rolls placed into buccal cavity for 5 minutes. Vital signs were monitored and ECGs were performed.

Results: The mean age of the patients was 67±12 years, 78% were males. Median disease duration=8 years. VAS score differences (baseline to 120min) were -0.55±0.54, -1.08±0.54, -1.53±0.52 and -0.81±0.51 for placebo and 0.3, 1 and 3mg tropicamide, respectively. While treatment effects were non-significant (F=0.6 p=0.6, ANOVA), the 1mg tropicamide resulted in a significant decrease in the VAS score. Saliva volume was reduced by 11-33% after tropicamide vs. 5% with placebo (p=0.3, Friedman). No adverse events were detected.

Conclusion: Results of this pilot, proof-of-concept study show that NH004 was safe and exerted effects worthy of further exploration as a possible treatment for sialorrhea in PD.

P1474

AN OPEN-LABEL STUDY TO ASSESS THE LONG-TERM EFFECTS OF RASAGILINE ON CUMULATIVE DISABILITY IN PARKINSON’S DISEASE: DESIGN AND BASELINE DATA FROM THE ADAGIO FOLLOW-UP STUDY

F. Stocchi1, R.A. Hauser2, C.W. Olanow3, O. Rascol4
1Department of Neurology, Institute for Research and Medical Care IRCCS, Rome, Italy, 2Department of Neurology, Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL, 3Department of Neurology, Mount Sinai School of Medicine, New York, NY, USA, 4Department of Clinical Pharmacology, Faculty of Medicine, Toulouse University Hospital, Toulouse, France

Introduction: The 18-month ADAGIO delayed-start study demonstrated that rasagiline 1mg/day slows progression of clinical symptoms as measured by deterioration in total-UPDRS scores. The aim of the ADAGIO Follow-Up (AFU) study is to assess whether the effect of early-start rasagiline treatment provides long-term benefits over delayed-start as well as to investigate the long-term effects of rasagiline.

Methods: Ongoing open-label, 2-year follow-up of subjects who entered the active phase of ADAGIO. AFU subjects continue to receive rasagiline 1mg/day; patients who stop treatment will be followed until study end. Main outcomes are the emergence of unsteady gait and balance impairment, falls, freezing of gait and cognitive decline. Functional decline, QoL; and time to additional treatment are also assessed.

Results: 683 subjects have been enrolled (58% of ADAGIO ITT population & 75% of active phase completers) and all retain a diagnosis of PD. Baseline characteristics of AFU population at ADAGIO start are representative of the original ADAGIO population. The mean time from PD diagnosis to AFU study is 46.9 months. Due to the need for re-enrolment, there was a short gap (mean 26; range 16-39 months) between the end of ADAGIO and the start of the AFU study; 88% subjects were maintained on rasagiline during this period. At AFU baseline, 32% of subjects remain on rasagiline monotherapy and the rest are receiving additional dopaminergic medications.

Conclusions: The AFU study includes the majority of subjects from ADAGIO and will extend understanding of the effects of rasagiline on long-term patient functionality.
P1475

DE NOVO DOPAMINE DYSREGULATION SYNDROME AFTER SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION: REPORT OF THREE CASES
B. De la Casa-Fages, F. Grandas
Movement Disorders Research Unit, Hospital General Universitario Gregorio Marañon, Madrid, Spain

Introduction: The relationship between subthalamic nucleus deep brain stimulation (STN-DBS) and dopamine dysregulation syndrome (DDS) in patients with Parkinson’s disease (PD) remains unclear. DBS may improve, worsen or not affect preoperative DDS. Furthermore, de novo DDS may appear after STN-DBS.

Objective: To report three PD patients who developed DDS after STN-DBS.

Patients and methods: We identified three Parkinson’s disease patients who fulfilled dopamine dysregulation syndrome criteria for the first time within one year after STN-DBS surgery.

Results: 1 woman and 2 men aged between 45 and 59 years underwent STN-DBS for a PD complicated with motor fluctuations. They had no psychiatric or substance abuse history except depression in 1 patient. No cognitive decline was present before surgery. They had motor improvement as expected after DBS of the sensorimotor part of the STN and antiparkinsonian drugs were consequently reduced. Electrodes were well located in STN as postoperative MRI showed. DDS appeared between two weeks and three months after surgery. Antiparkinsonian drugs overused were levodopa, subcutaneous apomorphine and pramipexole. One patient developed also binge eating. Another patient had hypersexuality and compulsive coke drinking. All patients justified their overuse of drugs to avoid anxiety, dysphoria and other non-motor symptoms. Reduction or even withdrawal of dopamine agonists or levodopa, addition of antidepressants or quetiapine and adjustments of stimulation parameters induced a mild improvement of their behaviour.

Conclusions:
· DDS may be a complication of STN-DBS, perhaps related to the combination of stimulation of limbic STN area plus dopaminergic medication in vulnerable patients.
· Postoperative DDS has poor prognosis.

P1476

CLINICAL OUTCOME OF WILSON’S DISEASE PATIENTS DIAGNOSED BY FAMILY SCREENING
K. Dzieżyć1, A. Członkowska1,2
1Second Department of Neurology, Institute of Psychiatry and Neurology, 2Department of Clinical and Experimental Pharmacology, Medical University of Warsaw, Warsaw, Poland

Background: Wilson’s disease (WD) is an autosomal recessive inherited disorder of copper metabolism. First degree familial screening should be performed after WD was diagnosed in the proband, because early diagnosis and treatment can prevent symptoms development. The aim of the study was clinical outcome assessment in WD patients diagnosed by family screening who had no previous history of any clinical symptoms.

Methods: We have retrospectively analyzed data of 96 WD patients diagnosed by family screening in our center between 1964 and 2008. We gained information about medical history, physical and neurological examination, laboratory tests at the time of diagnosis and during last follow-up visit. Compliance on anti-copper treatment has been assessed. Clinically asymptomatic patients were defined as having any history of neurological or hepatic symptoms.

Results: 82 out of 96 WD patients diagnosed by family screening had no clinical symptoms, however raised aminotransferases level was present in 77 patients (93.9%) and only 5 subjects (6%) had normal laboratory tests. 61 out of 82 subjects without symptoms were again assessed after the follow-up (median follow-up period: 15 years): 41 (67%) remained without clinical symptoms, 6 (9.8%) had neuropsychiatric symptoms, 7 (11%) hepatic failure and 6 (9.8%) patients died (4 from liver failure, 2 from cancer). All patients who developed symptoms had irregular treatment.

Conclusions: Our observations indicate that anti-copper treatment prevents WD symptoms development in patients clinically asymptomatic at time of diagnosis, providing that there was good compliance to anti-copper therapy. Clinical deterioration is observed after irregular therapy.
P1477

INTERIM RESULTS FROM AN ONGOING, LONG-TERM, OPEN-LABEL, EFFICACY AND SAFETY STUDY OF LEVODOPA/CARBIDOPA INTESTINAL GEL IN PATIENTS WITH PARKINSON’S DISEASE AND SEVERE MOTOR FLUCTUATIONS


1Klinikum-Bremerhaven, Germany and Skane University Hospital, Lund, Sweden, 2Abbott, Weesp, The Netherlands, 3University of Cincinnati Academic Health Center, Cincinnati, OH, 4University of Alabama at Birmingham, Birmingham, AL, 5Cleveland Clinic, Cleveland, OH, 6Abbott, Abbott Park, IL, USA

Introduction: In Parkinson’s disease (PD), pulsatile dopaminergic stimulation may be associated with treatment-related complications. Levodopa/carbidopa intestinal gel (LCIG) is delivered continuously via an intrajejunal percutaneous endoscopic gastrostomy (PEG) tube.

Methods: An open-label, 54-week, international study of individually optimized LCIG therapy is underway in patients with advanced PD and severe motor fluctuations despite optimized therapy. Measures include patient-diary, Unified Parkinson’s Disease Rating Scale (UPDRS), Parkinson’s disease Questionnaire (PDQ-39), and safety.

Results: In this interim analysis, 192 patients received a mean ±SD of 256.7±126.0 days of LCIG via PEG. “Off” time was reduced and “on” time without troublesome dyskinesia (TD) was increased versus baseline.

