Movement disorders 1

P1521

Interim results from an international, open-label study of levodopa-carbidopa intestinal gel in patients with advanced Parkinson’s disease: efficacy results by country


1Klinikum-Bremerhaven, Bremerhaven, Germany, 2Skåne University Hospital, Lund, Sweden, 3University of Cincinnati Academic Health Center, Cincinnati, OH, 4Northwestern University, Chicago, IL, 5University of South Florida, Tampa, FL, 6Cleveland Clinic, Cleveland, OH, 7University of Alabama at Birmingham, Birmingham, AL, 8Abbott, Abbott Park, IL, USA

Introduction: Fluctuating blood levels of levodopa are associated with motor complications in Parkinson’s disease (PD). Levodopa-carbidopa intestinal gel (LCIG) is delivered continuously via a percutaneous endoscopic gastrojejunostomy (PEG-J) tube.

Methods: An international, 54-week, open-label study of LCIG in patients with advanced PD experiencing motor fluctuations despite optimized standard therapy is ongoing (NCT00335153). Individualized LCIG dosing was instructed to be 16 hr/day. Efficacy outcomes included “Off” time and “On” time with and without troublesome dyskinesia (TD). Adverse events (AEs) were monitored. This interim analysis included assessments performed on or prior to the data cut-off date of Nov. 25, 2011. Efficacy and safety endpoints were tabulated across 16 enrolling countries.

Results: At data cut-off, 354 subjects had nasojejunal tube insertion and 323 had received subsequent PEG-J tube. Across countries, mean [SD] baseline values ranged from: Age, 53.9[6.3]-70.1[6.9] yrs; PD duration, 9.2[3.9]-16.0[6.4] yrs; “Off” time, 5.7[1.9]-8.4[3.3] hr/day; “On” time without TD, 6.7[2.9]-8.5[2.7] hr/day; “On” time with TD, 0.2[0.6]-2.3[2.2] hr/day. In each country, the change from baseline in “Off” time and “On” time without TD was significantly improved (p<0.05) as early as week 4, and sustained through week 54. At week 54, mean [SD] “Off” time improvements ranged from -3.4[3.9] to -5.8[2.7] hr/day, and improvements in “On” time without TD ranged from 4.1[3.8]-6.3[3.5] hr/day. Additional analyses of baseline characteristics across countries will be included in the presentation. AE profiles were similar across countries.

Conclusions: LCIG consistently improved motor symptoms and resulted in similar AE profiles across countries.

Support: Abbott

P1522

A panel of five CSF biomarkers can be used with high accuracy in the differential diagnosis of patients with dementia and/or parkinsonism

S. Hall1,2, A. Öhrfelt3, R. Constantinescu4, U. Andreasson2, Y. Surova1,2, F. Bostöm5,6, C. Nilsson8, H. Widner2,7, H. Decraemer3, K. Nägga1,7, L. Minthon1,7, E. Londos1,7, E. Vanmechelen7, B. Holmberg1, H. Zetterberg1, K. Blennow1, O. Hansson1,2,5

1Department of Clinical Sciences, Lund University, 2Department of Neurology, Skåne University Hospital, Lund, 3Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at University of Gothenburg, 4Department of Neurology, Sahlgrenska University Hospital, Gothenburg, 5Neuropsychiatric Clinic, Skåne University Hospital, Malmö, 6Department of Cognitive Medicine, Skåne University Hospital, Lund, Sweden, 7ADx NeuroSciences, Gent, Belgium

Introduction: Due to overlapping symptomatology, it can be difficult to clinically distinguish Parkinson’s disease (PD) from atypical parkinsonism, i.e. multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD). There is also an overlap in clinical symptoms and brain pathologies between dementia disorders, including Alzheimer’s disease (AD), dementia with Lewy bodies (DLB) and PD with dementia (PDD). There is thus a need for biomarkers to improve the diagnosis of these disorders.

Method: CSF samples (n=453) were obtained from controls, subjects with PD, PDD, DLB, AD, PSP, MSA and CBD. A newly developed Luminex multiplex assay was used for simultaneous quantification of α-synuclein, Aβ42, T-Tau and P-tau. ELISA was used to analyze NF-L.

Results: CSF α-synuclein was decreased in patients with PD, PDD, DLB and MSA, but increased in AD. CSF β-amyloid1-42 was decreased in DLB, but even further decreased in AD. CSF T-Tau and P-tau were increased in AD. Multivariate analysis revealed that these four biomarkers could differentiate AD from DLB and PDD with an AUC of 0.90, where α-synuclein and T-Tau contributed most to the model. NF-L was substantially increased in AD. Multivariate analysis revealed that NF-L alone could differentiate PD from atypical parkinsonian disorders with an AUC of 0.93.

Conclusions: CSF α-synuclein improves the differential diagnosis of AD vs. DLB and PDD, and when combined with established AD-biomarkers the diagnostic accuracy reaches 90%. Neurofilament light chain alone can differentiate PD from atypical parkinsonian disorders with an accuracy of 93%.
Assessing postural stability in early Parkinson’s disease - how valid are commonly used clinical assessment tests?

I.M. Claesson1,2, A. Ståhle1

1Institution of Neurobiology, Care Sciences and Society, Karolinska Institutet, 2Division of Physiotherapy, Karolinska Universitetssjukhuset, Stockholm, Sweden

Background: Postural instability is an important symptom of Parkinson’s disease (PD) that may cause problems in daily life. It is, therefore, important to screen for this problem to identify those at risk for falling and to reduce hazardous falls. The primary aim of this study was to examine the suitability of different clinical assessment tests for the screening of postural stability in early PD.

Methods: 28 people with idiopathic PD were assessed with commonly used clinical assessment tests, i.e. the Berg Balance Scale (BBS), Timed Up and Go (TuG), Timed Up and Go-cognition (TuG-cog), the Modified Figure of Eight (MFE), walking 30 meters at self-paced and maximum speeds, together with disease severity rating, self-reported fall history, the Falls Efficacy Scale-International (FES-I) and the Freezing of Gait Questionnaire (FOG-Q). The Bäckstrand, Dahlberg, and Liljenäs Balance Scale (BDL), with more complex balance demands, was also validated. Correlations between the different assessment tests, questionnaires, ratings of disease severity, and fall history were calculated.

Results: Tests that included walking with a turning task were more predictive of risk of fall and more highly correlated to the disease severity rating scales than were the other tests. The questionnaires FES-I and FOG-Q did not correspond to actual falls or to disease severity.

Conclusions: To evaluate postural stability in early PD, we suggest a battery of tests that includes the TuG, the TuG-cog, and the MFE. For evaluating exercise intervention in early PD the BDL is a better test than the BBS.

Dystonia in corticobasal degeneration: a review of the literature on 404 pathologically proven cases

M. Stamelou, A. Alonso-Canovas, K. Bhatia

UCL Institute of Neurology, London, UK

Background: Dystonia is considered one of the classical features of corticobasal degeneration and is reported in up to 83% in clinical series.

Methods: We reviewed the literature on 404 pathologically proven cases and noted the presence, age at onset, distribution, evolution and treatment of dystonia, associated features and final clinical diagnosis.

Results: Dystonia was present in only 37.5% of the 296 cases, with adequate information. The majority of them presented with a corticobasal syndrome and dystonia occurred in the first two years from disease onset, affecting the upper limb. In phenotypes where dementia was the cardinal feature, dystonia tended to appear later in the disease course and to affect more cervical region and face. 54% of 374 cases, where the phenotype was available, presented as corticobasal syndrome, 15% as frontotemporal dementia and 10.7% as progressive supranuclear palsy. 48.8% of corticobasal syndrome cases presented with dystonia, 51.5% with myoclonus, 86.3% with apraxia and 100% with akinetic-rigid syndrome.

Conclusion: Despite dystonia being an inclusion criterion in all sets of clinical criteria for corticobasal degeneration, this was present in only one third of the pathologically proven cases presented here. Dystonia and myoclonus were present in about half of all cases with corticobasal syndrome, implying that these features may not be that frequent in corticobasal syndrome as are akinetic-rigid syndrome and apraxia. Dystonia and myoclonus almost co-occurred in our analysis, suggesting a possible association. More accurate characterization of dystonia in corticobasal degeneration would be of importance for clinical diagnosis and development of treatment strategies.
P1525

Clinical features of corticobasal syndrome with midbrain atrophy

R. Hayashi, T. Oeda, A. Umemura, M. Kousaka, S. Tomita, H. Nakano, H. Sawada

Clinical Research Center and Neurology, National Hospital of Utano, Kyoto, Japan

Introduction: Mesencephalic tegmentum atrophy can be a maker for progressive supranuclear palsy (PSP). However, patients with corticobasal syndrome (CBS) often share common pathological and clinical features with PSP, and some cases show midbrain atrophy (MA). The purpose of this study was to clarify clinical features in CBS with MA comparing that without MA.

Methods: 34 patients with CBS (male 32%, age 72.7±7.6), 46 patients with PSP (male 67%, age 73.1±7.3), and 31 healthy controls (male 45%, age 66.7±12.1) were investigated. Midbrain area was measured on planimetry using mid-sagittal MRI. The cut-off point of midbrain area discriminating between PSP and control was 112mm² (sensitivity 91.3%, specificity 90.3%). We classified CBS patients into two groups, CBS with MA (≤112mm²) and without MA (>112mm²), and compared clinical features such as age, sex, FAB, MMSE, postural instability with fall ≤2 years (PIF) and vertical gaze palsy (VGP) between the groups. The clinical factors which are independently associated with MA were identified by a general linear model.

Results: Comparing the clinical factors in the two groups, patients with MA were older and more often showed PIF and VGF than patients without MA. The general linear model analysis revealed that MA was independently associated with PIF (β 21.3, p=0.004), VGP (β 13.8, p=0.043) and FAB score (β 3.4, p=0.007).

Conclusion: MA in patients with CBS was associated with PSP-like features.

P1526

Characterization of gait disturbance in patients with normal pressure hydrocephalus

R. Schniepp¹, M. Wuehr², C. Pradhan², K. Jahn¹

¹Neurology, University of Munich, ²Integrated Research and Treatment Center for Vertigo, Oculomotor and Balance Disorders, University Munich, Germany

In normal pressure hydrocephalus (NPH) a disturbance of gait is typically the first symptom to appear. The most common test for the outcome of a shunt operation is a CSF tap test. In this study we investigated which gait parameters positively respond to CSF tapping and at which time period after tapping this response is most pronounced. The study cohort comprised 41 patients (72.2±10.0 years, 12 females). Gait analysis was performed on a pressure-sensitive gait carpet (GaitRITE®). Patients were tested under two different speed-, two cognitive dual-task- and one motor dual-task-condition. A Principal Component Analysis was performed in order to identify relevant gait parameters. Extracted parameters were then analyzed at different time points and under different gait analyses. Positive effects of CSF tapping were most pronounced during walking with preferred walking speed. Patients did also show improvements while walking with maximal speed and for the motor dual-task but not for the two cognitive dual task conditions. Velocity, stride length, stride time and double support time were the parameters that responded most positively (p<0.01). In nearly all cases improvements were detectable not till 12h or even 48h after the CSF tapping. These results indicate that in a multi-parametric analysis of the preferred walking pattern covers a positive CSF tap test best. In addition, gait examinations immediately after the CSF tap test will overlook most gait improvements and therefore gait assessments at later time points are necessary to detect all positive effects on the walking performance.
P1527  

Prepulse inhibition in idiopathic REM sleep behaviour disorder, Parkinson's disease and multiple system atrophy  

M. Zoetmulder1,2,3, H.B. Biernat1, M. Nikolic4, L. Korbo1, P.J. Jennum2,3  
1Neurological Department, Bispebjerg Hospital, Copenhagen, 2Danish Center for Sleep Medicine, Department of Clinical Neurophysiology, Glostrup Hospital, Glostrup, 3Center for Healthy Aging, University of Copenhagen, 4Department of Clinical Neurophysiology, Glostrup Hospital, Glostrup, Denmark  

Introduction: Prepulse inhibition (PPI) of the acoustic startle response is a measure of sensorimotor gating, in which a weaker prestimulus (prepulse) inhibits the reaction of an organism to a subsequent strong startling stimulus (pulse). The objective of this study was to determine whether patients with idiopathic REM sleep behaviour disorder (iRBD), Parkinson's disease (PD) and multiple system atrophy (MSA) have altered PPI.  

Methods: 21 PD patients with RBD, 20 PD patients without RBD, 12 with iRBD, 10 with MSA and 20 healthy and gender-matched controls entered and completed the study. A passive acoustic PPI paradigm was applied with prepulses 5dB and 15dB above background noise at 30-, 60-, 120- and 300-ms intervals.  

Results: Startle-response characteristics (latency and habituation) did not differ between patients and controls (p≤0.05). Non-parametric analyses showed that MSA patients had a significantly lower PPI than the other groups for the 60ms - 85dB and 120ms - 85dB prepulses. No differences in PPI were found between the other groups.  

Conclusion: The present study suggests that prepulse inhibition is markedly altered in MSA. Since striatal dopaminergic function and the pedunculopontine nucleus (PPN) play a major role in prepulse inhibition, these results are in line with the functional involvement of the striatum and PPN in the pathogenesis of multiple system atrophy.