UPDRS motor scores during “on” time improved from 28.4±12.9 at baseline to 20.9±11.2 and 20.4±11.5 at weeks 24 and 54 (both p<0.001). PDQ-39 summary index improved from 43.2±14.3 to 33.9±17.1 and 34.1±14.6 at weeks 24 and 54 (both p<0.001). Of 168 patients (87.5%) reporting ≥1 AE, the most common were abdominal pain (30.7%), complication of device insertion (21.4%), and procedural pain (17.7%). Serious AEs occurred in 60 (31.3%) subjects. 4 (2.1%) subjects died (none deemed related to LCIG treatment), and 14 (7.3%) discontinued due to AEs.

Conclusions: Interim results show that LCIG produces clinically meaningful long-term improvements and is generally well tolerated in patients with advanced PD and severe motor fluctuations. The most common AEs were related to PEG insertion.

Support: Abbott.
P1478
COMPARISON OF NON-MOTOR EFFECTS OF SUBCUTANEOUS APOMORPHINE INFUSION AND INTRAJEJUNAL LEVODOPA INFUSION IN ADVANCED PARKINSON’S DISEASE

P. Reddy1, P. Martinez-Martin2, A. Antonini3, P. Odin4, A. Martin5, D. Calandrella1, G. Durner4, H. Honig4, T. Henriksen6, A. Rizos5, K.R. Chaudhuri5, EUROPAR, We Acknowledge a Grant from Kings R&D

1Neurosciences and King’s R&D Department, King’s College Hospital, London, UK, 2National Centre of Epidemiology and CIBERNED, Carlos III Institute of Health, Madrid, Spain, 3Neurology, IRCCS San Camillo Venice and University of Padua, Venice, Italy, 4Neurology, Central Hospital Bremerhaven, Germany and Dept. of Neurology, University Hospital, Lund, Sweden, 5Neurology, King’s College Hospital, London, UK, 6Neurology, Central Hospital Bremerhaven, Bremerhaven, Germany

Objective: We compared non-motor effects of intrajejunal levodopa infusion (IJL) and apomorphine infusion (Apo) in PD (H&Y ≥3).

Methods: IJL: 22pts (16 M, mean age: 58.6±9.1 yrs, mean duration of disease: 15.32±5.8 yrs, median H&Y stage: 4). Apo: 17pts (11M, mean age 59.5±11.7 yrs, disease duration 12.05±4 yrs, median HY: 4). Non-motor symptom scale (NMSS) scores and health related quality of life (HRQol/ PDQ-8) collected before therapy and after 6 months.

Results:

<table>
<thead>
<tr>
<th>Domain of NMSS</th>
<th>% of change in Apo group</th>
<th>% of change in IJL group</th>
<th>Effect size in Apo group</th>
<th>Effect size in IJL group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>-41</td>
<td>-82</td>
<td>0.33</td>
<td>0.67</td>
</tr>
<tr>
<td>Sleep/Fatigue</td>
<td>-51</td>
<td>-63</td>
<td>0.99</td>
<td>0.72</td>
</tr>
<tr>
<td>Mood/Apathy</td>
<td>-50</td>
<td>-49</td>
<td>0.58</td>
<td>0.49</td>
</tr>
<tr>
<td>Perception/Hallucination</td>
<td>-59</td>
<td>-54</td>
<td>0.39</td>
<td>0.30</td>
</tr>
<tr>
<td>Attention/Memory</td>
<td>-32</td>
<td>-45</td>
<td>0.43</td>
<td>0.40</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>-40</td>
<td>-62</td>
<td>0.40</td>
<td>0.67</td>
</tr>
<tr>
<td>Urinary</td>
<td>-47</td>
<td>-58</td>
<td>0.56</td>
<td>0.62</td>
</tr>
<tr>
<td>Sexual</td>
<td>-21</td>
<td>-50</td>
<td>0.01</td>
<td>0.48</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>-49</td>
<td>-53</td>
<td>1.18</td>
<td>1.28</td>
</tr>
</tbody>
</table>

[Table 1]

Conclusions: Both Apo and IJL result in robust improvement in HrQol/PDQ-8 with a big effect size. Differential effects however, of Apo and IJL are observed in relation to motor effect, dyskinesias, cardiovascular, gastrointestinal and sleep function.

[Table 2]
P1479
A COHORT OF LATE-STAGE HUNTINGTON’S DISEASE (HD) FROM THE REGISTRY STUDY

M. Coelho, T. Mestre, J.J. Ferreira,
The European HD Network
Department of Neurology, University Hospital Santa Maria, Lisbon, Portugal

Objective: To describe clinical manifestations, medication use and caregivers’ burden in late-stage HD (LS-HD).

Background: Few data are available regarding LS-HD.

Patients and methods: Patients were extracted from the database of REGISTRY study between 2004 and 2007. LS-HD defined as a score in the Total Functional Capacity (TFC) ≤3. Demographics, Huntington’s Disease Rating Scale (HDRS), QoL (SF-36), resource utilization, caregiver burden (CARE), and medication use were extracted.

Results: 420 patients were included (26.7% of those in the REGISTRY): 54% females, mean age 54 years (SD±12.1), mean TFC score 1.97 (SD±1.0). Motor (mean HDRS motor score 62.2; SD±19.2) and cognitive (mean HDRS cognitive score 67.9; SD±54.8) symptoms were severe, while behavioural ones were moderate (mean HDRS behaviour score 18.4; SD±54.8). Functional status (mean HDRS functional score 7.1; SD±12.6). Quality of life was poor, and its most affected domains were physical functioning, emotional health and energy fatigue. Admission to residential home (12.8%) was infrequent, and associated with worse TFC scores (p<0.001). 75% needed informal care and 33% a wheelchair. QoL was mildly correlated with HDRS motor, behaviour and functional scores (p<0.05). Main reasons for prescription were anxiety, depression, agitation and hyperkinesias. Caregiver burden was low and moderately correlated with behavioural symptoms and functional status (p<0.001).

Conclusions: According to our definition, a high number of patients in the REGISTRY were in late-stage. LS-HD patients have a poor QoL but most of them live at home. Caregivers report low burden, correlated mostly with behavioural problems. These are major indications for drug prescription.

P1480
EXPERIENCE IN THE TREATMENT OF FRIEDREICH ATAXIA WITH DARBOPOETIN: AN OPEN STUDY

I. Sanz Gallego1, J. Arpa1, J. Medina1, F.J. Rodriguez de Rivera1, I. Pascual Pascual2
1Department of Neurology, 2Department of Neuropediatry, Hospital Universitario La Paz, Madrid, Spain

Objectives: There is evidence that recombinant human erythropoietine has a beneficial effect in patients with Friedreich ataxia (FRDA) increasing frataxin levels (Boesch et al. 2008). Our objective is to study the efficacy of alpha dabopoitin in patients with FRDA.

Material and methods: A 12-month open label study including patients with FRDA genetically confirmed. All patients were treated with 150mg of alpha dabopoitin (Aranesp, Lab Amgen Europe B.V.) for 2 weeks (subcutaneous). The patients were evaluated for 2 weeks with blood tests and functionally for 4 months with the SARA scale (Schmitz-Hübsch et al. 2006).

Results: 7 women were included with mean age of 30 years (12.1 SD). Basal mean SARA score 20.5 points (7.3 SD). 1 woman withdrew from the study because of elevated haemoglobin levels. 1 woman withdrew the study voluntarily. No other side effects were observed. An improvement in SARA score was observed within the first year of treatment.

Conclusions: Alpha darbopoitin produces a functional improvement in patients with FRDA within the first year of treatment.
**P1481**

**IMPROVEMENTS IN SLEEP AND MOOD AFTER SWITCH OF PARKINSON’S DISEASE PATIENTS FROM SELEGILINE TO RASAGILINE**

T. Müller¹, J.A. Hoffmann², W. Dimpfel³, C. Oelwein⁴
¹St. Joseph Hospital Berlin-Weissensee, Berlin, ²TEVA Pharma GmbH, Moerfelden, ³University of Giessen c/o NeuroCode AG, Wetzlar, ⁴Private Practice, Berlin, Germany

**Introduction**: Parkinson’s disease (PD) patients often suffer from nocturnal sleep disturbances. This can be caused by disease progression and/or as a consequence of antiparkinsonian therapy. In particular, the MAO-B inhibitor selegiline is metabolised to amphetamines, which decrease subjective sleepiness during the night and increase subjective sleep latencies during a post-testing sleep period. Switch from selegiline to rasagiline may improve sleep, as rasagiline is not metabolised to amphetamine-like derivatives in contrast to selegiline.

**Aim**: To assess the benefits of switching treatment from selegiline to rasagiline on sleep and mood in PD patients.

**Methods**: 30 PD patients (66.6±6.5 [mean±SD, years]; 18 men/12 women) on combination therapy with selegiline 7.5mg/day and other antiparkinsonian agents (dopamine agonists, L-Dopa, amantadine) with sleep disturbances were included. Patients were assessed with the Parkinson’s Disease Sleep Scale (PDSS), Hamilton Depression Scale (HAMD) and the Unified Parkinson’s Disease Rating Scale (UPDRS) before and four months after the switch to rasagiline 1mg/day. Concomitant drugs remained unchanged. Methamphetamine serum levels were determined 2 hours after the administration of the MAO-B inhibitor.

**Results**: After 4 months of treatment with rasagiline, PDSS-scores improved from (mean±SD) 111.33±15.59 to 126.01±11.18 (p<0.001; paired t-test), HAMD-scores from 8.07±3.28 to 6.87±3.56 (p=0.012), UPDRS scores from 22.63±9.82 to 21.89±10.30 (p=0.012). High blood methamphetamine levels were measured 2 hours after the last drug intake of selegiline and were not detectable after switching to rasagiline.

**Conclusion**: Switch from selegiline to rasagiline significantly improved both nocturnal sleep disturbances and mood in PD patients and provided a better motor symptom control.

---

**P1482**

**INTRACORTICAL INHIBITION OF THE MOTOR CORTEX IN HYPERGLYCAEMIC HEMICHOREA-HEMIBALLISM**

J.-Y. Li
Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan R.O.C.

**Introduction**: Hyperglycaemic hemichorea-hemiballism (HC-HB) in uncontrolled diabetes mellitus is an uncommon manifestation of hyperglycaemia and typically shows high signal intensity lesions in the putamen and sometimes in the caudate head on T1-weighted MRI. However, the pathophysiology of hyperglycaemic HC-HB is not well understood.

**Objective**: To investigate motor cortex (MC) excitability in patients with hyperglycaemic HC-HB.

**Patients and methods**: We studied 15 patients with mean age 71.5 years (range 48 to 94 years) and 12 age-matched healthy subjects. TMS studies included motor evoked potential, recruitment curve, GABAA mediated short interval intracortical inhibition (SICI), intracortical facilitation (ICF) and GABAB mediated silent period (SP) duration and long interval intracortical inhibition (LICI). The conditioning and test pulses were applied to the same MC at the ISI of 2ms for SICI, 10ms for ICF, and 50, 100, 150 and 200ms for LICI in both rest and active conditions.

**Results**: There was no significant difference in motor threshold, recruitment curve response, SICI, ICF in both rest and active conditions between patients with hyperglycaemic HC-HB and normal subjects. However, LICI was significantly increased during muscle activation (p=0.0005) but not at rest in patients with hyperglycaemic HC-HB. The SP duration is also increased in patients with hyperglycaemic HC-HB (p=0.0005).

**Conclusion**: LICI and SP are increased in the MC contralateral to the hemichorea in hyperglycaemic HC-HB, but only during muscle activation. This suggests that HC-HB is associated with increased GABAB receptor mediated inhibitory activity in the MC.
P1483
LTD-LIKE PLASTICITY OF THE TRIGEMINAL BLINK REFLEX FOR THE TREATMENT OF BLEPHAROSPASM
G. Krantz1,2, S.A. Ejaz2, L.T. Peter2, G.S. Kranz3, M. Hallett2
1Department of Neurology, Medical University of Vienna, Vienna, Austria, 2Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA, 3Department of Biological Psychiatry, Medical University of Vienna, Austria

Our prior work has shown a beneficial therapeutic effect on benign essential blepharospasm (BEB) with long-term depression-like (LTD)-rTMS. High frequency supraorbital electrical stimulation (HFS) asynchronous with the R2 of the blink reflex induces LTD-like effects on the blink reflex circuit. As abnormal plasticity of this circuit was demonstrated in BEB, LTD of the blink reflex might be a therapeutic tool. Randomized, sham-controlled, observer-blinded prospective study. In 14 patients with BEB, we evaluated the effects of HFS on three separated treatment days: we applied 28 trains of 9 stimuli, 400Hz, either BEFORE or AFTER the R2 component of the blink reflex or used SHAM stimulation. Primary outcome was the clinical effects on BEB (video rating by a blinded physician and patient rating before, immediately after and one hour after stimulation during rest, reading and talking); secondary outcome was the blink reflex recovery curve (BRR). HFS-BEFORE and HFS-AFTER showed the same improvement on BEB as HFS-SHAM in physician rating but patients found a significant improvement only in the BEFORE condition immediately after stimulation. Similarly, improved recovery of the BRR was seen only in the BEFORE condition immediately after stimulation. Clinical symptoms differed in the three baseline conditions (rest, reading, talking). HFS in the BEFORE condition reduced enhanced LTP-like plasticity of trigeminal blink reflex circuits in BEB toward normal values but did not show an objective improvement on clinical symptoms. Modulation of other brain regions like cortical areas seems to be essential to normalize blink patterns in BEB.

P1484
EARLY DETECTION OF WEARING OFF (WO) IN PARKINSON’S DISEASE: PRELIMINARY RESULTS OF THE DEEP STUDY
G. Abbruzzese1, A. Antonini2, P. Barone3, F. Stocchi4, V. Posocco5, D. Colombo6, On Behalf of DEEP Study Group
1Università degli Studi di Genova - Centro Parkinson - Dipartimento Neuroscienze, Genoa, 2U.O. Malattia di Parkinson, IRCCS San Camillo Venice, Venice, 3Centro Parkinson Dipartimento Scienze Neurologiche, Università Federico II Napoli, Naples, 4Dipartimento di Neurologia, IRCCS San Raffaele Pisana di Roma, Roma, 5Novartis Pharma S.p.A, 6Novartis Farma SpA, Varese, Italy

Background: WO occurs in the majority of Parkinson’s disease (PD) patients, even in the early stage of disease; it can impair quality of life and enhance disability. Early recognition of WO is critical in order to develop strategies to manage these symptoms, and to prevent troublesome complications.

Objective: To evaluate the prevalence of motor and non-motor symptoms of WO in a PD population. Furthermore, to compare usefulness of patients’ self-assessment versus neurologists’ evaluation for the detection of WO, in Italian office-based practice.

Methods: We performed an observational cross-sectional multicentre study on 634 consecutive ambulatory non-demented PD patients, who had been under dopaminergic agents for at least one year. During a single visit, WO was diagnosed by the neurologists’ evaluation, and on the basis of the Italian validated version of a patient self-rated 19-questions Wearing-Off Questionnaire (WOQ-19).

Results: 617 patients completed the study. Mean age was 66.8±9.2 years, and mean duration of PD symptoms was 8.0±4.7 years. WO was diagnosed by the neurologists in 57% of the patients, whilst analysis of responses to WOQ-19 found that WO symptoms were reported by 67% of patients (p<0.0001); this discrepancy was more marked in patients with <2.5 years disease duration (22% vs. 40%). WO was positively associated with disease duration, H&Y staging, UPDRS part II+III score, length of dopaminergic treatment.

Conclusions: WO symptoms are common since the early stage of disease, probably underestimated by routine clinical evaluation. WOQ-19 is a useful screening tool to diagnose WO.
P1485
RISK ANALYSIS FOR DROPPED HEAD IN PARKINSON’S DISEASE
T. Oeda, A. Umemura, S. Tomita, R. Hayashi, K. Masayuki, K. Yamamoto, H. Sawada
Clinical Research Center and Department of Neurology, Utano National Hospital, Kyoto, Japan

Objective: Patients with Parkinson’s disease (PD) often show abnormal postures including dropped head, camptocormia and Pisa syndrome, which disturb quality of life; however, the etiology of these symptoms was unknown. The purpose of this study was to identify risk factors for dropped head in patients with PD in the light of clinical backgrounds and drugs.

Methods: We enrolled 221 consecutive patients with PD. On photos, neck flexion angles were measured. Dropped head was defined as those with the angle more than 3SD of healthy controls. A nested case-control study was conducted, in which, patients with dropped head were assigned as cases and remains were designated as controls. The clinical profiles including age, sex, Hoehn and Yahr (H-Y) stages, onset age, initial symptoms, disease duration, mini-mental state examination, histories of psychosis and orthopedical spine lesions, stereotaxic operation and drugs were analyzed using multiple logistic regression models.