P1528  

Hip fractures in people with idiopathic Parkinson's disease: incidence and outcomes  

R. Rutherford1, R. Hancock1, A. Chaplin2, W. Gray3, R. Walker1  
1Medical School, Newcastle University, Newcastle Upon Tyne, 2Medicine, Northumbria Healthcare NHS Foundation Trust, Ashington, 3Medicine, Northumbria Healthcare NHS Foundation Trust, North Shields, UK  

Introduction: People with Parkinson’s disease (PD) are thought to be at increased risk of hip fracture compared to the general population, with poorer outcomes post-surgery. The aim of this audit was to establish the incidence of, and outcomes from, hip fracture in people with and without PD living in north-east England.  

Methods: Data from two previous prevalence studies in the same geographical area was used to estimate the number of people with PD living in the study area. Using data collected prospectively for the UK national hip fracture database, the annual incidence of hip fracture in people with and without PD was calculated. Type of fracture, time to surgery, time to discharge and 30-day outcomes from surgery were compared for PD and non-PD patients.  

Results: The annual incidence of hip fracture was significantly higher in people with PD across all age bands. In those aged 60 years and over it was 2032 (95% CI 1945 to 2121) per 100,000 in people with PD and 552 (95% CI 507 to 599) per 100,000 in people without PD. The experience of PD and non-PD patients within hospital was remarkably similar. However, PD patients had poorer mobility prior to hip fracture, took longer to be discharged to the community, and were less mobile post-surgery.  

Conclusions: People with PD have a significantly higher incidence of hip fracture than people without PD and post-surgical outcomes are poorer. Specific guidelines for managing people with PD who sustain a hip fracture may improve outcomes.
P1529

Cost effectiveness of Apomorphine infusion in the treatment of advanced Parkinson’s disease in the UK

E. Walter, D. Merksans
Institute for Pharmaeconomic Research, Vienna, Austria

Objectives: Parkinson’s disease (PD) is the second commonest neurological disability and affects 100-180 people per 100,000 of the population and increases with age. Continuous subcutaneous apomorphine represents an alternative treatment option of advanced PD with motor-fluctuation. The purpose of this analysis was to estimate the cost-effectiveness of Apomorphine infusion (APO) compared with Levodopa/carbidopa intestinal gel (LCIG), Deep-Brain-Stimulation (DBS) and Standard-of-care (SOC).

Methods: We developed a Markov-Model to simulate the long-term consequences, disease progression (Hoehn&Yahr-stages 3-5, percentage of waking-time in the OFF-state), complications and adverse-events. Complications are different for the alternatives (e.g. pump problems in case of LCIG, temporary/permanent complications in case of DBS). We include moderate and severe adverse-events and death. Monte-Carlo-simulation accounted for uncertainty. The model includes 25 health-states. Probabilities were derived from RCT and open-label studies; direct costs (2012 £) from published sources from the payer’s perspective. QALYs, life-years and costs were projected over a life-time horizon and discounted at 3.5%.

Results: Over a life-time horizon, costs associated with apomorphine amounts to 46,053.42£ and 2.05 QALYs (4.4 LYs). Costs associated with LCIG are 92,753.42£ and 2.40 QALYs (5.3 LYs). The cost-saving amounts to 46,700£ per patient and the incremental-cost per QALY gained (ICER) was 129,903£. Costs associated with DBS are 61,893.08£ and 2.16 QALYs (4.98 LYs). Apomorphine dominates DBS. ICER amounts to 143,215.73£ favourable for apomorphine. SOC associated total-costs are 60,312.19£ and 1.75 QALYs (4.04 LYs). Apomorphine dominates SOC.

Conclusion: Apomorphine is a cost-effective alternative, reducing OFF-time and improving quality-of-life, and is associated with a cost-advantage.

P1530

The influence of striatal dopamine on the modulation of upper limb locomotor synergies

I.U. Isaias¹²³, A. Cattaneo¹, J. Volkmann¹, A. Marzegan¹, G. Marotta⁴, P. Cavallari¹, G. Pezzoli²
¹Dipartimento di Fisiologia Umana, L.A.M.B. P.&L. Mariani, Università degli Studi di Milano, ²Centro per la Malattia di Parkinson e i Disturbi del Movimento, Istituti Clinici di Perfezionamento, Milan, Italy, ³Neurologische Klinik und Poliklinik, Universitätäsklinik Würzburg, Germany, ⁴Dipartimento di Medicina Nucleare, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy

Introduction: Reduced arm swing while walking is a clinical hallmark of Parkinson’s disease (PD) suggesting a direct involvement of the basal ganglia.

Aim: We investigated the role of striatal dopamine on the modulation of upper limb synergies during walking at different velocities.

Method: Patients were recruited according to several inclusion criteria, including normal spatio-temporal parameters of the stride at preferred gait speed. After 3-day drugs-off state, 13 patients and 10 healthy controls (HC) were asked to walk at preferred, slow and fast speed (12 trials). Kinematics were measured using an optoelectronic system. Striatal dopaminergic innervation was measured by FP-CIT and SPECT.

Result: At preferred gait speed, all patients showed reduced range of motion (ROM) at one arm and four bilaterally. In PD, ROM of the most affected arm (median: 7°, range: 3.9°-16.3°) was significantly reduced compared to HC (median: 25.27°, range: 14.6°-29.1°; p<0.01). The range of gait velocities (Km/h) was similar between patients (range: 1.93-7.81, median: 3.49) and HC (range: 1.24-8.15, median: 3.76). While walking at different velocities, patients modulated arm swing similarly to HC (RSquare average, PD: 0.51; HC: 0.71; p<0.001 both), although to a lesser extent (no statistical significance). Such a modulation, measured as linear correlation slope, as well as arm ROM reduction at preferred gait speed, was not predicted by contralateral striatal dopaminergic loss and clinically tested rigidity or bradykinesia.

Conclusion: Rather than striatal dopaminergic tone per se, mesencephalic centres (i.e. PPN and reticular system) might be involved in the modulation of upper limb locomotor synergies.
P1531

Association between irritable bowel syndrome and restless legs syndrome: a comparative study with control group

R. Borji1, S.-M. Fereshtehnejad2, S. Tabataba Vakili3, N. Ebrahimi Daryani2, H. Ajdarkosh1
1Tehran University of Medical Sciences, Tehran, Iran, 2Neurobiology, Care Sciences & Society (NVS), Karolinska Institutet, Stockholm, Sweden, 3Shaheed Beheshti University of Medical Sciences, Tehran, Iran

Background: As a common gastrointestinal (GI) disorder, irritable bowel syndrome (IBS) has been reported to be associated with some psychological and neurological factors. This study aimed to evaluate the prevalence rate of restless legs syndrome (RLS) in a sample of IBS patients and to compare this prevalence with that of matched healthy controls.

Methods: This prospective comparative study was conducted in Tehran, Iran during 2010 and 2011. Based on the Rome III criteria, a total number of 225 definite IBS patients and 262 age- and sex-matched healthy controls were recruited in the final assessment to compare the prevalence rate of RLS between the two groups.

Results: RLS was significantly more frequent in IBS group (25.3% vs. 6.5%, p<0.001) which leads to an odds ratio (OR) of 4.89 (95%CI: 2.75-8.70). IBS patients with comorbid RLS suffered significantly more from stomach pain [96.5% vs. 86.3%, OR=4.36 (95%CI: 1.91-9.60)], nausea [40.4% vs. 21.4%, OR=2.48 (95%CI: 1.3-4.73)] and vomiting [10.5% vs. 2.4%, OR=4.82 (95%CI: 1.31-17.76)].

Conclusion: Having enrolled a considerable number of IBS patients and healthy controls, our study showed a significantly higher prevalence of RLS in IBS patients. Surprisingly, a higher prevalence rate of RLS was also accompanied by a more severe discomfort and stomach pain in IBS patients. It seems that screening patients with IBS for RLS may lead to greater identification of RLS and improved treatment of both conditions.

P1532

Longstanding idiopathic dystonia preceding Parkinson’s disease

R. Modreanu, Y. Compta, M.J. Marti
Parkinson’s Disease & Movement Disorders Unit, Hospital Clinic, Barcelona, Spain

Introduction: There are few descriptions of idiopathic dystonia preceding in years or even decades the onset of idiopathic Parkinson’s disease (PD). These reports pointed to a possible common etiologic mechanism.

Patients and methods: We reviewed the medical records of patients with initial focal dystonia who had been followed in our clinic and further developed PD. Data about demographic, clinical and genetic features, and response to treatment of dystonia and parkinsonism were collected retrospectively.

Results: There were 7 patients (5 men and 2 women), with a mean age of dystonia onset of 47 (35 to 52) years and a mean age of PD onset of 60 (55 to 63) years. The time between dystonia and parkinsonism ranged from 3 to 28 years (median 15.3). 2 patients presented with writer’s cramp, 3 with blepharospasm, 1 with cervical and 1 with segmental (cranio-cervical) dystonia. 5 patients had a mixed parkinsonism (with resting tremor) and 2 a rigid-akinetic type. Genetic tests for LRKK2 and parkin mutations were performed in 5 patients and were negative. 5 patients received anticholinergics for dystonia without improvement. All received levodopa and 5 of them also dopaminergic agonists with good response of parkinsonism, but no changes in dystonia.

Conclusions: The co-existence of dystonia with parkinsonism suggests a possible common pathophysiological mechanism. The previous descriptions of dystonia preceding parkinsonism in PD antedated the discovery of monogenetic causes of parkinsonism which can in turn present with dystonia, but in our short series such mutations do not appear to underlie this uncommon association.
**P1533**

**Unmyelinated axons are more vulnerable to degeneration than myelinated axons of the cardiac nerve in Parkinson's disease**

S. Orimo1, T. Uchihara2, Y. Itoh1, A. Kakita4, K. Wakabayashi3, H. Takahashi4

1Kanto Central Hospital, 2Tokyo Metropolitan Institute of Medical Science, 3Yokufukai Geriatric Hospital, Tokyo, 4University of Niigata, Niigata, 5Hirosaki University Graduate School of Medicine, Hirosaki, Japan

**Aims:** The aim of this study is to determine whether there is a difference in the degenerative process between unmyelinated and myelinated axons of the cardiac nerve in Parkinson's disease (PD).

**Background:** We recently reported cardiac sympathetic denervation in PD and dementia with Lewy bodies, which accounts for the reduced cardiac meta-iodobenzylguanidine (MIBG) uptake on MIBG myocardial scintigraphy in these disorders. Furthermore, we demonstrated accumulation of [alpha]-synuclein aggregates of the cardiac sympathetic nerve in PD and a possible relationship between degeneration of the cardiac sympathetic nerve and [alpha]-synuclein aggregates.

**Methods:** We immunohistochemically examined cardiac tissues from 4 pathologically verified PD patients, 9 patients with incidental Lewy body disease (ILBD) and 5 control subjects, using antibodies against neurofilament, myelin basic protein (MBP) and α-synuclein. First, we counted the number of neurofilament-immunoreactive axons not surrounded by MBP (unmyelinated axons) and those surrounded by MBP (myelinated axons). Next, we counted the number of unmyelinated and myelinated axons with α-synuclein aggregates.

**Results:** (i) The percentage of unmyelinated axons in PD (77.5±9.14%) was significantly lower compared to that in control subjects (92.2±2.40%). (ii) The ratio of unmyelinated axons with α-synuclein aggregates to total axons with α-synuclein aggregates in ILBD ranged from 94.4 to 100 (98.2±2.18%). Among axons with α-synuclein aggregates, unmyelinated axons were the overwhelming majority, comprising 98.2%.

**Conclusion:** These findings suggest that in PD unmyelinated axons are more vulnerable to degeneration than myelinated axons of the cardiac nerve, because α-synuclein aggregates accumulate much more abundantly in unmyelinated axons.

---

**P1534**

**Eye movement abnormalities in essential tremor and other neurodegenerative diseases (Parkinson's disease, spinocerebellar ataxia, Huntington's disease)**

M. Wojcik-Pedziwiatr1, M. Rudzinska1, K. Zajdel2, T. Tomaszewski1, A. Szczudlik1

1Department of Neurology, 2Department of Otolaryngology, Jagiellonian University Medical College, Krakow, Poland

**Introduction:** Eye movement abnormalities are a common sign of many neurodegenerative diseases like Parkinson’s disease (PD), spinocerebellar ataxia (SCA) or Huntington’s disease (HD). Even though essential tremor (ET) is the most prevalent movement disorder, the spectrum of eye movement abnormalities for this disease has not been entirely explored yet.

**Aim:** To evaluate eye movement abnormalities in ET patients in comparison with controls matched according to age and gender and patients with other neurodegenerative diseases like PD, SCA and HD and to assess the relations between eye movement abnormalities and other signs as well as course of ET.

**Material and methods:** 50 ET and 50 PD matched according to age and gender, 42 SCA, 50 HD patients as well as 42 healthy controls were included in the study. Saccades were recorded using portable Saccadometer from Ober Consulting company. EOG (Hortman) was used for recording of smooth pursuit, OKN and fixation.

**Results:** The study showed that eye movement abnormalities are considerably more common in ET patients than in healthy subjects and their frequency in ET is similar to other neurodegenerative diseases like PD, SCA and HD. The most typical eye movement disturbances in ET were: reflexive saccades dysmetria, smooth pursuit and OKN impairment. In ET patients with concomitant cerebellar signs volitional saccade latency prolongation was additionally detected. The frequency of reflexive saccades dysmetria in ET increases with disease progression.

**Conclusion:** Eye movement abnormalities are a common sign of ET like other neurodegenerative diseases and their frequency increases with disease progression.
P1535

White matter damage in Parkinson’s disease patients with glucocerebrosidase gene mutations: a study using diffusion tensor imaging

F. Agosta1, K. Davidovic1, L. Sarro2, N. Kresojević3, M. Svetel1, I. Stanković3, N. Kresojević3, M. Filippi2

1Neuroimaging Research Unit, 2Neuroimaging Research Unit and Department of Neurology, Vita-Salute San Raffaele University and San Raffaele Scientific Institute, Milan, Italy, 3Clinic of Neurology, Faculty of Medicine, University of Belgrade, Serbia, 4Department of Neurology, Vita-Salute San Raffaele University and San Raffaele Scientific Institute, Milan, Italy, 5Clinic of Neurology, Faculty of Medicine, University of Belgrade, Serbia

Objective: To investigate brain white matter (WM) damage in patients with Parkinson’s disease (PD) carrying glucocerebrosidase (GBA) gene mutations.

Methods: Among 360 PD patients screened for mutations of the GBA gene, 19 (5.3%) heterozygous mutation carriers were identified. 15 (mean age 64 years, mean age at onset 57 years, median Hoehn and Yahr [HY] stage score 3.0), were found to be heterozygous for N370S (6 cases), D409H (6 cases), D380V (1 case), E388K (1 case) and L444P (1 case) GBA mutations, were enrolled in this study. 20 PD patients without GBA mutations (mean age 63 years, mean age at onset 56 years, median HY stage score 3.0) and 16 healthy controls (mean age 64 years) were also studied. Diffusion tensor imaging (DTI) scans were obtained from all subjects. Tract-based spatial statistics were used to perform a brain voxel-wise analysis of mean diffusivity (MD) and fractional anisotropy (FA).

Results: Compared to controls, GBA mutation PD carriers showed an increased MD of the genu of the corpus callosum and a decreased FA of the corpus callosum, cingulum, external capsule, anterior thalamic radiations, bilaterally, and right superior longitudinal fasciculus (p<0.05, family-wise error corrected). PD patients without GBA mutations did not show significant DT MRI abnormalities when compared with healthy controls.

Conclusions: PD patients carrying GBA mutations show WM abnormalities involving the interhemispheric, limbic and associations tracts. Future research will clarify whether WM damage in these patients may have an impact on the clinical phenotype, in particular on the development of cognitive impairment.

P1536

Clinicopathological correlation of progressive supranuclear palsy presenting with corticobasal syndrome

H. Ling1, R. de Silva1, L. Massey1, N. Bajaj2, J. Lowe2, J. Holton3, A. Lees1, T. Revesz5

1Reta Lila Institute of Neurological Studies, Institute of Neurology, University College London, 2University of Nottingham, 3Queen Square Brain Bank for Neurological Studies, Institute of Neurology, University College London, UK

Aim: We aimed to characterise the clinical and pathological features of 10 progressive supranuclear palsy (PSP) cases with a clinical presentation of corticobasal syndrome (PSP-CBS) and to compare these with 10 PSP cases with a classical presentation of Richardson’s syndrome (PSP-RS).

Background: The clinical presentation of CBS has been associated with PSP pathology and is clinically characterized by asymmetric limb dystonia, rigidity, apraxia, the alien limb phenomenon and cortical sensory loss.

Methods: Morphometry with a stereological approach was used for tau load quantitation.

Results: Only 3.9% of PSP cases in the Queen Square Brain Bank presented with a CBS. All PSP-CBS cases had marked asymmetrical features with a clumsy useless limb, in association with apraxia, hand dystonia, myoclonus and the alien limb phenomenon, cortical sensory loss and delayed initiation of horizontal saccades. Neuropathologically, both PSP groups had similar total tau load (p=0.18). However, analysis of the regional tau load revealed a shift of tau pathology from the basal ganglia (p=0.003) towards the cortical regions (p<0.001) in PSP-CBS when compared to PSP-RS.

In PSP-CBS, the presence of delayed initiation of horizontal saccades was associated with a greater parietal tau load (r=0.6; p<0.001).

Conclusions: We conclude that PSP-CBS is a cortical predominant subtype of PSP characterized by a shift of tau burden from the basal ganglia towards the cortices. Early falls and vertical supranuclear gaze palsy, when present, might be helpful in predicting PSP pathology in patients presenting with CBS.
P1537
Randomized, double-blind, double-dummy study of levodopa-carbidopa intestinal gel in patients with advanced Parkinson’s disease: efficacy analyses by subgroups
1IRCCS San Camillo, Venice, 2University of Padua, Italy, 3Abbott, Abbott Park, IL, USA

Introduction: Fluctuating blood levels of levodopa are associated with motor complications in Parkinson’s disease (PD). Levodopa-carbidopa intestinal gel (LCIG) is delivered continuously via an intrajejunal percutaneous gastrostomy tube.

Methods: A double-blind, double-dummy trial evaluated LCIG compared with oral levodopa-carbidopa immediate-release (IR) therapy in patients with advanced PD and motor fluctuations. Levodopa-responsive patients received LCIG infusion+placebo capsules or encapsulated levodopa-carbidopa IR tablets+placebo gel infusion for 12 weeks. The primary endpoint was the change from baseline to week 12 in “Off” time normalized to 16 waking hours. “On” time without troublesome dyskinesia was a key secondary outcome. Efficacy was analyzed by subgroups including gender, age (<65 or ≥65 years), disease duration (<10 or ≥10 years), and number of PD medications at baseline (≤2 or ≥3).

Results: 71 patients were randomized (n=37 LCIG; n=34 IR), and 66 (93%) completed the trial. LCIG significantly improved “Off” time (LS mean difference = -1.91hr; p=0.0015) and “On” time without troublesome dyskinesia (LS mean difference =1.86hr, p=0.0059) compared with IR. Subgroup analyses of the change from baseline in “Off” time revealed no statistically significant interaction of treatment group by gender (p=0.589), disease duration (p=0.135), age (p=0.935), or number of PD medications at baseline (p=0.237).

Conclusions: These results demonstrate the robust and consistent efficacy of LCIG, compared with optimized oral levodopa-carbidopa therapy, irrespective of differences in gender, age, PD duration, or number of PD medications at baseline.

Support: Abbott

P1538
Recognition of adult-onset dystonia over time (1970 to 2007): data from a multicenter Italian series
A. Macerollo1, G. Abbruzzese2, A.R. Bentivoglio3, R. Liguori4, L. Santoro5, A. Berardelli6, G. Defazio1
1Dept. of Neurosciences and Sense Organs, University of Bari, 2Department of Neuroscience, University of Genoa, 3Department of Neurosciences, Catholic University of Rome, 4Department of Neurological Sciences, University of Bologna, 5Department of Neurological Sciences, University ‘Federico II’ of Naples, 6Department of Neurology and Psychiatry, Sapienza University of Rome, Italy

Introduction: A dataset of 470 Italian patients, recruited between 2007 and 2008 at 7 Italian movement disorder centres, was checked in order to analyse the time elapsing between dystonia onset and diagnosis taking into account sex, education, place of birth and residence, year of birth, and type of dystonia.

Methods: The dataset included 318 women and 155 men with adult-onset dystonia aged 62±14 years. Mean age at dystonia onset was 51±14 years. Dystonia at presentation was blepharospasm (BSP, n=235), cervical dystonia (CD, n=185) and hand dystonia (FHD, n=50).

Results: The time elapsing from dystonia onset to diagnosis was 6 years on average. The diagnostic delay was less marked in the patients presenting with blepharospasm than in the other groups (5±7 vs. 8±8 years, p<0.05). The time elapsing from dystonia onset to diagnosis significantly decreased by increasing the year of diagnosis, but the percentage of patients who had <1 year elapsing between dystonia onset and diagnosis did not exceed 50% in the most recent time bin (> year 2000) (all patients, 47%; cranial dystonia, 50%; extra-cranial dystonia, 43%). It was chosen “one year” because this is the average diagnostic delay for Parkinson’s disease in western countries.

Confirmation that the year of diagnosis is a significant predictor of the percentage of patients who had <1 year elapsing between dystonia onset and diagnosis was obtained by binomial regression models.

Conclusions: Outside movement disorder centres the recognition of dystonia in Italy remains poor even in the years 2000. We suspect that a similar situation may be present in other western countries.
P1539

Nutritional status as a predictor of the mortality in patients with Parkinson’s disease

R. Motoyama1,2, T. Oeda1,2, Y. Hari1, R. Hayashi1,2, A. Umemura1,2, S. Tomita1,2, M. Kohsaka1,2, K. Yamamoto1,2, T. Konishi2, H. Sawada1,2
1Clinical Research Center; 2Department of Neurology, Utano National Hospital, Kyoto, Japan

Purpose: It has been reported that hypoalbuminemia increases the mortality rates in cancer or surgical operations. To evaluate the association between the nutritional status and mortality in patients with Parkinson’s disease (PD).

Methods: The cohort of 501 consecutive PD patients enrolled from July 2004 to March 2010 was followed until June 15th 2010. The concentrations of serum albumin, urea nitrogen, and creatinine, the lymphocyte counts and the body mass index (BMI) were regarded as nutritional status, and in addition, age, sex, disease duration, Hoehn-Yahr stages (HY), and dementia (yes/no according to DSM-IV) were obtained at the study entry. The association between the nutrition status and mortality was analyzed using Cox proportional hazard models and the relative risk of death was estimated as hazard ratios (HR).

Results: In the study period 22 patients died. Serum albumin concentration was negatively associated with the mortality in the Cox model adjusted for age, sex, disease duration, HY and dementia (yes/no) (p=0.014). The HR was 0.38 (per 0.5g/dl, 95% CI 0.18-0.82). Patients with albumin <3.8g/dl had a shorter lifetime than those with albumin ≥3.8g/dl (Log rank test p=0.010).

Conclusion: Serum albumin concentrations were a significant prognostic factor for the mortality in patients with PD.

P1540

Maintenance of constant steady state therapeutic plasma concentrations of levodopa following its continuous subcutaneous administration with carbidopa

O. Yacoby-Zeevi1, S. Oren1, P.A. LeWitt2
1Neuroderm, Ltd., Ness-Ziona, Israel; 2Neurology, Wayne State University School of Medicine and Henry Ford Hospital, West Bloomfield, MI, USA

Objective: To determine the pharmacokinetic (PK) profile of levodopa (LD) following continuous subcutaneous (SC) administration of carbidopa (CD) / LD.

Background: In PD, wearing-off between doses and dyskinesias are often related to variable circulating concentration of LD occurring with oral administration. Unfortunately, with available oral LD preparations, most patients with treatment fluctuations do not experience much improvement and the option of administering LD intravenously or intraduodenally (Duodopa) is costly, and invasive. Neuroderm proposes a practical alternative for maintaining more constant plasma concentrations of LD.

Methods: A proprietary LD/CD solution (designated ND0612), was continuously administered SC in pigs with PK measurements of LD and CD.

Results: Constant, dose-dependent steady-state plasma concentrations of LD were achieved during continuous SC administration of ND0612 for both LD and CD. By using only 2-4ml/day of SC ND0612, constant LD plasma concentrations could be maintained at values that are generally effective at maintaining anti-Parkinsonian control in humans. No safety or tolerability issues were detected.

Conclusions: The limitation of oral LD products is the marked variability in plasma concentrations of the drug. Using SC delivery of an LD/CD solution, we demonstrated a promising option for achieving consistency in plasma LD concentrations. A clinical application of this approach should achieve improved control of motor fluctuations in PD. Furthermore, frequent daily oral dosing with CD/LD can be avoided. This approach is currently under investigation in a randomized clinical trial (double-blind) of ND0612, evaluating the plasma LD PK profile as well as safety and tolerability.
**P1541**

**Rapid eye movement (REM) sleep behaviour disorder (RBD): a risk factor for cognitive impairment in Parkinson’s disease (PD)?**

R. Di Giacopo, D. Quaranta, C. Piccininni, C. Marra, A.R. Bentivoglio  
Neuroscience, Catholic University of Rome, Italy

**Background:** RBD is strongly associated with synucleinopathies, often heralding and later accompanying motor symptoms of PD and Lewy Body Dementia (DLB). The neuropsychological assessment in 24 idiopathic RBD patients revealed a cognitive impairment similar to those observed in patients with PD and DLB; it suggests a common pathophysiological mechanism underlying these conditions, according to Braak’s hypothesis. However, this theory in not confirmed in all PD cases. Our objective is to assess the relationship between the presence of RBD and the cognitive profile of non-demented patients with PD.

**Methods:** 47 patients with PD without dementia were evaluated by a standard neuropsychological battery assessing intelligence, episodic verbal and spatial memory, recall capacity, fluency, executive and visuospatial abilities. 25 patients fulfilled polysomnographic criteria for RBD. Bilateral t-tests were performed to compare differences between RBD-PD group and non-RBD-PD group.

**Results:** No significant differences between groups were found regarding age, schooling, depression assessment, Hoehn and Year stage (I-II), UPDRS III score, disease duration, levodopa equivalent daily doses (LEDD). Groups differed significantly for execution time in interference condition of the Stroop colour word test (p=0.002).

**Conclusions:** Our data confirm a previous study in that RBD-PD patients showed a lower cognitive performance compared to non-RBD-PD. The cognitive involvement in executive functions is very early, because our patients presented a mild motor phenotype (H&Y:1.87) compared to literature. Thus RBD may indicate a more pervasive neurodegenerative process in PD and can increase the risk of cognitive impairment in patients.