Results: Patients with dropped head were 23 cases in a total of 221 subjects. Case patients showed more severe H-Y stages than control (p=0.001). Multiple logistic regression analysis revealed H-Y stage as the only significant risk factor for dropped head (p< 0.05, Odds Ratio 2.5).

Conclusion: Dropped head of PD patients was significantly related to the disease severity.

P1486
A VIRTUAL ARENA TEST INDICATES IMPAIRED STRIATAL SPATIAL MEMORY STRATEGIES IN MILD TO MODERATE PARKINSON’S DISEASE
T. Gudmundsdottir1, C.F. Doeller2, N. Burgess2, F. Bergquist1,3
1Neurology, Sahlgrenska University Hospital, Gothenburg, Sweden, 2Inst Cognitive Neuroscience, University College London, London, UK, 3Pharmacology, University of Gothenburg, Inst Neuroscience and Physiology, Gothenburg, Sweden

Spatial memory is encoded in at least two different memory systems in the brain, a hippocampus-based and a striatum-based system. A recent fMRI study shows distinct and separate activation of these systems when subjects collect and replace objects paired to a movable landmark (striatal system) or borders and distant cues (hippocampal system) in a virtual arena[1]. We hypothesised that the striatal dopamine denervation in Parkinson’s disease leads to compromised landmark based spatial orientation. A pilot study was performed with 17 patients with left sided or bilateral parkinsonism with mild clinical symptoms (median Hoehn and Yahr =1, UPDRS =8±7), and 13 age matched controls. Participants collected and replaced two objects in the virtual arena and were given visual feedback on their performance at each trial. By moving the landmark it is possible to determine if the subject is biased towards landmark (striatal) or border (hippocampal) orientation strategies. Control subjects were biased towards landmark strategy, something we found was not the case with Parkinson’s patients (unpaired t-test vs. controls, p= 0.029, t=2.301 df=28). This finding suggests that striatal spatial memory strategies are compromised early in Parkinson’s disease. Deficient striatal memory functions may lead to poor judgement of distance at close range and could contribute to disturbed motor planning, balance problems and falls, problems known to have considerable clinical impact in advanced Parkinson’s disease.

Reference:
THE EFFECTS OF RASAGILINE ON COGNITIVE DEFICITS IN PARKINSON’S DISEASE PATIENTS WITHOUT DEMENTIA: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTI-CENTER STUDY

H.A. Hanagasi1, H. Gurvit1, P. Unsalan1, H. Horozoglu2, N. Tuncer2, A. Feyzioglu2, D. Ince Guna1, R. Cakmur3, G. Yener3, H.A. Sahin4, M. Emre1

1Department of Neurology, Istanbul Faculty of Medicine, 2Marmara University, Istanbul, 3Dokuz Eylül University, Izmir, 4Ondokuz Mayıs University, Samsun, Turkey

Objective: To assess the effects of rasagiline (1mg/day) on cognitive deficits in cognitively impaired, non-demented patients with PD.

Background: Cognitive impairment associated with Parkinson’s disease (PD) can occur at all stages of the disease. Dopamine is thought to be involved in certain cognitive processes such as working memory. Rasagiline is a selective MAO-B inhibitor, which enhances central dopaminergic transmission.

Methods: Randomized, double-blind, placebo-controlled, prospective study. Parkinson’s disease patients receiving stable dopaminergic treatment were assigned to receive rasagiline 1mg/day or placebo for 3 months. Patients were eligible if they had impairment in 2/4 cognitive domains (attention, executive functions, memory, visuo-spatial functions) in the screening neuropsychological tests, but did not fulfill criteria for PD dementia.

Results: 55 patients were randomized and 48 patients completed the study. At week 12, patients in the rasagiline group showed significant improvement in digit span-backward as compared to placebo (p=0.04), with trends favouring rasagiline in digit span total and digit ordering tests. Verbal fluency total score showed a significant difference in favour of rasagiline (p=0.038), with trends favouring rasagiline in semantic fluency test and Stroop spontaneous corrections. The composite cognitive domain Z scores revealed a significant difference in favour of rasagiline as compared to placebo for attention (p<0.005). There were no significant differences between the two groups in cognitive tests assessing memory, language and visual-spatial functions.

Conclusions: Rasagiline may exert beneficial effects on certain aspects of attention and executive functions in non-demented PD patients with cognitive impairment.

INSULIN RESISTANCE IN NORMOGLYCEMIC PATIENTS WITH SPINOCEREBELLAR ATAXIA TYPE-1

N. Dragasevic1, N. Lalic2, E. Stefanova1, I. Petrovic1, V. Kostic1

1Movement Disorders, Clinic for Neurology, 2Clinic for Endocrinology, Belgrade, Serbia

Objective: We have recently shown impairment in insulin sensitivity and insulin secretion in normoglycaemic patients with Huntington’s disease (HD). In order to investigate whether such observations are HD-specific or may be common to other polyglutamine diseases, we wanted to investigate glucose homeostasis in patients with spinocerebellar ataxia type 1 (SCA 1), another entity from the family of polyglutamine diseases.

Methods: Glucose homeostasis was studied in 12 unrelated, untreated normoglycaemic patients with SCA 1 and in 24 healthy, matched controls. Metabolic investigations included

(a) glucose tolerance assessment based on glucose curve during oral glucose challenge;
(b) insulin sensitivity assessment by the homeostasis model assessment (HOMA) and the euglycemic insulin clamp (M value); and
(c) insulin secretion by acute insulin response (AIR) and insulinogenic index.

Results: The evaluation of insulin sensitivity demonstrated higher HOMA-insulin resistance indices, and lower M values (p<0.001 and p<0.05, respectively), while both the AIR and the insulinogenic index were lower in patients with SCA 1 compared to controls (p<0.001 and p<0.05, respectively).

Conclusion: Our data suggested impairment in insulin secretion capacity, as well as simultaneous decrease in insulin sensitivity, with an increase in insulin resistance level in patients with SCA1.
P1489
DEEP BRAIN STIMULATION IN A 60-YEAR-OLD MAN WITH FRAGILE X TREMOR ATAXIA SYNDROME
K.A. Roberts, S. Cronin, K. O’rourke, T. Lynch, Dublin Neurological Institute
Neurology, Dublin Neurological Institute, Dublin, Ireland
Introduction: Fragile X Tremor Ataxia Syndrome (FXTAS) is an X-linked recessive late-adult-onset neurodegenerative disease. It primarily affects male carriers of a premutation expansion of the fragile X mental retardation 1 gene (FMR1). It is characterised by action tremor and cerebellar ataxia. Associated features include cognitive impairment and parkinsonism (DAT normal). Treatment options are limited.
Methods: Chart and videotape review of a patient with genetically-confirmed FXTAS, pre and post-DBS.
Case report: A 60-year-old man was referred with a ten-year history of progressively worsening tremor of his head, upper limbs, voice and a diagnosis of Benign Essential Tremor (BET). The tremor was functionally disabling and non-responsive to medications. He had a positive family history for tremor including a sister and a maternal aunt. He had 2 nephews with mental retardation. MRI brain showed hyperintensities in the middle cerebellar peduncle and genetic testing confirmed he was a carrier of the Fragile X premutation. Subsequently his siblings were found to be positive for this and two nephews were diagnosed with Fragile X syndrome. Our patient underwent DBS which resulted in marked tremor suppression and had a lasting improvement on his quality of life one year later.
Conclusion: FXTAS can mimic BET. FXTAS is underdiagnosed due to variable phenotype. Neurologists must have low threshold to screen for FXTAS especially if family history is positive for learning disability or if there is a suggestive MRI sign. DBS can be a successful treatment option for the medically intractable FXTAS tremor.