---

**P1542**

**Motor learning in primary cervical dystonia**

P. Katschnig1,2, P. Schwingenschuh1,2, M. Davare1, A. Sadnicka1, R. Schmidt2, J.C. Rothwell1, K.P. Bhatia1, M.J. Edwards1  
1Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, London, UK,  
2Department of Neurology, Medical University of Graz, Austria

**Introduction:** Motor sequence learning and motor adaptation rely on overlapping circuits predominantly involving basal ganglia and cerebellum. Given the importance of these neuro-anatomical structures to the pathophysiology of primary dystonia, and the previous finding of abnormal motor sequence learning in DYT1 gene carriers, we explored motor sequence learning and motor adaptation in patients with primary cervical dystonia.

**Methods:** 12 patients with cervical dystonia and 11 healthy age-matched controls were included. Subjects used a joystick to move a cursor from a central starting point to radial targets as fast and accurately as possible. Using this device, we recorded baseline motor performance, motor sequence learning and a visuomotor adaptation task.

**Results:** Baseline motor performance with random target presentation was normal except for higher peak velocity in patients with cervical dystonia. Patients and controls had similar levels of motor sequence learning and motor adaptation.

**Conclusion:** Our patients had significantly higher peak velocity compared to controls, with similar movement times, implying a different performance strategy. The preservation of motor sequence learning in cervical dystonia patients contrasts with the previously observed deficit seen in patients with DYT1 gene mutations, supporting the hypothesis of differing pathophysiology in different forms of primary dystonia. Normal motor adaptation may signify that previously documented cerebellar abnormalities in cervical dystonia might simply reflect unimportant “contamination” of a structure directly connected to the basal ganglia, or might represent a compensatory response to the primary pathophysiology within the basal ganglia.
P1543
PRRT2 mutations are a major cause of paroxysmal kinesigenic dyskinesia in the European population
INSERM, UMRS 975 and CNRS 7225 - CRICM, Paris, France

Introduction: Paroxysmal kinesigenic dyskinesia (PKD) is a rare disorder characterized by recurrent attacks of hyperkinetic movements. Mutations in the PRRT2 gene were recently identified in PKD patients. We studied the prevalence of PRRT2 mutations and characteristics of the patients in a European PKD population.

Methods: 34 consecutive PKD index cases (20 sporadic cases and 14 cases with family history) were recruited through the 1996-2011 database of our DNA bank. Each patient had a standardized neurological assessment. Molecular analysis of the PRRT2 coding sequence was performed in all index cases and their family members when available. In addition, 3 microsatellite markers were genotyped in the patients and their relatives.

Results: Mutations introducing premature termination codons were identified in 22/34 patients (65%) including 13/14 families and 9/20 sporadic cases. The previously described c.649dupC/pArg217ProfsX8 and c.629dupC/pAla211SerfsX14 were present in 19 and 1 cases respectively; we also report 2 novel mutations, each in one case: c.562C>T/pGln188X and c.649C>T/pArg217X. Segregation analysis of the mutations in the parents of 6 sporadic cases revealed 3 de novo mutations and incomplete penetrance in a transmitting parent in the 3 other cases. No founder effect was found for the c.649dupC mutation. The mutated group was characterized by a younger age of onset (9 years) compared to the negative patients (15 years; p<0.01).

Conclusion: Mutations in PRRT2 are a major cause of PKD in familial and sporadic cases in the European population.

P1544
Peripheral selective denervation for torticollis - long-term follow-up
T. Bergenheim1, M. Hariz2, R. Libelius3, E. Nordh3, E. Larsson1

Introduction: Spasmodic torticollis is a focal cervical dystonia that most often responds to botulinum toxin. However, not all patients respond to this treatment and some develop secondary resistance. In those cases, there are two surgical options, selective peripheral denervation (Bertrand procedure) and pallidal Deep Brain Stimulation (DBS). We report here on the Umeå experience of selective denervation.

Methods: 63 patients were operated. 4 patients were later re-operated due to recurrence or change in the pattern of the dystonia. The patients were assessed with the Tsui torticollis scale, VAS for pain, and the Fugl-Meyer Life Satisfaction scale before surgery, at 6 months, and long-term follow-up (mean 42 months).

Results: 6 months follow-up was available for 57 patients and long-term for 35. Mean score of Tsui scale was preoperatively 10.2, early post-op 4.1 (p<0.001), 6 months post-op 4.8 (p<0.001), and at long-term follow-up 5.3 (p<0.001). Mean VAS for pain was pre-operatively 6.2, at 6 months 4.3 (p<0.001), and at long-term follow-up 4.1 (p<0.01). Life satisfaction total score improved moderately from a mean of 43.3 to 46.6 at 6 months (p<0.05), and to 51.4 at long-term follow-up (p<0.05). No severe or long-lasting side effects were noted.

Conclusions: From our experience it can be concluded that selective peripheral denervation is a satisfactory neurosurgical option for treatment of otherwise refractory spasmodic torticollis when the muscles involved are surgically accessible for denervation. In patients with a widespread muscular involvement, pallidal DBS may be preferable.
P1545

Familial congenital mirror movements: phenotype and neurophysiological findings in a new family with incomplete penetrance

M. Bologna¹, A. Fasano¹, E. Iezzi¹, F. Di Biasio¹, L. Rocchi², M. Srour¹, A. Levert³, G. Rouleau³, A. Berardelli¹,²
¹Neuromed Institute, Pozzilli, ²Sapienza University of Rome, Italy, ³Hôpital Notre Dame, Montréal, QC, Canada

Introduction: Mirror movements (MMs) are involuntary movements of one side of the body that accompany intentional movements on the opposite side. Few families with members presenting MMs without other neurological disorders have been reported and mutations in DCC gene were found to underlie this condition. In the present study we aimed to report the clinical and neurophysiological features of a novel family with congenital MMs.

Methods: 13 members of a 4-generation family with individuals affected with congenital MMs were clinically evaluated using the Woods & Teuber scale. Subjects were blood sampled for the screening of the DCC gene mutations. 5 subjects underwent neurophysiological evaluation including recordings of voluntary and involuntary EMG activity, motor evoked potentials (MEPs) and interhemispheric inhibition (IHI) studied with transcranial magnetic stimulation. The neurophysiological parameters were recorded before and after delivering continuous theta burst stimulation (cTBS) on the dominant primary motor cortex.

Results: Transmission of MMs was consistent with an autosomal dominant fashion with incomplete penetrance and variable degree of expression. The screening of the DCC gene mutations was negative. Among the subjects who underwent neurophysiological evaluation, ipsilateral MEPs were detectable in the two most severe cases. IHI did not correlate with MMs severity; cTBS tended to reduce the EMG mirror activity and this was clinically relevant in one of the two most affected case.

Conclusions: Neurophysiological features suggest that MMs in this newly reported family are mainly mediated through uncrossed cortico-spinal tracts and that cTBS might be a potential therapeutical tool in congenital MMs.

P1546

Copper metabolism and diagnostic problems in clinically asymptomatic Wilson's disease patients

K. Dzieżyc¹, A. Członkowska¹,²
¹2nd Department of Neurology, Institute of Psychiatry and Neurology, ²Department of Clinical and Experimental Pharmacology, Medical University of Warsaw, Poland

Background: Wilson's disease (WD) is a rare autosomal recessive inherited disorder of copper metabolism. Diagnosis of WD is based on combination of clinical, biochemical, genetic testing and may be problematic. The aim of the study was the evaluation of initial copper metabolism parameters in asymptomatic cases diagnosed upon family history of WD.

Methods and results: We have assessed 85 WD patients diagnosed by family screening in our center between 1964 and 2010. All of them had no history of hepatic or neurological symptoms and were without any symptoms at the time of diagnosis. WD diagnosis was based on copper metabolism, DNA analysis and in uncertain cases using radiocopper study. The initial copper metabolism test results of asymptomatic patients were compared to their symptomatic siblings (n=60). Serum ceruloplasmin levels were decreased in asymptomatic patients but were significantly higher than in symptomatic siblings (14.3±7.7mg/dl vs. 10.2±6.2mg/dl, respectively, p=0.001), in 11 (13%) cases were even in normal range. Urinary copper excretion was significantly lower in asymptomatic patients (168±181.5ug/24h vs. 388.2±678.6ug/24h, p=0.003), and was normal in 11 (15%) patients. Total copper serum concentration levels were similar in both groups.

Conclusion: Copper metabolism test results in clinically asymptomatic patients may cause diagnostic difficulties. Ceruloplasmin levels and urinary copper excretion may be less significant for diagnosis comparing with symptomatic patients. In case of lack of genetic confirmation, further diagnostics such as the radiocopper study may be necessary, because missed diagnosis and delay of therapy may lead to development of symptoms.
P1547
The impact of micro-electrode recording on selecting the most optimal trajectories for electrode implantation

N. Kovacs, E. Gasparics, E. Bosnyák, F. Nagy, J. Janszky, I. Balás, G. Deli
Department of Neurology, University of Pecs, Hungary

Background: Micro-electrode recording (MER) is an electrophysiological tool for finding the most optimal trajectory and level during implantation of chronic stimulation electrode. Although it might be associated with a higher risk for intra-operative intracranial bleedings, most DBS center routinely apply it.

Objectives: To analyze the number of DBS surgeries in a large prospective cohort where the planned trajectory was modified by the results of MER signals.

Methods: 184 DBS electrode implantations were evaluated. We applied Leadpoint 5 system (Medtronic Inc, MN) to MER. Simultaneously 5 micro-electrodes were inserted (center, anterior, posterior, medial and lateral) 2mm and the electrophysiological activity was recorded in the level of -10 and +5mm from the planned target level. The signals were evaluated offline and macro-electrode stimulation was performed subsequently.

Results: The central electrode at the level of the planned target demonstrated pathological activity during 134 electrode placements (72.8%); however, the central trajectory was used for chronic stimulation only in 102 (55.4%) of instances. Anterior trajectory was chosen in 53 cases (28.8%). Chronic electrodes were placed in the lateral, medial and posterior positions less frequently (12, 15 and 6 instances, respectively).

Conclusion: Although we reached the planned target in the vast majority of cases, we selected the central trajectory for electrode implantation only in nearly half of the cases based on signal quality and intra-operative stimulation.

P1548
Epidemiological (cross-sectional) study to evaluate and describe fatigue in patients with Parkinson's disease in Italy - The FORTE Study

F. Stocchi1, G. Abbruzzese2, R. Ceravolo1, P. Cortelli1, M.F. De Pandis1, G. Fabbrini6, W. Liboni7, C. Pacchetti8, G. Pezzoli6, M. Canesi9, C. Iannacone10, M. Zappia11, FORTE Study Investigators
1Institute of Neurology, IRCCS San Raffaele Pisana, Rome, 2Department of Neurosciences, Ophthalmology, Rehabilitation and Genetics, University of Genoa, 3Department of Neuroscience, University of Pisa, 4Department of Neurological Sciences, Alma Mater Studiorum, IRCCS, Institute of Neurological Sciences, University of Bologna, 5Parkinson Operative Unit, San Raffaele Institute, Cassino, 6Department of Neurology and Psychiatry and IRCSS Neuromed, 'La Sapienza' University of Rome, 7Complex Structure of Neurology, Gradengo Hospital, Turin, 8Parkinson Operative Unit, IRCCS 'National Neurological Institute C. Mondino' Foundation, Pavia, 9Parkinson Institute, I.C.P., 10SPARC Consulting, Milan, 11Department 'G. F. Ingrassia', Neurosciences Area, University of Catania, Italy

Introduction: Fatigue is a common non-motor symptom in patients with Parkinson’s disease (PD) and one of the most disabling symptoms of this disease, as reported by patients, with serious impact on patients’ quality of life. It is generally accepted that about 50% of PD patients will complain of fatigue and clinical observation revealed that its severity remained mostly unchanged during progression of the disease. This study aims to assess, in a non-interventional epidemiological setting, the incidence and severity of fatigue in PD patients and its correlation with PD severity.

Methods: This is an epidemiological, cross-sectional, multicentre study, in patients diagnosed with PD according to the 'UKPDS brain bank diagnostic criteria'. The primary objectives included the evaluation of the incidence and severity of fatigue in PD patients measured by Parkinson Fatigue Scale (PFS-16) and assessment of its predisposing factors (age, gender, marital status, disease duration, presence of depression, presence of sleep disorders, PD severity, UPDRS total score).

Results: 402 patients (mean age: 66.9 years; mean disease duration: 7.5 years) were enrolled in 27 PD centres in Italy. 33.8% of them showed fatigue (PFS-16 score ≥ 3.3 points). Logistic regression analysis showed that UPDRS total score, female gender, presence of depression and presence of sleep disorders significantly increase the odds of occurrence of fatigue in patients with PD.

Conclusion: FORTE is the largest study ever conducted in Italy to assess fatigue in PD patients. The large amount of data collected will allow us to investigate in depth the fatigue in these patients.
P1549

Usefulness of brain perfusion SPECT for differentiation between idiopathic Parkinson's disease and multiple system atrophy

K.-S. Lee¹, I.-U. Song¹, J.-W. Park¹, Y.-A. Chung²
¹Department of Neurology, ²Department of Nuclear Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Objectives: Statistical parametric mapping was performed to investigate differences in regional cerebral blood flow (rCBF) between patients with idiopathic Parkinson's disease (IPD), patients with multiple system atrophy (MSA), and healthy volunteers.

Methods: Tc-99m HMPAO SPECT was performed on 23 IPD patients (10 men, 13 women; aged 57-80 y), 9 MSA patients (4 men, 5 women; aged 60-83 y), and 12 age-matched healthy volunteers (5 men, 7 women; aged 56-81y).

Results: Significant hypoperfusion was observed in IPD compared with healthy subjects in a symmetric subcortical-cortical network including the basal ganglia, thalami, prefrontal and lateral frontal cortex, and parietal cortex (voxel size: 50, corrected p<0.001). For MSA, only symmetric hypoperfusion was seen in both prefrontal cortices with respect to healthy subjects and to IPD (voxel size: 50, corrected p<0.001).

Conclusions: Tc-99m HMPAO perfusion SPECT shows detailed differences between IPD and MSA, which may be of use in the differentiation of both disease entities.

P1550

Early-onset dystonia with brain manganese accumulation due to SLC30A10 mutations: a new treatable disorder

M. Stamelou¹, K. Tuschl², P. Mills², K. Chong³, A. Burroughs⁴, P. Clayton², K. Bhatia¹
¹UCL Institute of Neurology, ²UCL Institute of Child Health, ³Department of Radiology, ⁴The Wellington Hospital, London, UK

Background: Recently, the first gene causing early-onset generalised dystonia with brain manganese accumulation has been identified. Mutations in the SLC30A10 gene, encoding a manganese transporter, cause a syndrome of hepatic cirrhosis, dystonia, polycythemia and hypermanganesemia.

Methods: We present ten-year longitudinal clinical features, magnetic resonance imaging data, and treatment response to chelation therapy of the originally described patient with proven SLC30A10 mutation.

Results: The patient presented with early-onset generalized dystonia and jaundice accompanied by elevated whole blood manganese levels. T1 sequences in magnetic resonance imaging showed manganese deposition in the basal ganglia and cerebellum. Treatment with intravenous disodium calcium edetate, led to a slow but continuous clinical improvement and reduction of the manganese deposition in brain imaging.

Conclusions: We wish to highlight this rare disorder which, together with Wilson's disease, is the only potentially treatable inherited metal storage disorder to date, that otherwise can be fatal due to complications of cirrhosis.
P1551

Digitalised spirography and clinical examination based decision support system for differentiating between tremors

D. Georgiev1, V. Groznik2, A. Sadikov2, M. Možina2, M. Guid3, V. Kragelj3, I. Bratko2, S. Ribarič3, Z. Pirtošek1
1Laboratory for Movement and Gait Disorders, Department of Neurology, University Medical Centre Ljubljana, 2Artifitial Intelligence Laboratory, Faculty of Computer and Information Science, University of Ljubljana, 3Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Objective: To analyse the usefulness of computer decision support system (DSS) that combines digitalised spirography and clinical data for differentiating between essential tremor (ET) and Parkinson’s disease (PD), including the mixed type tremor (MT) (comorbidity).

Introduction: ET and PD are very often misdiagnosed when standard clinical examination is applied (37-50% and 24%, respectively, Quinn et al., 2011). DaTSCAN can be used to more precisely differentiate between ET and PD, but it is costly and not widely available. In a previous work (sample size 69 patients), we have estimated the accuracy of the argument-based machine learning (AMBL) DSS for tremor differentiation as 81%.

Methods: 122 (median age 69 years) patients with ET, PD or MT were included in the study. DSS was built using ABML, which combines machine learning (ML) with expert knowledge based on the clinical as well as quantitative data from digitalised spirography.

Results: The estimated classification accuracy of the model was 91%, which shows an improvement of 10% compared to the previously reported model. Measured specificities of the model were 0.97 for ET, 0.89 for PD, and 0.98 for MT; measured sensitivities were 0.93 for ET, 0.97 for PD, and 0.70 for MT.

Conclusions: Digitalised spiography has a potential to be used as a stand-alone screening method for tremor analysis. We plan to further evaluate and validate the system by enrolling a larger number of patients and compare it to DaTSCAN, in order to improve the diagnostic precision of the system.

P1552

Movement disorders in Ethiopia

D.K. Worku
Addis Ababa University, Addis Ababa, Ethiopia

Introduction: In a country of 80-million plus people, there is a shortage of physicians - only 15 neurologists serve the entire country and most are concentrated in the capital city - making it difficult for all who need care to see a neurologist.

Methods: A review of journals was done on papers: movement disorders in Ethiopia available until the end of June, 2011 at the main Library of Addis Ababa University, Department of Neurology.

Results: In one retrospective study done over a 1-year period a total of 15.1% of the neurological patients were seen for movement disorders. Of these, most were parkinsonism (47.7%), followed by ataxia (16.5%), dystonia (8.3%), essential tremor (8.3%), chorea (7.3%), and miscellaneous (11.9%). Data on Parkinson’s disease in sub-Saharan Africa is limited but it appears that the age-adjusted prevalence may be a little lower than in other parts of the world. The likely explanation for this is a lack of diagnosis, and therefore treatment, leading to early fatality. Different studies indicated that movement disorders is one of the neurologic disorders associated with malnutrition which is rampant in the country. HIV/AIDS adds more to this problem and makes the diagnosis and the management even more challenging. Diagnostic evaluations are limited, but treatment is available, although expensive. In spite of the limitations, patients with movement disorders require and seek care in Ethiopia in proportions comparable to developed nations.

Conclusion: These findings underline the need for adequate training in movement disorders for physicians and neurologists, and community education in Ethiopia.
P1553

**Obliquus capitis inferior muscle plays an important role in dystonic torticcaput**

A. Stenner, G. Reichel  
*Movement Disorders Department, Paracelsus Clinic, Zwickau, Germany*

**Introduction:** Idiopathic cervical dystonia (CD) is the most prevalent defined dystonia in adults. The response rate to botulinum toxin in open and double-blind studies is usually about 60-70%. Nevertheless, there are cases of primary treatment failure or unsatisfactory treatment outcomes. The main reasons for this are most probably the selection of muscles to be injected. In addition, in such cases the problem is probably not only that not all affected muscles are treated, but that healthy muscles are also affected by the application of botulinum toxin.

**Methods:** The results of the examinations of 94 patients with primary CD treated in our clinic, were analysed. The cervical spine and the soft parts of the neck, including deep neck muscles, were examined by CT in 5mm slices. For comparison, the CT-images of 50 patients who did not suffer from CD were analyzed.

**Results:** Measurement of the maximum muscle diameters by CT revealed one distinctive feature: in 73% of the patients the only small muscle that was asymmetrical, in addition to the large neck muscles, was the obliquus capitis inferior muscle. Dystonia of this muscle induced rotation to the same side in the lower head joints.

**Conclusions:** Obviously, the obliquus capitis inferior muscle plays an important role in the dystonic rotation of the head. If treatment of the large neck muscles with Btx does not show satisfactory results, this small muscle should be included in the therapy plan.

P1554

**Dopamine therapy in primary pain syndromes in patients with Parkinson’s disease**

A. Alekseev, E. Podchufarova, M. Nodel  
*First Moscow Medical University, Moscow, Russia*

**Introduction:** Many researchers discussed the role of dopamine in the functional activity of the anti-nociceptive system (ANS). Parkinson’s disease (PD) is an example of common dopaminergic failure, accompanied by widespread pain syndromes.

**Aim:** To investigate the relationship of primary pain (pain without peripheral sources) in patients with PD and activity of ANS using nociceptive-flexion reflex (NFR).

**Patients and methods:** 12 patients with PD and primary pain (PD+PP), mean age 63.35±9.04, mean duration of PD 5.68±0.48, 15 patients with PD and low back pain (PD+LBP), mean age: 63.23±10.11, mean duration of PD 5.42±4.8, and 20 patients with low back pain without PD (LBP), mean age: 62.09±9.27, were enrolled in the study. Pain intensity by visual analogue scale (VAS), NFR thresholds (NFRTh) were determined. Patients underwent clinical examination before and after treatment of motor sign by dopaminergic drugs. Patients had no significant differences in the therapy received, the stage of PD or motor symptoms PD.

**Results:** Patients PD+PP had significantly (p<0.05) higher pain intensity (7.25±1.76 VAS) than PD+LBP (6.73±1.39 VAS), not significantly different from LBP (7.38±1.50 VAS). Patients PD+PP had significantly (p<0.05) more types and localizations of pain (2.75±1.48), than PD+LBP (1.63±0.67) and LBP (1.12±0.38). NFRTh was significantly (p<0.05) higher in PD+PP (19.25±6.21), and PD+LBP (18.31±4.76), than in LBP (18.3±4.76). After dopaminergic therapy all PD patients showed decreased intensity of pain. Decreasing was more significant (p<0.05) in PD+PP (5.1±1.72 VAS). NFRTh significantly (p<0.05) decreased (14.37±4.78). Any correlations between pain reduction or NFRTh increase and improvement of motor signs were not noted.

**Conclusion:** Primary pain in PD may be an example of dopaminergic-associated pain due to dopaminergic dysfunction and incompetence of ANS.
P1555

Surface electromyogram of neck extensor and flexor muscles in Parkinson’s disease patients with antecollis and retrocollis

K. Kashihara, T. Imamura
Neurology, Okayama Kyokuto Hospital, Okayama, Japan

Objective: Patients with Parkinson’s disease (PD) may present with abnormal neck posture, including antecollis and retrocollis. In order to study the mechanism of such postural disorders of the neck, we evaluated the electrical activity of the neck extensor and flexor muscles in PD patients presenting with postural disorders.

Methods: We examined 15 PD patients without postural disorder of the neck, 14 with antecollis, and 6 with retrocollis. Surface electromyogram (EMG) was recorded from the splenius capitis, trapezius, sternocleidomastoideus, and deltoid muscles on both sides of the spine while the subjects were at rest in the sitting position and while they tried to lift their head in the same position.

Results: The EMG amplitude of the sternocleidomastoideus muscles at each position was the highest. The amplitude at the spine position was at maximum in patients with retrocollis, followed by those with antecollis, and then by those without neck postural disorder. In PD patients with antecollis, the amplitude increased in the sitting position and showed a greater increase when patients tried to lift their head. In patients with retrocollis, changes in position from supine to sitting hardly produced increased muscle discharges.

Conclusion: Antecollis in PD patients may be associated with disproportionately increased muscle tonus of both flexor and extensor muscles, though antecollis of the sternocleidomastoideus is the most prominent. In case of patients with retrocollis, muscle tonus increased to the maximum level.

P1556

Xenologous transplantation of human adipose derived mesenchymal stem cells in an animal model of Huntington’s disease: behavioural and micro-anatomical outcomes

1Department of Physiology, Science & Research Branch, Islamic Azad University, Shiraz, 2School of Medicine, Islamic Azad University, Mashhad Branch, 3Neuroscience Research Center and Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, 4Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Iran

Introduction: Human adipose derived mesenchymal stem cells (hMSCs) have been proposed as alternative sources of cells for transplantation into the brain in neurodegenerative disorders. We tested the efficacy of hMSCs transplants to reduce behavioural and micro-anatomical deficits in a Quinolinic acid (QA) rat model of Huntington’s disease.

Methods: After unilateral lesion in striatum was caused by QA, hMSCs, which were isolated and purified from liposuction of healthy male donors, were transplanted into the damaged striatum of rats. Animals were tested by motor function tests at different times after cell transplantation. The volume of striatum, lateral ventricles and atrophy percentage of striatum and volume extension of lateral ventricles were measured in all treated rats.

Results: MSCs survived 42 days without inducing a strong inflammatory response from the striatum. Behavioural amelioration was observed on tests of apomorphine induced rotation, cylinder, beam balance and rotarod tasks for MSCs-treated rats. Relative to QA controls, the MSCs treated group was protected from QA-induced enlargement of the lateral ventricles. Histological results showed significant difference in amount of striatum atrophy between QA controls and MSCs-treated rats.

Conclusions: These results confirm the potential of hMSCs in treatment of behavioural and micro-anatomical defects in Huntington’s disease. Taken together, these data demonstrate that xenologous transplantation of hMSCs could be considered as a good candidate for treatment of neurodegenerative diseases, especially Huntington’s disease.
P1557

Neuromelanin activates dendritic cells: implications for Parkinson's disease

U. Oberländer1, E. Gschmack1, K. Pletinckx1, A. Döhler1, N. Müller1, M.B. Lutz1, T. Arzberger2, P. Riederer3, M. Gerlach4, E. Koutsilieri1, C. Scheller1
1Institute of Virology and Immunobiology, University of Würzburg, 2Institute of Neuropathology, University of Munich, 3Clinical Neurochemistry (National Parkinson Foundation Center of Excellence Research Laboratory), Clinic and Polyclinic of Psychiatry. Psychosomatics and Psychotherapy, 4Laboratory of Clinical Neurobiology, Department of Child and Adolescent Psychiatry. Psychosomatics and Psychotherapy, University of Würzburg, Germany

Introduction: Neuromelanin (NM) is a complex polymer pigment that is present in the dopaminergic neurons of the substantia nigra (SN). It is these neurons that degenerate in PD. In the past decade evidence for an autoimmune mechanism in PD pathogenesis has accumulated. NM represents an attractive potential target for an autoimmune pathomechanism, as the distribution of NM in the brain correlates with the pattern of neurodegeneration in PD. Here we investigated whether NM triggers maturation of dendritic cells (DCs), the major antigen-presenting cell type involved in adaptive (auto-) immune response. Moreover, we studied whether NM-mediated DC-activation is functional in order to trigger a T-cell response.