P1490
FREE URINARY CATECHOLAMINES EXCRETION PROFILE IN PATIENTS SUBMITTED TO BILATERAL DEEP BRAIN STIMULATION
J. Guimarães1, M.A. Vieira-Coelho2, E. Moura2, C. Andrade3, M.J. Rosas4, R. Vaz5, C. Garrett3
1Neurology Department, Faculty of Medicine, University of Porto, Hospital de São João, 2Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, 3Neurology Department, Faculty of Medicine, University of Porto, 4Neurology Department, Hospital de São João, 5Neurosurgery Department, Faculty of Medicine, University of Porto, Porto, Portugal
Introduction: Deep brain stimulation of the subthalamic nucleus (DBS-STN) is thought to continuously alter the activity of STN neurones in Parkinson’s disease (PD), whereas oral levodopa therapy has a pulse effect. It has been suggested that chronic decrease in the levodopa dose with continuous STN stimulation can induce plastic neuronal changes. However this change in the dopaminergic system is not known.
Aim: To study urinary excretion of catecholamines in patients with PD before and after DBS-STN and try to define a profile of variation in dopaminergic system activity.
Patients and methods: 20 patients were submitted to STN-DBS and evaluated before and one week after surgery for: 1) UPDRS-III; 2) mean dose of levodopa; 3) catecholamines and metabolites in 24h urine measured by HPLC-ED.
Results: UPDRS-III was significantly improved after DBS-STN (p<0.005), 52±8 to 16±8, with a reduction of levodopa dosage (mg/day) from 1037±499 to 550±441. Urinary excretion (in µmol/24h) of L-DOPA, noradrenaline, adrenaline, dopamine and DOPAC were: 455±41, 32±5, 5±2, 180±29, 310±44 before surgery and 300±54, 28±7, 3±1, 147±29, 274±68 after surgery, respectively. The DA/L-DOPA and DOPAC/DA ratios were 0.4±0.1, 2.3±0.1 before surgery and 0.6±0.1, 2.0±0.1 after surgery, respectively. Urinary L-DOPA excretion and DA/L-DOPA ratio after surgery were significantly different (p<0.05) from values before surgery.
Conclusion: As expected with a lower oral dose of levodopa, urinary excretion of L-DOPA was significantly reduced in patients after DBS-STN surgery. Unexpectedly the DA/L-DOPA ratio, an indirect measure of dopamine synthesis, was significantly increased. These results show that DBS-STN may improve the efficacy of oral levodopa.
P1491

SEVERITY OF LIVER DISEASE IN EXTRAHEPATIC FORMS OF WILSON’S DISEASE

J. Domingos1, H.P. Miranda2, M. Magalhães1
1Neurology, 2Gastroenterology, Centro Hospitalar Porto - Hospital de S. António, Porto, Portugal

Introduction: Wilson’s disease (WD) is a rare genetically autosomal recessive inborn error of copper metabolism leading to its accumulation since early life, which invariably causes subclinical liver disease. The severity of liver involvement in extrahepatic forms of WD is unknown.

Aim: To evaluate clinical and histopathological hepatic involvement in extrahepatic WD patients.

Methods: Between 1980 and 2011, 54 WD patients (24 male; 30 female) were observed. At presentation, patients were classified into three main groups: presymptomatic, hepatic and extrahepatic (involving also other systems). The severity of hepatic involvement was evaluated according to liver histopathology and Child-Pugh score.

Results: 24 out of 54 WD patients were classified as extrahepatic. All of them had some degree of hepatic dysfunction. 15 patients were classified as Child-Pugh “A”, 3 as “B” and 4 as “C”. All had abnormal liver histology (Fatty change-1; Inflammation-2; Fibrosis-6 and Cirrhosis-11). 14 out of the 24 extrahepatic had isolated neurological symptoms. 11 were classified as Child-Pugh “A”, 2 as “B” and none as “C”. In the performed liver biopsies, 2 patients had inflammation, 4 fibrosis and 6 cirrhosis. The mean age of the subgroups was similar (21.9±15.6 presymptomatic versus 20.6±8.4 extrahepatic versus 20.8±10.9 years hepatic).

Conclusion: We found liver disease in all the extrahepatic groups of WD; as we expected, many of them severe, although mostly asymptomatic. We found similar age of presentation in three groups of WD, suggesting there are still important unknown factors that explain the highly variable clinical course.

P1492

OSCILLATORY ACTIVITY IN THE HUMAN GLOBUS PALLIDUS DURING WALKING

A. Singh1, A. Plate1, S. Kammermeier1, J. Ilmberger2, K. Böetz1
1Neurology Department, 2Physical Medicine Department, LMU, Germany, Munich, Germany

Introduction: Nowadays, globus pallidum internum (GPI) represents the most therapeutic target for deep brain stimulation (DBS) in dystonia. Pallidal recordings of local field potentials (LFPs) in patients with dystonia have demonstrated 3-12Hz pathophysiological oscillatory activities. Gait disturbance, one of the axial symptoms, may also be caused by basal ganglia disease and can be seen as a symptom of dystonia. DBS electrodes also give us an opportunity to investigate basal ganglia involvement in gait cycle phase during steady-speed human walking.

Methods: We recorded LFPs from deep brain stimulation electrodes implanted into the GPI of dystonic patients during rest (sitting and standing) and walk on a treadmill machine. All subjects walked bare-foot with preferred velocity.

Results: There was not any difference in the power of frequency bands during sitting and standing conditions. LFP power in the theta (4-8Hz), alpha (8-12Hz) and gamma (60-90Hz) frequency bands was higher during walking as compared to resting condition (sitting). Oscillatory activities were observed higher in lower contact as compared to upper contact of macroelectrode. Synchronized alpha frequency modulation was observed in the beginning of stance and swing phase of a gait cycle.

Conclusions: In the present study, we were able to show that prominent activity in the theta, alpha and gamma frequency bands significantly contribute to the involvement of the human globus pallidus during walking. The dynamic organization of frequency band activities in the human GPi therefore provide information of pathophysiological circuit of basal ganglia involved in movement disorders during walking.
P1493

MOVEMENT DISORDERS ARE PREVALENT IN PATIENTS WITH FAMILIAL CREUTZFELDT JAKOB DISEASE (f-CJD) CARRYING THE E200K MUTATION


1Sheba Medical Center, Ramat-Gan, Israel, 2Mount Sinai Medical Center, New-York, NY, USA, 3Tel Aviv University, Tel-Aviv, 4Barzilai Medical Center, Ashkelon, 5Hadassah University Hospital, Jerusalem, Israel

Background: Although myoclonus and ataxia are considered common in patients with familial Creutzfeldt-Jakob Disease (fCJD); other movement disorders are considered less prevalent.

Objectives: To systematically evaluate the prevalence of extrapyramidal signs and movement disorders (MD) in patients with fCJD.

Methods: 43 consecutive symptomatic CJD patients (26 males, mean age 58.7±8.9 yrs, range 43-77 yrs) carrying the E200K mutation in the PrP gene underwent a detailed neurological examination, with special emphasis on MD and extrapyramidal signs.

Results: 38 patients (88%) (37/43, 86% at presentation) had limb or gait ataxia. Myoclonus was evident in 25/43 patients (58%) (21/43, 49% at presentation). 95% of the patients (41/43) had at least one extrapyramidal sign throughout the disease course (37/43, 86% at presentation), the most prevalent of which was rigidity (28/43, 65% of the patients and 22/43 51% at presentation), followed by the glabellar sign (24/43, 56% of the patients and 22/43, 51% at presentation), bradykinesia (19/43, 44% of the patients and 15/43, 35% at presentation), dystonia (15/43, 35% patients, 12/43, 28% at presentation) and tremor (13/43 patients, 30%, 12/43, 28% at presentation).

Conclusion: In this unique population of patients with familial CJD myoclonus was less prevalent than previously reported while other extrapyramidal signs were very common occurring at a relatively early stage of the disease. The high prevalence of MD can be added to other phenomena characteristic to the familial disorder in Libyan Jews. Whether it is attributed to the E200K mutation itself or to some other mechanism has still to be elucidated.

P1494

FACTORS INFLUENCING SYMPTOMS IMPROVEMENT OF INDIVIDUAL BODY PARTS IN PATIENTS WITH DYT1 GENERALIZED DYSTONIA TREATED BY INTERNAL GLOBUS PALLIDUS DEEP BRAIN STIMULATION

L. Cif, D. Ruge, V. Gonzalez, P. Coubes

1Neurosurgery, Gui de Chauliac Hospital, Montpellier, France, 2Sobell Department of Motor Neuroscience and Movement Disorders, University College London UCL-Institute of Neurology, London, UK, 3Neurosurgery, Gui de Chauliac University Hospital, Montpellier, France

Objectives: We studied dystonic symptoms evolution of individual body parts in primary generalized dystonia (PGD) patients chronically benefiting from internal globus pallidus (GPi) deep brain stimulation (DBS) and the influence of DBS related factors (stimulated volume in the GPi, active contact position) on the clinical outcome.