Methods: Murine DCs were treated for 48h with NM from human SN and synthetic dopamine melanin (DAM) in a concentration of 50µg/ml. Uptake of NM was studied by confocal microscopy. Characterization of activation/maturation of DCs was performed by flow cytometry and ELISA. T-cell activation was assessed with mixed lymphocyte reaction (MLR).

Results: DCs phagocytosed NM, leading to DC maturation (CD86high, MHC-IIhigh), activation (release of proinflammatory cytokines TNF-α and IL-6) and T-cell proliferation in a mixed lymphocyte reaction. DAM was also phagocytosed, but did not cause significant DC activation.

Conclusions: The maturation and activation of DCs following contact with NM represents the initial step in triggering an adaptive immune response. If operative in vivo, this could lead to an autoimmune response directed at NM and subsequent degradation of dopaminergic neurons in PD. (The data has been published in BMC Neurosci., doi:10.1186/1471-2202-12-116.)

P1558

Brain MRI apparent diffusion co-efficient (ADC) in Parkinson’s disease with dementia

A. Umemura, T. Oeda, M. Kohsaka, S. Tomita, R. Hayashi, K. Yamamoto, H. Sawada
Clinical Research Center and Neurology, Utano National Hospital, Kyoto, Japan

Purpose: ADC reflects pathological changes in the brain. To evaluate ADC in the brain regions and explore which brain regions are associated with dementia in Parkinson’s disease.

Methods: In 249 patients with Parkinson’s disease (157 without dementia and 92 with dementia), ADC was obtained in the hippocampus, amygdala, putamen, thalamus, caudate, the superior frontal, middle frontal, superior temporal, and inferior temporal gyri, the anterior cingulate, the posterior cingulate, the primary visual area and the substantia nigra. By a logistic regression model using a likelihood test it was determined, which brain regions were associated with dementia.

Results: The ADC in the amygdala was significantly increased in demented patients compared to the non-demented after adjustment for age, sex and Hoehn-Yahr (p=0.005). The odds ratio was 2.1 (>0.1 x 10-3 mm²/s, 95% CI 1.25-3.56).

Conclusion: It was supposed that dementia was related to degeneration in the amygdala in Parkinson’s disease.
P1559

Prognostic value of nocturnal stridor in multiple system atrophy

F. Mastrolilli1, P. Guaraldi2, G. Calandra-Buonaura2, G. Barletta2, A. Cecere2, L. Sambati2, F. Provini2, F. Vernieri2, P. Cortelli2

1Policlinico Universitario Campus Bio-Medico, Roma, 2IRCCS, Istituto delle Scienze Neurologiche, University of Bologna, Italy

Introduction: Multiple system atrophy (MSA) is a neurodegenerative disease characterized by parkinsonian, cerebellar and autonomic features. Nocturnal stridor is frequent associating with poor prognosis. We conducted a retrospective study to determine the survival of 111 patients and examine the incidence and prognosis of stridor in relation to standard therapy.

Methods: 111 patients were analyzed (68 MSA-P, 43 MSA-C; mean age at motor onset was 58±9 years). 86 of 111 patients died; mean disease duration was 8±4 years. 80 of 111 patients underwent polysomnography.

Results: Stridor was diagnosed by polysomnography in 36 patients. Mean disease duration was 9±4 years in patients with stridor; 8±4 years in patients without stridor. Disease duration after stridor onset was 7±4 years. 28 of 36 patients with stridor died: 14 underwent tracheostomy (6±2 years after disease onset), 5 were treated with CPAP (4±1 years after disease onset), 9 patients refused any treatments. Statistical analyses showed a mean survival from disease onset of 10 years for tracheotomised patients and 8 years for CPAP treated patients after stridor therapy.

Conclusions: In our series stridor does not appear to be a marker for reduced life expectancy in MSA. Despite the treatment, the mean survival time is not significantly different. A prospective study is needed to shed light on the prognostic effect of the nocturnal stridor and its treatment that is one of the most reliable clinical hallmarks of MSA.

P1560

Pharmacokinetics, pharmacodynamics and tolerability of opicapone, a novel COMT inhibitor, during the first administration to healthy male subjects

T. Nunes1, J.-F. Rocha1, R. Pinto1, R. Machado1, L. Wright1, A. Falcão2, L. Almeida3, P. Soares-da-Silva1,4

1Research & Development, BIAL - Portela & Cª S.A., 2Faculty of Pharmacy, University of Coimbra, 3Health Science Section, University of Aveiro, 4Dept. Pharmacology & Therapeutics, Faculty of Medicine, University of Porto, Portugal

Introduction: Opicapone was developed to fulfil the need for more potent, safer and longer acting catechol-O-methyltransferase (COMT) inhibitors (1). This study was aimed to assess the tolerability, pharmacodynamics, and pharmacokinetics of single oral doses of opicapone in healthy male subjects.

Methods: Single rising oral doses of 10mg to 1,200mg of opicapone were studied under a double-blind, randomised, placebo-controlled design. 8 sequential groups of 8 subjects were enrolled. Within each group, 6 subjects were randomised to receive opicapone and 2 subjects to receive placebo. Opicapone/placebo was administered after a 10h overnight fasting.

Results: The extent and rate of systemic exposure (AUC and Cmax) to opicapone increased in an approximate dose-proportional manner. Despite the relatively short half-life of opicapone (1 to 4h), inhibition of soluble COMT (S-COMT) activity in erythrocytes was long-lasting, ranging from 6% (10mg) to 55% (1,200mg) at 72h post-dose. Maximum S-COMT inhibition (Emax) occurred between 1 and 6 h post-dose (tEmax), and was 34.5%, 71.7%, 93.8%, 96.3%, 100%, 100%, 100% and 100% with the doses of 10, 25, 50, 100, 200, 400, 800 and 1,200mg, respectively. Urine levels of opicapone and its metabolites usually remained below the limit of quantification, showing that the kidney is not the primary route of excretion. Opicapone was well tolerated at all doses tested.

Conclusion: Opicapone was well tolerated at oral single doses of 10 to 1,200mg, presented a dose-proportional kinetics and effectively inhibited erythrocyte soluble COMT activity.

P1561

Effect of verbal auditory cues on cortical motor excitability in Parkinson’s disease. Evidence from motor evoked potentials

E. Shahine1, N.A. Elsawy1, G.A. Achmawi2
1Physical Medicine and Rehabilitation, 2Neurology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

Introduction: Parkinson’s disease (PD) patients rely on external sensory inputs to guide movements.

Aim: To study the effect of verbal auditory cues on cortical motor excitability of PD patients.

Participants and methods: The study included 17 PD patients and 15 healthy controls. Motor evoked potential (MEP) was recorded from abductor pollicis brevis muscle at baseline, following repetitive rhythmic thumb abduction-adduction at preferred speed and with verbal cues. Number of repetitive movement cycles (RMC), resting motor threshold (RMT), central motor conduction time (CMCT), MEP amplitude ratio and cortical silent period (CSP) mean duration were measured.

Results: At baseline, PD patients had significantly higher MEP amplitude ratio and shorter CSP mean duration than controls (p=0.9, 0.01, respectively). At their preferred speed, PD patients had significantly lower RMC compared to controls (p=0.005); and compared to baseline, they had significantly lower RMT, prolonged CMCT and increased CSP mean duration (p=0.04, 0.05 and 0.01, respectively). With verbal cues, both PD patients and controls could increase significantly RMC (0.000, 0.028 respectively) but still lower in patients (p=0.002). Following verbal cues, none of the MEP parameters had changed significantly among patients compared to controls and compared to performance without cues. Controls had significant shortening in CMCT and prolongation of CSP mean duration (p=0.046, 0.001 respectively).

Conclusion: Parkinson’s disease patients have significant cortical hyperexcitability compared to healthy subjects. Performing a repetitive motor task with or without verbal auditory cues may normalize cortical excitability level in PD patients.

P1562

Genetic features and dopaminergic imaging in benign hereditary chorea

T. Konishi1, S. Kono1, M. Fujimoto2, T. Terada1,3, Y. Ouchi3, H. Miyajima1
1First Department of Medicine, Hamamatsu University School of Medicine, Hamamatsu, 2Department of Neurology, Iwata City Hospital, Iwata, 3Laboratory of Human Brain Imaging Research, Molecular Imaging Frontier Research Center, University School of Medicine, Hamamatsu, Japan

Introduction: Benign hereditary chorea (BHC) is a rare autosomal dominant movement disorder caused by a mutation in the TITF-1 gene, which is essential for the development, differentiation and organization of the basal ganglia. Previously reported TITF-1 mutations were located in the exons or splice sites adjacent to the exons. Some patients showed a response to levodopa therapy, suggesting a functional impairment in the dopamine neuronal pathway of the basal ganglia.

Methods: We investigated the clinical features in Japanese BHC family members by genetic analyses of the TITF-1 gene and positron emission tomography (PET) imaging to assess the integrity of the striatal dopaminergic system using [11C]-CFT for the presynaptic dopamine transporter function and [11C]-raclopride for the postsynaptic D2 receptor function.

Results: The BHC patients presented non-progressive generalized choreic movements initiated in childhood and no response to levodopa treatment. The genomic DNA analyses showed a novel heterozygous c.464-9C>A mutation in intron 2. A sequencing analysis of the lung TITF-1 mRNA by a reverse transcription-PCR assay revealed an abnormal transcript with a 7bp insertion, identical to sequence in intron 2, at the boundary of exons 2 and 3. Dopaminergic PET studies revealed decreased raclopride binding in the striatum compared to age-adjusted control values, while the CFT binding was not altered.

Conclusions: The intronic mutation created a new acceptor splice site leading to the production of an aberrant transcript affecting the expression of TITF-1 gene. Dopaminergic PET imaging revealed striatal D2 receptor impairment which may be attributed to a lack of response to levodopa.
P1563

Ocular application of oxybuprocaine hydrochloride against apraxia of lid opening: a randomized controlled trial

M. Kohsaka, T. Oeda, H. Nakano, A. Umemura, S. Tomita, R. Hayashi, K. Yamamoto, H. Sawada
Clinical Research Center and Neurology, Utano National Hospital, Kyoto, Japan

Introduction: Apraxia of lid opening (ALO) is often seen in patients with Parkinson’s disease. ALO is usually aggravated by bright lights or irritants to the cornea such as cold wind, suggesting that it could be caused by abnormal reaction to trigeminal sensory input from the cornea. The purpose of the study is to examine an effect of corneal anesthesia against ALO.

Methods: A randomized placebo-controlled cross-over trial of ocular application of oxybuprocain hydrochloride, a short acting corneal anesthetic, was conducted in 8 Parkinson’s disease patients. Time to complete opening after 10 minutes eye closure (complete opening time (COT)) was measured 14 times (before and every minute from 1 to 13 minutes after eye drops of oxybuprocain hydrochloride or saline as placebo). Primary outcome measure was a difference of % change of COT (Δ%COT) from baseline between the two arms. The data were analyzed statistically by a two-way repeated-measure ANOVA.

Results: In the oxybuprocaine hydrochloride arm, the mean COT was reduced from baseline COT at every point. In contrast, every mean COT was increased in the saline arm. Comparing Δ%COTs between the two arms, eye drop of oxybuprocaine hydrochloride improved COT significantly compared to saline eye-drop (p<0.05). In 5 patients (63%), the effect of oxybuprocain hydrochloride appeared within 1 minute after the eye drop.

Conclusion: Oxybuprocain hydrochloride is useful for ALO in Parkinson’s disease patients as a rescue drug.

P1564

Resting state functional connectivity in early Parkinson’s disease

K. Szewczyk-Krolikowski1,2, R. Menke3,4, M. Hu1,2, K. Talbot1,2, C. Mackay1,2,3
1Nuffield Department of Clinical Neurosciences, 2Oxford Parkinson Disease Centre (OPDC), 3FMRIB Centre, 4Department of Psychiatry, University of Oxford, UK

Background: RS-fMRI is a promising new method for developing an imaging biomarker in PD. It investigates functional connectivity between different brain regions at rest and requires minimal cooperation from the patient. Previous resting state studies in PD used Region of Interest (ROI) analyses which are very investigator-dependent. In our study we employed a data driven approach of Independent Component Analysis to look at changes in Resting State Networks (RSN).

Methods: 19 early stage idiopathic PD patients and 19 normal controls (NC) were selected from the Oxford Parkinson Disease Centre cohort. Patients were scanned on two sessions: OFF and ON medication. Scans were performed under resting conditions with eyes open in a 3T MRI scanner. Data was analysed with Independent Component Analysis implemented in MELODIC, FSL.

Results: We isolated 25 components. Comparing OFF state PD patients to NC, the Basal Ganglia/Thalamic network showed reduced connectivity in the putamen bilaterally. The left putamen showed increased connectivity with the Default Mode network. Dopaminergic medication normalised all the differences. We found significant correlations with UPDRS part III subscores in the Sensorimotor and Cerebellar networks.

Conclusions: Independent Component Analysis of RS-fMRI is a sensitive method for investigation of functional connectivity in PD. Identified connectivity differences correspond very well to results of task-related fMRI studies. In particular, reduced activation in the basal ganglia has been one of the most commonly reported findings. Our study shows additionally that this phenomenon may be related to a stronger correlation of the putaminal activity with the Default Mode Network.
P1565

Differences in non-motor symptoms in patients with young-onset and late-onset Parkinson's disease

I. Stankovic¹, V. Markovic¹, M. Svetel¹, T. Pekmezovic², V. Kostic¹
¹Movement Disorders Department, Neurology Clinic, Clinical Center of Serbia, ²Neuroepidemiology Unit, Institute of Epidemiology, School of Medicine, University of Belgrade, Serbia

Objective: To assess prevalence of different non-motor symptoms (NMS) in young-onset Parkinson's disease patients (YOPD) in comparison to their older counterparts (LOPD).

Introduction: In some studies it was suggested that YOPD patients have an increased risk of non-motor symptoms.

Methods: This cross-sectional study comprised 101 consecutive YOPD and 107 LOPD patients. All PD patients were clinically evaluated and completed the revised NMS Quest. The two separate backward stepwise linear regression analyses were used to examine how the various demographic and clinical characteristics contribute to the total number of NMS.

Results: The mean total NMS (NMSQ-T) was 11.9±6.0 in LOPD and 7.7±5.8 in YOPD (p<0.05). Dribbling of saliva, loss of taste/smell, nocturia, forgetfulness, loss of interest, hallucinations, lack of concentration, anxiety, change in libido and difficulty in sexual activities were more prevalent in LOPD. The only NMS more prevalent in YOPD were restless legs and sweating. Significant positive correlations were registered between the NMSQ-T and actual age (r=0.480; p=0.001 and r=0.261; p=0.007), duration of PD (r=0.499; p=0.001 and r=0.359; p=0.001) and H&Y stage (r=0.607; p=0.001 and r=0.556; p=0.001) in both YOPD and LOPD groups, respectively. In the multivariate linear regression model, in the YOPD group only the H&Y stage of the disease appeared to be a significant predictor of an increasing number of NMS, while in the LOPD group significant contributors were also age at onset and duration of PD.

Conclusions: NMS were less frequent in our YOPD patients and had different predictors than in LOPD group.

P1566

Botulinum toxin therapy of cervical dystonia (CD): duration of therapeutic effects

D. Dressler, P. Tacik, F. Adib Saberi
Movement Disorders Section, Department of Neurology, Hannover Medical School, Hannover, Germany

Introduction: We sought to explore the duration of therapeutic effect of botulinum toxin (BT).

Methods: Patients with CD, receiving Xeomin®, Botox® or both treatments in sequence, entered a non-interventional study. Outcome measures included treatment duration (TD; time between application of BT and patient-reported waning of therapeutic effect), inter-injection interval (II) and excess time (ET; ET=II-TD).

Results: 59 patients (male, n=22; mean age, 52.6 years; mean Tsui score, 9.0) and 1289 treatment cycles (mean number per patient, 21.8; standard deviation [SD], 14.0; range, 4-66) were evaluated. Mean (SD) TD per patient ranged from 7.8 (1.4) to 21.0 (3.9) weeks (overall mean, 11.8 [2.7]). Mean TD was ≤12 weeks in 83.1% of patients and ≤10 weeks in 35.6%. Mean (SD) II per patient ranged from 11.3 (1.3) to 27.8 (11.6) weeks (overall mean, 15.4 [3.4]). Overall mean (SD) ET was 3.5 (2.4) weeks (22.7% of overall mean II). TD and II were generally stable, although 16.9% of patients experienced treatment delays, most frequently due to appointment difficulties. Prolonged treatment effects, probably due to CD fluctuations, occurred in 18.6% of patients. Singular unexplained therapy failure (SUTF) occurred following 0.4% of injection series. No antibody-induced therapy failure occurred.

Conclusion: TD and II were generally stable with long-term BT application, but could be influenced by treatment delays, CD fluctuations or SUTF. ET indicated that patients were treated suboptimally for ~23% of their treatment cycle, supporting a reduction of II. BT formulations associated with low antigenicity may be useful if II is reduced to ≤12 weeks.
P1567

**Dysautonomic dysfunction in Parkinson’s disease evaluated by SCOPA-AUT scale**


*Dipartimento di Biomedicina Sperimentale e Neuroscienze Cliniche, Università degli Studi di Palermo, Italy*

**Introduction:** Non-motor symptoms of PD are common, occur across all stages of PD, and are under-reported. Dysautonomic symptoms generally associated with more advanced Hoehn and Yahr (H&Y) stages, further aggravate quality of PD patients’ life.

**Objective:** To assess frequency of dysautonomic symptoms in PD patients and to correlate to PD related characteristics.

**Method:** All consecutive non-demented PD patients who underwent an extensive evaluation including UPDRS, and Scale for Outcomes in PD for autonomic symptoms (SCOPA-AUT) were enrolled. SCOPA-AUT evaluates the involvement of gastro-intestinal, urinary, cardiovascular, thermoregulatory, pupillomotor and sexual dysfunction. Supine to standing position blood pressure and cardiac frequency changes were measured. Orthostatic hypotension (OH) was diagnosed according to consensus statement on the definition of OH (Freeman, Clin Auton Res. 2011).

**Results:** 89 PD patients were included (mean age at interview was 67.7). Patients were stratified according to the medium score of SCOPA-AUT scale (17.1). Those with higher SCOPA-AUT score had more frequently an older age at PD onset (77%; 62.4 years), higher UPDRS IV score (61%; 30.1) and longer disease duration (64%; 5.2 years). Mean SCOPA-AUT score was significantly higher (21.8±8.2) among those patients (5; 5.6%) who showed OH compared to those without (16.9±30.2).

**Conclusion:** Our study remarks the role of autonomic dysfunction in PD. In our population characterized by mild to moderate disease severity, in most of patients the autonomic system was involved. In these symptoms frequency increases with duration and severity of disease, might be present also at onset, suggesting therefore evaluating their presence also in the earliest stage.

P1568

**A meta-analysis of cognitive deficits in clinical subtypes of multiple system atrophy**

E. Lyros1,2, A. Tsapanou3, L. Messinis4, P. Papathanasopoulos5, K. Fassbender6

1Neurology, University of Saarland, Homburg, Germany, 2Neurology, Medical School, University of Patras, 3University of Athens Medical School, Athens, 4University of Patras Medical School, Patras, Greece, 5University of Saarland, Homburg, Germany

Dementia and severe cognitive impairment are considered as non-supporting features for the diagnosis of multiple system atrophy (MSA). Several studies however suggest that neuropsychological deficits are frequent in this condition. It would also be interesting to see whether the magnitude of these deficits would be any different among MSA with predominant parkinsonism (MSA-P) and MSA with predominant cerebellar ataxia (MSA-C). Therefore we conducted a meta-analysis to increase power by pooling data from individual relevant studies based on a Pubmed database search (studies that qualified had to include both patient groups or clearly defined only MSA-P or MSA-C group, a control group, a battery of diverse neuropsychological tests, statistics that were convertible to affect size g and be written in English). Eligible studies reached the number of 7. The overall mean effect size for each cognitive domain was computed using a random effects model and adjusted for sample size. Our preliminary results indicate that significant decrements in neuropsychological performance loading on executive functions are present in both patient groups with their magnitude however being greater for the MSA-P group. Reasoning, psychomotor speed and memory recognition were less severely impaired. It is implied that dysfunction in the frontostriatal circuits but also of its cerebellar connections may underlie the observed deficits.
P1569
Validation study of genetic factors contributing to Parkinson's disease in Spanish and Latin American populations

A. Sesar1, P. Cacheiro2-3, M. Camiña-Tato3, M. Lopez2, B. Quintáns2-3, E. Alonso2, E. Cebrián1, A. Castro1, A. Carracedo2,3, M.J. Sobrido2,3
1Neurology, Santiago de Compostela Clinical Hospital, University of Santiago de Compostela, 2Neurogenetics Group, Fundacion Publica Galega de Medicina Xenoomic-SERGAS, 3Genomic Medicine Group, School of Medicine-University of Santiago de Compostela, Spain

Introduction: In past years some genes have been associated with predisposition to Parkinson’s disease (PD). The aim of this study was to analyze several candidate genes as susceptibility factors to PD in populations from Spain and Latin America.

Methods: PD cases defined by the Gelb criteria were compared with controls selected after family history and clinical exam. SNPs in 12 previously reported genes and intergenic regions were genotyped by SNPlex. After quality control by genotyping rates, minor allele frequency and Hardy-Weinberg equilibrium - no significant population substructure is known in the Galician population; 71 SNPs were analyzed in 268 patients and 257 controls. Quality control and association tests were carried out with the R package SNPassoc. Imputation of additional markers was performed using HapMap panels.

Results: Nominally significant associations (P<0.05) were found for SNPs belonging to MAPT, SNCA and SYT11 genes. Only the MAPT association remained significant after multiple testing correction (False Discovery Rate). These results were also checked in a Mexican cohort.

Conclusions: Genetic variation in MAPT and SNCA have been associated with PD in independent populations. The replication of MAPT and SNCA association confirms the participation of these genes in susceptibility to PD while serving as a quality indicator of our sampling protocol. Regarding SYT11 there is only a meta-analysis of GWAS suggesting association with PD. Our data, together with previous results, suggest that SYT11 encoding synaptotagmin XI, substrate for parkin may play a so far under-recognized role in the pathogenesis of PD.

P1570
Leukoaraiosis as a predictor of cognitive decline in patients with Parkinson's disease submitted to STN-DBS

F. Sousa1, J. Rocha1, H. Costa2, C. Sousa2, J. Lima3, R. Figueiredo2, C. Reis2, J. Massano1, M. Basto4, P. Linhares5, R. Vaz2, M.J. Rosas5
1Neurology Department, Hospital de Braga, 2Neurology Department, 3Neuropsychology Unit, 4Neuroradiology Department, 5Movement Disorders Unit - Functional Surgery, Hospital de São João, Porto, Portugal

Introduction: Subthalamic nucleus deep brain stimulation surgery (STN-DBS) may lead to selective cognitive decline. Leukoaraiosis is a cognitive decline predictor in patients with cerebrovascular disease. The aim of the study is to evaluate the influence of leukoaraiosis on cognitive decline after STN-DBS in Parkinson’s disease (PD).

Methods: From October 2002 and December 2010, neuropsychological studies pre- and post-DBS (12-18 months) were prospectively registered and Fazekas classification of leukoaraiosis in pre-DBS MR imaging was evaluated in patients with PD undergoing STN-DBS. Demographics, disease duration, educational level, Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB), categorical (Fvcat) and phonemic (Fvfon) verbal fluency tests were compared.

Results: 91 patients were enrolled, 64 with leukoaraiosis. In this group there was a decrease in MMSE (27.94 to 26.94 p<0.05), FAB (13.02 to 11.80 p<0.05), Fvcat (13.76 to 10.77 p<0.05) and Fvfon (18.48 to 13.86 p<0.05). In patients without leukoaraiosis, MMSE (27.94 to 26.94 p<0.05), FAB (13.62 to 13.33 p<0.05), Fvcat (14.73 to 11.81 p<0.05) and Fvfon (20.56 to 14.48 p<0.05) decreased, but not MMSE (27.74 to 27.89 p<0.05). The mean value of MMSE and FAB post-DBS was lower in subjects with leukoaraiosis (p<0.05). There were no differences in score variations between Fazekas 0-1 and 2-3, progression to dementia or educational level.

Conclusion: These results confirm the trend for cognitive decline in the evaluated areas after DBS. Patients with leukoaraiosis have lower scores on evaluated domains, but only MMSE and FAB differences were significant.
P1571
What is the diagnosis behind patients with parkinsonian syndrome and normal 123I-Ioflupane SPECT? A clinical follow-up study

M. Menéndez1,2, F. Tavares1, M. Martínez1, A. López-Muñiz2, J.A. Vega2
1Hospital Álvarez-Buylla, Mieres, 2Morfología y Biología Celular, Universidad de Oviedo, Spain

Introduction: Making the diagnosis of Parkinson’s disease (PD) is a common clinical situation faced by neurologists, geriatricians, and general physicians. The Food and Drug Administration (FDA) recently approved [123I]ioflupane ([123I]-fluoropropyl CIT, DaTSCAN), a dopamine transporter (DAT) radioligand, for SPECT to assist in the evaluation of adult patients with suspected parkinsonian syndromes (PS). We aimed what is the diagnosis of patients with PS and normal DaTSCAN.

Methods: A series of 30 patients with parkinsonism and normal 123I-Ioflupane SPECT. They were followed up for at least 2 years; and then a second DaTSCAN was performed. The diagnosis was reconsidered at endpoint.

Results: The second DaTSCAN changed from normal to abnormal only in 4 patients. Final diagnosis included cases of essential tremor (4), SWEDD (2), FTAX (1), iatrogenic parkinsonism (1), vascular parkinsonism (2), corticobasal degeneration (2), multisystem atrophy (4) and PD (8). The diagnosis remained uncertain in 6 cases.

Conclusion: DaTSCAN can help the diagnostic process in certain situations but it should not be relied on as a substitute for careful, experienced clinical assessment and follow up. There is a list of alternative diagnoses to consider when a PD patient presents with normal DaTSCAN. Following cases of uncertain diagnosis with DaTSCAN studies does not seem to be useful.