Patients and methods: 11 patients with DYT1 PGD treated with GPi DBS were enrolled. Dystonic symptoms evolution was monitored during 48 hours DBS discontinuation. Severity of dystonia in nine individual body parts was evaluated at baseline and postoperatively using the Burke Fahn Marsden dystonia rating scale. The evolution of dystonia between baseline and DBS-ON, DBS immediate switch-off (OFF-DBS1) and after 48 hours of DBS switch-off (OFF-DBS2) was monitored. For correlations between symptoms distribution and DBS linked factors, the cranial, axial and appendicular subscores have been used.

Results: Trunk and lower limb dystonia improved, the effect still lasting after DBS arrest. There was no significant difference between preoperative and DBS-OFF2 assessments for upper limbs. A correlation was found between the axial subscores and the total score for the three conditions. A correlation was found for the left stimulated GPi volume and the right limb, the axial subscore and the total scores.

Conclusions: 48 hours DBS arrest could be used for assessment of the DBS efficacy in PGD. The left GPi seems to have a prominent role in the achievement of DBS global therapeutic effect.
**P1495**

**BRAIN IRON ASSESSED AT 3-T IN HEALTHY CONTROLS AND PATIENTS WITH PARKINSON’S DISEASE**

H. Antell¹, M. Pohja², J. Numminen¹-³, P. Häkkinen², T. Parviainen⁴, T. Annanmäki⁵, V.-P. Poutanen⁶, K. Murros²

¹Neurosurgery Research Group, Biomedicum Helsinki, Helsinki, ²Jorvi Hospital, Helsinki University Central Hospital, Espoo, ³Helsinki Medical Imaging Center, Töölö Hospital, Helsinki University Central Hospital, Helsinki, ⁴Low Temperature Laboratory, Brain Research Unit, Aalto University, Espoo, ⁵Meilahti Hospital, Helsinki University Central Hospital, Helsinki, ⁶Kanta-Hämeen Sairaanhoidopiirin Kuntayhtymä, Hämeenlinna, Finland

**Introduction:** Abnormal brain iron levels are seen in PD. Iron causes oxidative stress, thought to have a key role in the pathogenesis of PD.

**Patients and methods:** 11 patients (mean disease duration 5.0 yrs) with hypokinetic-rigid PD and their 11 spouses underwent MRI of the brain. Brain iron was quantified by measuring R2, R2*, and R2’ relaxation rates on a 3-tesla system.

**Results:** In controls, R2* (p≈0.006) and R2’ (p≈0.026) were greater in the left medial SNc. R2* was greater in the left GPe (p=0.026), and in the right cerebellum (p=0.041). R2’ was greater in the left putamen (p=0.021).

In patients, R2 of SNc was greater contralaterally to the clinically most affected side (p=0.010). R2 of contralateral medial SNc was greater in patients (p=0.041). R2* (p=0.041) and R2’ (p=0.047) of ipsilateral cerebellum were greater in patients. R2 of contralateral FWM was smaller in patients (p=0.026).

**Conclusions:** In healthy controls, iron accumulates in medial SNc, GPe, and putamen of the left hemisphere, and in the right cerebellum. In PD patients, iron accumulates in contralateral SNc. Contralateral FWM iron content is slightly lower in PD patients, and ipsilateral cerebellar iron content is slightly increased. We hypothesize, that oxidative stress in PD may disrupt normal axonal transport from deep gray matter nuclei to cortical regions, leading to increased retrograde neuronal transport of iron from contralateral deep gray matter nuclei via thalamus to ipsilateral cerebellum.

**P1496**

**FLUOXETINE DOES NOT IMPAIR MOTOR FUNCTION IN PATIENTS WITH PARKINSON’S DISEASE: CORRELATION BETWEEN MOOD AND MOTOR FUNCTIONS WITH PLASMA CONCENTRATIONS OF FLUOXETINE/NORFLUOXETINE**

E.D. Dzoljic¹, T. Zoran², M. Mijajlovic¹, M. Pokrajac³, I. Kovacevic³, M. Prostran⁴, V. Kostic¹

¹Clinic of Neurology, ²Department of Pharmacology, ³Faculty of Pharmacy, ⁴School of Medicine, University of Belgrade, Belgrade, Serbia

**Objective:** To assess the influence of fluoxetine (Flu) on motor function in patients with Parkinson’s disease (PD).

**Methods:** In this prospective, controlled, open-label study, 18 patients with PD and mild depression (10<HDRS<23) without dementia (25<MMSE) were treated with Flu. Both single and repeated dose effects of Flu were assessed on days 1-80. Plasma concentrations of Flu and norfluoxetine (NORFlu) were correlated with the results of selected motor function performance scores (UPDRS, FTT and PPT). Severity of PD, depression and dementia were evaluated using standard tests (HY, ADL, HDRS, MMSE).

**Results:** Steady-state for Flu/NORFlu was reached after 18 days of treatment. Such a plateau correlated with significant improvements in both scores of depression and Parkinson’s disease (HDRS, UPDRS-motor score, and ADL, respectively), while HY did not change. In addition, FTT and PPT scores also increased until day 18, with further slight fluctuations around the plateau. According to the factor analysis, optimal motor performances correlated with Flu concentrations of 60-110 microg/L.

**Conclusions:** Flu (20mg/day) significantly reduced depression in PD patients while it did not impair their motor performances. Because substantial placebo effects may arise in studies of PD and depression, large, prospective, randomized, placebo-controlled clinical trials are warranted.
P1497
AN INTERNATIONAL, OBSERVATIONAL STUDY TO IDENTIFY IN REAL LIFE PRACTICE PROGNOSTIC FACTORS FOR RESPONSE TO BOTULINUM TOXIN TYPE-A INJECTION IN SUBJECTS WITH CERVICAL DYSTONIA (CD)
V.P. Misra1, B. Zakine2, P. Maisonobe2
1The National Hospital for Neurology & Neurosurgery, London, UK, 2Ipsen Pharma, Boulogne-Billancourt, France

Introduction: Efficacy/safety of Botulinum toxin type A (BoNT-A) is well-established in randomized controlled trials, but real life data are lacking.

Patients and methods: 404 adult subjects with idiopathic CD from 9 countries were included in this international observational study. Response was assessed after one injection cycle with BoNT-A, using a challenging multidimensional definition: TWSTRS, duration of action, related adverse event and subject’s satisfaction. Exploratory analyses based on the above endpoints and the intent to treat population was conducted to identify prognostic factors for response.

Results: Depending on the duration of action criterion used for the analysis, the responder rate varied from 28.6% (subject’s assessment by phone; primary analysis) to 55.8% (time between inclusion and subsequent visit; post-hoc analysis). A multivariate logistic regression (testing for the following variables: demographic data, duration of CD, CD subtypes, severity of CD, injection protocols) showed that the most strongly associated factors were age (<40 years) and absence of baseline head tremor. Odds Ratio (OR) were 3.9 (p<0.05) using the original responder definition (ORD) and 2.5 (not significant) using the post hoc responder definition (PHRD). Similarly for the absence of baseline head tremor, OR were 1.5 (not significant) using the ORD and 2.1 (p<0.05) using the PHRD. Other trends with less statistical evidence were observed.

Conclusion: Logistic regression for primary responder and post hoc responder definitions primarily identified that age (<40 years) and absence of baseline head tremor were potential prognostic factors for improved response in subjects suffering from CD.

P1498
PREFRONTAL STIMULATION IN TOURETTE’S SYNDROME
S. Lalli1, S. Piacentini1, O. Gambini2, A. Franzini3, F. Ferrè1, G. Messina3, D. Perani4, A. Albanese5
1Neurology 1, IRCCS Besta Neurological Institute, 2DMCO, State University of Milan, 3Neurosurgery, IRCCS Besta Neurological Institute, 4Nuclear Medicine, IRCCS San Raffaele, Vita e Salute University, Milan, 5Neurology, Università Cattolica del Sacro Cuore, Rome, Italy

Introduction: Pharmacological treatment of Tourette’s syndrome is based mainly on neuroleptics and other agents interacting with the dopaminergic system, with major side effects. Recently it has been shown that slow repetitive magnetic stimulation to supplementary motor area resulted in a significant clinical improvement

Aim of this study: To evaluate safety and efficacy of prefrontal cortical stimulation in patients affected by Tourette.

Methods: 6 patients were selected for cortical stimulation (5 men, 1 woman, mean age 36.3±8.6). 4 patients underwent a bilateral implant of electrodes for epidural pre-frontal stimulation. Psychiatric, behavioural and cognitive evaluations were performed before surgery and 1, 3, 6 and 12 months from surgery. Each subject underwent three resting 18F-fluorodeoxyglucose PET scans before and 6 and 12 months after surgery.

Results: No adverse events have been reported by our group of patients. Analysis of the clinical data up to 6 months shows that all patients improved the scores for assessment, in different percentage, after surgery. Hamilton scale for depression (HAM-D 21 items) and Hamilton for anxiety (HAM-A) show an improvement both for anxiety and depression symptoms after surgery.

Conclusions: All 4 patients responded well to prefrontal cortical stimulation, although to differing degrees. The procedure is safe and effective on motor and phonemic tics. Tics did not disappear entirely. After CS, 1 patient required no medication. Among the 3 left patients, drug requirements remained stable or slightly reduced. More data on long-term follow-up will be required before for proposing prefrontal stimulation for treatment of pharmacological resistant cases.
P1499

TRANSCRANIAL SONOGRAPHY: A RELIABLE DIAGNOSTIC TOOL IN DIAGNOSIS OF PARKINSON’S DISEASE

A. Jesic, L. Sakalas, N. Delibasic, D. Stefanovic, M. Semnic, I. Divjak, P. Slankamenac

Neurology Clinic, Clinical Centre of Vojvodina, Novi Sad, Serbia

Transcranial sonography (TCS) is a reliable method in the diagnosis of Parkinson’s disease (PD) and the differential diagnosis of atypical parkinsonism. Finding of hyperechogenicity of substantia nigra (SN), which is the result of iron deposition in this midbrain structure, is highly suggestive of PD.

Material and methods: We performed a study on 67 PD patients and 33 healthy controls in order to determine sensitivity and specificity of TCS in diagnosis of PD.

Results: Due to insufficient or impenetrable acoustic temporal bone TCS could not be performed in 10.2% of PD patients and 15.1% of healthy controls. Significant SN hyperechogenicity was recorded in 77.6% of PD patients and 12.1% of healthy controls. The sensitivity of TCS was 86.6% and specificity 86.2%, with the positive predictive value of 92.8%. In the PD group, SN hyperechogenicity was generally more pronounced on the side which was contralateral to the side of dominant clinical presentation.

Conclusions: Our results are in line with the data reported by other investigators. With its high reliability, harmlessness and low cost, TCS is a diagnostic method that is today widely used in the diagnosis of PD.

P1500

HEMICHOREA-HEMIBALLISM INDUCED BY NON-KETOTIC HYPERGLYCAEMIA

T. Argun, P. Dogan Ak, C. Dayan, A. Soysal, B. Arpaci

Bakirköy Neuro-Psychiatry Training and Research Hospital, Istanbul, Turkey

Introduction: Hemichorea-hemiballism (HCHB) is a clinical spectrum of continuous, irregular, involuntary movements involving one side of body. We have reported 2 cases with HCHB induced by non-ketotic hyperglycaemia.

Case 1: A 71-year-old woman, with history of diabetes mellitus type-2 (DM), admitted with involuntary movements of the left arm. Examination was normal except choreiform movements of left upper limb and tongue. The blood glucose, HbA1c and serum osmolality were high. Urinalysis was positive for glucose but negative for ketones, protein. Other blood tests were normal. Brain computerized tomography (CT) and MRI showed lesion on right putamen and caudate; MRI revealed hyperintensity on T1-weighted and flair images and hypointensity on T2-weighted images.

Case 2: A 71-year-old man with 8-year history of DM was admitted with left hemichorea. He was taking, irregularly, oral hypoglycaemic agents. Neurological examination was normal except the choreiform movements of left upper and lower limbs. The blood glucose, HbA1c and serum osmolality were high. Urinalysis was positive for glucose, negative for ketones and protein. Other routine blood tests were normal. CT showed hyperdensity on right caudate. MRI of brain demonstrated a hyperintense lesion on T1-weighted images which was hypointense on T2-weighted images localized to right caudate.

Discussion: Non-ketotic hyperglycaemia associated with chorea and ballism are most commonly seen in female diabetic patients. Neuroimaging shows involvement in putamen, caudate nucleus, and globus pallidus. The underlying mechanisms are not clear. Many different causes have been suggested including vascular insufficiency, dysfunction secondary to hyperglycaemic, hyperosmolar insult, hypertoviscosity, petechial haemorrhage and decreased GABA, acetylcholine synthesis.
P1501

BOTULINUM TOXIN TYPE-A IN PATIENTS WITH PARKINSON’S DISEASE AND REFRACTORY DETRUSOR OVERACTIVITY

A. Giannantoni1, A. Conte2, S. Proietti1, S. Giovannozzi1, M. Gubbiotti1, A. Berardelli2

1Department of Urology and Andrology, University of Perugia, Perugia, 2Department of Neurology and Psychiatry and Neuromed Institute ‘Sapienza’, University of Rome, Rome, Italy

**Aim of the study:** To evaluate the effects of Botulinum Toxin-A (BoNT/A) injected intradetrusorially in patients with Parkinson’s disease (PD) affected by refractory detrusor overactivity (DO).

**Materials and methods:** 8 patients underwent the recording of urinary frequency and episodes of urinary incontinence, completed a quality-of-life questionnaire on incontinence (I-Qol) and underwent urodynamics. Then they received a single intradetrusorial treatment of BoNT/A 100 U. Clinical and urodynamic evaluations were repeated at one, three and six months after treatment.

**Results:** During follow-up, BoNT/A injections induced a decrease in daytime and night-time urinary frequency (p=0.003 and p=0.006), and urinary incontinence episodes (p=0.008) in all patients. I-Qol scores significantly improved (p=0.002). DO disappeared in 3/8 patients after treatment. 2 cases with high post-void residual (PVR) volume needed daily intermittent catheterizations (IC). Urodynamic results are shown in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (mean ± SD)</th>
<th>1 months (mean ± SD)</th>
<th>6 months (mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max bladder capacity (ml)</td>
<td>270±88.6</td>
<td>432±116.9</td>
<td>487±113.3</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>UDC threshold (ml)</td>
<td>246±107</td>
<td>303±90.1</td>
<td>330±48.2</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>UDC max pressure (cmH20)</td>
<td>21.5±7.3</td>
<td>18.4±3</td>
<td>17.8±3.3</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Post-void residual volume(ml)</td>
<td>25±28.3</td>
<td>162.5±92.1</td>
<td>90±60.2</td>
<td>&lt;0.05*</td>
</tr>
</tbody>
</table>

**Discussion:** 100U of BoNT/A induced clinical and urodynamic improvements, which lasted for at least six months. Despite of lower injected BoNT/A doses, these patients presented with increased PVR volume. Nevertheless, the need to perform IC in 2 cases was well accepted.

**Conclusion:** Intradetrusorial injection of BoNT/A 100U induced clinical and urodynamic improvements in PD patients that lasted for at least six months.

P1502

SIMILAR NUMBER OF NON-MOTOR SYMPTOMS IN EARLY-ONSET VERSUS LATE-ONSET PARKINSON’S DISEASE PATIENTS

D. Crosiers1,2,3, B. Pickut1, J. Theuns2,4, P. De Deyn5,6, C. Van Broeckhoven2,4, P. Cras1,3

1Department of Neurology, Antwerp University Hospital, Edegem, 2Neurodegenerative Brain Diseases Group, VIB-Department of Molecular Genetics, 3Laboratory of Neurobiology, Institute Born Bunge, 4Laboratory of Neurogenetics, Institute Born-Bunge, University of Antwerp, Wilrijk, 5Department of Neurology, ZNA Middelheim Hospital, Antwerpen, 6Laboratory of Neurochemistry, Institute Born-Bunge, University of Antwerp, Wilrijk, Belgium

**Aim:** To compare self-reported non-motor symptoms in early-onset and late-onset Parkinson’s disease (PD) patients.

**Methods:** Consecutive PD patients completed the Dutch translation of the Non-Motor Symptoms Questionnaire (NMS-Quest) in a hospital-based setting in Flanders.

**Results:** The NMS questionnaire was completed by 192 PD patients with a mean onset age of 60 years (range: 28-88 years). The mean disease duration of the patients was 7.5 years. A median number of 9 non-motor symptoms (NMS) were reported per patient. A significantly higher number of NMS was reported by patients with longer disease duration. However, in early-onset patients (onset age <50 years) a similar number of NMS was present as in late-onset PD patients. Moreover, the most frequently reported non-motor symptoms were identical in both groups: urinary urgency, nocturia and attention problems. Interestingly, significantly more early-onset patients indicated to suffer from unexplained pain complaints than late-onset patients (38.5 vs. 13.5%).

**Conclusions:** Non-motor symptoms are equally prevalent in early-onset and late-onset Parkinson’s disease. The number of reported NMS is associated with disease duration rather than with onset age. Sensory symptoms were overrepresented in the early-onset PD patients. Further research is needed to improve treatments for non-motor symptoms in PD.
P1503
PARKINSON’S DISEASE DISABILITY STATISTICS IN UKRAINE (4 YEARS OF EXPERIENCE)
V. Golyk¹, T. Mischenko²,³, A. Ipatov¹
¹Neurology and Border States, Ukrainian State Institute of Medical and Social Problems of Disability, Dnipropetrovsk, ²Institute of Neurology, Psychiatry and Narcology, Ukrainian Academy of Sciences, Kharkiv, ³Ministry of Health, Kiyv, Ukraine

P1504
MULTIFOCAL DYSTONIA AS A RESULT OF HIV INFECTION: A CASE REPORT
V. Miletić, M. Relja
Department of Neurology, University of Zagreb, School of Medicine and University Hospital Centre Zagreb, Zagreb, Croatia

P1505
THE ROLE OF DAT-SPECT IN DIFFERENTIAL DIAGNOSIS OF PARKINSONISM - FIRST EXPERIENCES IN THE SERBIAN POPULATION
T. Stojkovic¹, L. Brajkovic², E. Stefanova¹, V. Obradovic², V.S. Kostic¹
¹Movement Disorders Department, Neurology Clinic, Clinical Center of Serbia, ²Institute for Nuclear Medicine, Clinical Center of Serbia, Belgrade, Serbia

P1506
PERIPHERAL CROSS-NEUROTIZATION INDUCING UNAFFECTED HEMISPHERE REORGANIZATION TO ENHANCE THE MOTOR CONTROL OF THE SPASTIC HEMIPLEGIC HAND IN CENTRAL NEUROLOGIC INJURY
W.-D. Xu, J.-G. Xu, Y.-D. Gu
Department of Hand Surgery, Huashan Hospital, Fudan University, Shanghai, China

P1507
MIRROR MEETING AS A WAY TO EVALUATE PATIENTS’ IMPRESSIONS OF TREATMENT EFFECTS OR COMPLICATIONS IN DUODOPA THERAPY
S.W. Pedersen, J. Clausen
University of Copenhagen, Glostrup, Denmark

P1508
QUANTITATIVE DIFFERENTIATION OF PARKINSON’S DISEASE (PD), MULTIPLE SYSTEM ATROPHY (MSA), AND PROGRESSIVE SUPRANUCLEAR PALSY (PSP): IN VIVO 1H MRS AND DWI STUDY
I. Karaban¹, Z. Rozhko², N. Karaban¹
¹Extrapyramidal Disorders, Institute of Gerontology of the Academy of Medical Sciences of Ukraine, ²Radiology, Medical Clinic ‘BORIS’, Kiev, Ukraine

P1509
SYNERGETIC EFFECT OF INTRATHECAL BACLOFEN AND DEEP BRAIN STIMULATION IN TREATING DYSTONIA
Y. Awaad
KFMC, Riyadh, Saudi Arabia

P1510
ACUTE REVERSIBLE CHOREODYSTONIA AND BASAL GANGLIA LESIONS ASSOCIATED WITH HEMODIALYSIS
A.S.A. Correia¹, C. Jordão², C. Santos³, J. Vale⁴, P. Alegria⁴
¹Neurology, ²Neuroradiology, Hospital Egas Moniz (Centro Hospitalar de Lisboa Ocidental), Lisbon, ³Nephrology, Nephrocare Torres Vedras, Torres Vedras, ⁴Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisbon, Portugal

P1511
A CASE OF COMORBIDITY BETWEEN MULTIPLE SCLEROSIS AND MULTIPLE SYSTEM ATROPHY
M. Baldini¹, L. Kiferle¹, L. Petrucci¹, P. De Feo¹, C. Pecori¹, L. Pasquali¹, U. Bonuccelli¹,²
¹Department of Neuroscience, University of Pisa, Pisa, ²Neurology Unit, Hospital of Viareggio, Viareggio, Italy

P1512
FATIGUE IN DE NOVO PARKINSON’S DISEASE
S.Y. Kang¹, H.-I. Ma², Y.J. Kim², S.-B. Kwon¹, S.H. Hwang¹
¹Department of Neurology, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, ²Department of Neurology, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Republic of Korea
P1513
SIGNIFICANCE OF DIFFERENTIAL NEUROSCIENTIFIC ANALYSES OF BODY-BRAIN-BEHAVIOR RELATIONSHIPS IN PATIENTS WITH PARKINSON’S DISEASE
M. Gospodinov
Independent, Sofia, Bulgaria

P1514
VISUAL FIXATION CAN BE A PROMISING SENSORY-TRICK MANEUVER IN PATIENTS WITH CERVICAL DYSTONIA
D.-Y. Kwon, W.K. Seo, M.H. Park, K.W. Park
Neurology, Korea University College of Medicine, Ansan-City, Republic of Korea

P1515
INDICATION FOR MOTOR-LEARNING IN PATIENTS WITH PARKINSON’S DISEASE
J.P. Jakobsen¹, M.H. Rose¹, T.-T. Nielsen¹, A. Lokkegaard², S. Sonne-Holm³, B.R. Jensen¹
¹Department of Exercise and Sport Sciences, University of Copenhagen, ²Department of Neurology, Bispebjerg University Hospital, ³Department of Orthopaedic Surgery, Hvidovre University Hospital, Copenhagen, Denmark

P1516
THE USE OF POSTURAL STABILITY TESTS IN THE DIAGNOSIS OF HEREDITARY ATAXIA
J. Schwabova¹, F. Zahálka², P. Hrásky², V. Komárek³, A. Zumrová³
¹Department of Neurology, ²2nd Medical Faculty and Motol Hospital, ³Biomedical Laboratory, Faculty of Physical Education and Sport, ³Department of Pediatric Neurology, ²2nd Medical Faculty and Motol Hospital, Prague, Czech Republic

P1517
PSYCHIATRIC ADVERSE EFFECTS IN PARKINSON’S DISEASE PATIENTS TREATED WITH LEVODOPA OR DOPAMINE AGONISTS
C.-J. Lu, Y. Sun
En Chu Kong Hospital, Taipei, Taiwan R.O.C.

P1518
PAIN AND OTHER NON-MOTOR SYMPTOMS IN PARKINSON’S DISEASE
N. Demchuk
Neurology, Perm State Academy of Medicine, Perm, Russia

P1519
THE CLINICAL AND PSYCHOLOGICAL PECULIARITIES OF RESTLESS LEGS SYNDROME IN PATIENTS WITH LUMBOSACRAL RADICULOPATHY
A. Cucovici, I. Moldovanu, S. Pleșća
Neurology, State Medical and Pharmaceutical University ‘Nicolae Testemitanu’, Chisinău, Moldova

P1520
YOUNG-ONSET CORTICOBASAL DEGENERATION
E.C. Rosca¹, M. Simu¹, S. Ples², R.D. Chirileanu¹
¹Department of Neurology, University of Medicine and Pharmacy ‘Victor Babes’ Timisoara, ²Department of Neurosurgery, Clinical Emergency County Hospital Timisoara, Timisoara, Romania

P1521
VEGETATIVE MANIFESTATIONS OF PARKINSON’S DISEASE
R.I. Matmurodov, K.M. Khalinova, M.M. Raimova
Tashkent Medical Academy, Tashkent, Uzbekistan

P1522
STIMULATION INDEPENDENT SUSTAINED REMISSION FOLLOWING THE LONG-TERM PALLIDAL DBS IN AXIAL DYSTONIA
A. Tomskiy¹, A. Gamaleyev², N. Fedorova², V. Shabalov¹
¹Burdenko Neurosurgical Institute RAMS, ²Russian Medical Academy of Postgraduate Education, Center for Extrapyramidal Disorders, Moscow, Russia