P1572
CSF uric acid as an anti-oxidant in Parkinson’s disease

M. Pohja1, K. Murros2
1Helsinki University Central Hospital, 2Helsinki University Central Hospital, Jorvi Hospital, Espoo, Finland

Oxidative stress is thought to be an important factor in the pathogenesis of Parkinson’s disease (PD). Low serum uric acid (UA) has been associated with faster clinical progression of the disease. UA is an antioxidant having interactions with another important antioxidant, ascorbic acid (AA). We studied if UA or AA or total antioxidant capacities in plasma and CSF are altered in PD. 16 PD patients (52-73 yrs, 50% males, mean disease duration 4 years, mean UPDRS motor score 21) were recruited. 16 gender- and age-matched healthy subjects served as controls. UA in CSF was statistically lower in PD patients than in controls (19.6 umol/l vs. 25.6umol/l, p=0.03). In plasma, the corresponding difference was trend-like (p=0.07). The CSF/plasma ratio was the same in both groups but strong correlation between serum and CSF UA was seen in PD but not in the control group (0.77, p=0.01 vs. 0.42, p=0.10). In PD group, AA was higher both in plasma (77umol/l vs. 56umol/l, p=0.03 ) and in CSF (206 umol/l vs. 156umol/l, p=0.01) suggesting higher vitamin C intake but no difference in active transport mechanism across BBB. Antioxidant capacities in serum and CSF estimated by TRAP were similar in both groups. Our novelty finding was that in PD patients CSF uric acid concentrations are lower than in healthy, gender- and age-matched controls. In addition, plasma and CSF uric acid concentrations are more tightly coupled suggesting potentially different or altered UA regulation mechanism in PD.
P1573

Does Rivastigmine improve balance control in Parkinson’s dementia?

E. Pourcher1,2, A. Nadeau1, M. Jaime3, P. Corbeil4,5
1Clinique Sainte-Anne, 2Department of Medicine, Faculty of Medicine, Laval University, 3Department of Kinesiology, Laval University, 4Groupe de Recherche en Analyse du Mouvement et Ergonomie, Faculty of Medicine, Laval University, 5Centre de Recherche FRSQ, Centre Hospitalier Affilié Universitaire de Québec, QC, Canada

Introduction: According to Allcock et al. (2009), impaired attention predicts falling in Parkinsonian patients, however the contribution of attention improvement with cholinesterase inhibitors on balance control in Parkinson’s disease has never been formally explored.

Methods: 20 patients with idiopathic Parkinson’s disease and mild to moderate dementia (PDD) were randomized to receive either Rivastigmine trans-dermal patches or oral capsule for 24 weeks. Postural control using a force platform was assessed at baseline and 24 weeks under four conditions: eyes open/eyes closed with static support surface/sway referenced to body sway form support surface. Other outcomes included scores of the MATTIS Dementia Rating Scale (global and attention sub-scores) and the UPDRS motor sub-section.

Results: At 24 weeks, there was no difference in measures of postural control at rest, with a static support surface, however, a significant reduction was observed in sway velocity when the support surface was sway-referenced to body sway (p<0.01). Participants UPDRS III scores did not differ. Better performances on the MATTIS Dementia Rating Scale global scores were observed after 24 weeks (p=0.052). However neither the global score, nor the attention sub-score of the MATTIS correlated with improvement in sway velocity. No difference was observed in balance performance between patients on patches and patients on oral form.

Conclusion: In PDD, Rivastigmine improves adaptive balance control independently of an improvement on the attention MATTIS score. This result tends to support an improvement of balance driven by a sub-cortical cholinergic modulation.

P1574

Correlation between severity of cognitive deficit and motor symptoms in patients with Parkinson’s disease

S. Tomić1, M. Vlađetić1, K. Solić2, S. Misevic1, S. Juric1, L. Knezevic Poljak1, S. Butkovic Soldo1
1University Hospital Center Osijek, 2Medical School University of J.J. Strossmayer in Osijek, Croatia

Aim: To determine the existence of cognitive deficits in patients with idiopathic Parkinson’s disease (PD) compared to a control group and to find a correlation between the severity of cognitive deficits and motor symptoms in order to prove influence of dopamine on cognition.

Patients and methods: Demented and depressed PD patients were excluded from the study. Patients with PD were scored with UPDRS III and both groups made tests of cognitive function: Dementia Rating Scale (DRS), Raven progressive coloured matrices (RPCM) and Mill Hill Vocabulary (MHV) test. To analyse data we used the methods of descriptive statistics, Student T-test, Mann-Whitney U-test, Pearson and Spearman correlation co-efficient with p<0.05.

Results: We found statistically significant differences in MHV test and the frequency of pathological tests of construction and conceptualization (DRS subscales) between PD patients and control groups. We found no correlation between the results of cognitive tests and UPDRS part III in the PD patients group. There are no connections between cognitive deficit and duration of disease and type of PD (rigid or tremorous form). There is a possible connection between damaged visual-spatial perception and lesion of right side of brain.

Discussion: Patients with PD more often had cognitive deficit (dysexecutive syndrome, synonym finding and impaired visual-spatial perception) when compared to the control group. There is no correlation between cognitive deficits and severity of motor symptoms in PD patients.

Conclusion: These results suggest that cognitive deficits are not only due to dopamine depletion, but etiology is probably more complex.
P1575

The Rome tremor scale: an easy instrument for the evaluation of tremor

F. Puledda, L. Troilo, G. Lenzi
Neurology and Psychiatry, University of Rome Sapienza, Rome, Italy

Background: Tremor is a movement disorder that affects more than 10% of the general population. However, few clinical scales are available for tremor evaluation: the Clinical Tremor Rating Scale (CTRS) and the UPRS. The CTRS needs 30-90 minutes, and a fully compliant patient to be carried out. The UPRS is utilised in PD, with just a few of the 42 evaluations concerning tremor.

Objectives: In the planning of a clinical trial on tremor, we designed a user-friendly tremor scale, the Rome Tremor Scale (RTS) and tested it against the CTRS.

Materials and methods: RTS consists of six items: 0=no tremor; 1=tremor present in emotional situations, not invalidating; 2=tremor present, affects writing; 3=tremor present, affects daily activities; 4=tremor present, patients require constant help; 5=disabling tremor.

Results: 40 outpatients attending our Clinic because of neurological problems including tremor completed both CTRS and RTS. The mean score was 15.85±1.33 for CTRS and 2.025±0.094 for RTS. Correlation between CTRS and RTS shows r=0.943. By dividing patients into two cohorts, PD and essential tremor, correlation remains highly significant, r=0.971 and r=0.907 respectively.

Conclusions: The high correlation between RTS and CTRS indicates that RTS appears to be a valid and easy instrument for the clinical evaluation of tremor in an out-patient neurological setting, both in PD patients and patients affected by tremor due to other causes.

P1576

Expanding the spectrum of chorea associated with immune-mediated diseases: two case reports

E. Unti1, S. Mazzucchi1, D. Martino2, F. Vanelli1, R. Ceravolo1
1Department of Neuroscience, University of Pisa, 2Department of Neurological and Psychiatric Sciences, University of Bari, Italy

Introduction: Wegener Granulomatosis (WG) and psoriasis are diseases in which neurological involvement is quite rare; up to our knowledge, there are no cases associated with movement disorders in literature.

First case: A 72-year-old male, with a diagnosis of WG since 1999. Since 2003 he presented simple verbal tics, four limbs involuntary movements, and an amnestic mild cognitive impairment. No steroids were given. Hyperkinetic syndrome improved with low dosages of tetrabenazine.

Second case: A 67-year-old woman presented with choreic movements mainly in the left limbs, slight dysarthria and painful tumefaction of left wrist. Neuropsychological evaluation showed a mild frontal dysfunction. Within four months diagnosis of psoriasis was made. Methylprednisolone was given with improvement of chorea.

Methods: Genetic tests for HD, HDL2, SCA-17 and research for acanthocytis were negative. FDG-PET showed right caudo-putaminal hypermetabolism in the first patient and bilateral basal ganglia hypermetabolism in the second patient. Brain MRI did not show any significant alterations. CSF examination, iron and copper sieric values were in the normal range. Sieric anti-basal ganglia antibodies (ABGA) showed auto-antigen of 45 kDa.

Conclusions: Evidence of striatal hypermetabolism on FDG-PET with chorea associated with SLE and primary antiphospholipid syndrome has been reported probably due to auto-antibodies versus basal ganglia neurons. The ABGA positivity previously reported in autoimmune movement disorders, does not imply a pathogenetic relationship, however along with the striatal hypermetabolism in both and the good response to steroids in the second, one might extend the spectrum of chorea associated with autoimmune diseases.
P1577

Frequency distribution of orthostatic hypotension, nocturnal hypertension and postprandial hypotension in patients with Parkinson’s disease: a case-control study

A. Chitsaz

Neurology, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Etiology of orthostatic hypotension include sympathetic denervation and treatment with dopaminergic drugs.

Methods: The current study was conducted as a case-control study in the second half of 2008 and first half of 2009. The study population included Parkinsonian patients who received levodopa, >500mg/day for over 6 months. Patients who had not received any levodopa until the time of the study were in the control group. Exclusion criteria included having a concomitant disease or taking medications that cause orthostatic hypotension. Study variables included demographic characteristics, severity of disease, orthostatic hypotension, postprandial hypotension and nocturnal hypertension. Using the mercury barometer, the presence or absence of orthostatic hypotension was determined in all patients. The postprandial hypotension and nocturnal hypertension were identified using the portable device of ambulatory blood pressure monitoring.

Findings: The frequency distribution of orthostatic hypotension was 12% and 20% in the case and control group, respectively. The frequency distribution of postprandial hypotension was 12% and 24% in the case and control group, respectively. The frequency distribution of nocturnal hypertension was 40% and 56% in the case and control group, respectively.

Conclusion: Although the prevalence of orthostatic hypotension between the case and the control group was different, the difference was not meaningful.

P1578

A randomized, double-blind, placebo-controlled trial of hydrogen water in Parkinson’s disease

A. Yoritaka1,2, M. Takanashi2, M. Hirayama3, S. Ohta4, N. Hattori2

1Neurology, Juntendo Koshigaya Hospital, Koshiya-shi, 2Neurology, Juntendo University School of Medicine, Bunkyo-ku, 3Pathophysiological Laboratory Science, Nagoya University Graduate School of Medicine, Nagoya, 4Biochemistry and Cell Biology, Development and Aging Sciences, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan

Background: The major pathological hallmarks of Parkinson’s disease (PD) are cellular energy depletion and oxidative stress leading to cellular dysfunction and death. Molecular hydrogen (MH) selectively reduces the hydroxyl radical, the most reactive oxygen species, and can thereby effectively protect cells. MH water has been reported to prevent dopaminergic cell loss in rat models of PD.

Method: To determine that intake of MH water is safe and a disease-modifying treatment of PD, we conducted a double-blind, placebo-controlled trial of MH water in levodopa-treated patients with PD. The subjects prepared MH water (1.6ppm) by using Aquela blue (ecom International) and consumed 1,000ml of MH water divided per day for 48 weeks. The primary end-point was the change from baseline in the total score of the Unified Parkinson’s disease Scale (UPDRS). Additional analysis is the change of part of II and III of UPDRS and Hoehn and Yahr stage after 8, 24, 48 weeks and 8 weeks after treatment compared with the data at baseline.

Result: 18 subjects (7 male, 11 female) were enrolled in the treatment protocol. The changes in the total UPDRS score will be calculated with Mann-Whitney U-test after blinding will be opened after all subjects have finished protocol.

Conclusion: No doubt on safety of MH water intake has been found until now. We will demonstrate if MH may be applicable or not for the therapy in Parkinson’s disease.
P1579
The prevalence of non-motor symptoms and restless legs syndrome in Parkinson’s disease: correlation with quality of life
K.A. Abdul Manaf1, W.N.N. Wan Yahya1, H.J. Tan1, R. Azman Ali1, H. Othman2, S. Azhar3, N. Mohamed Ibrahim1
1Internal Medicine, 2Pathology, 3Community Health, University Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Introduction: The non-motor symptoms (NMS) are important determinants of health and quality of life (QoL) in Parkinson’s disease (PD). It occurs early and may even predate the diagnosis of PD. NMS are not well recognized in clinical practice despite their impact.

Aims: This study was conducted to determine the prevalence of NMS and restless legs syndrome (RLS) in PD and their impact on QoL.

Methods: This was a cross-sectional study involving patients with idiopathic PD. Prevalence of NMS using the NMS questionnaires was determined. The QoL and severity of NMS were assessed with PDQ-39 questionnaires and NMS Assessment Scale, respectively. Patients who met the criteria of International RLS Study Group criteria for the diagnosis of RLS were identified and blood samples to test serum iron were taken.

Results: A total of 113 patients consisting of 60 males and 53 females were recruited. The mean age was 64.8±9.0 years. The median duration of illness was 5.0 (2.0-8.0) years. 97.3% of patients reported the presence of NMS. The most common symptoms were gastro-intestinal symptoms (76.1%) followed by neuropsychiatric symptoms (72.6%) and autonomic dysfunction (64.6%). 11 patients (9.7%) had RLS. Patients with PD/RLS had a younger age of PD onset (p=0.023) and lower serum ferritin levels (p=0.616). NMS affected the QoL significantly in all dimensions of PDQ-39. Each dimension of PDQ-39 correlated strongly with the severity of NMS.

Conclusions: NMS was highly prevalent in our patients. The presence and severity of NMS adversely affected the QoL.

P1580
Transcranial sonography in differential diagnosis of restless legs syndrome
M. Budisic, Z. Trkanjec, V. Supanc, A. Lovrenic-Huzjan, V. Bašić-Kes
University Hospital Sestre Milosrdnice, Zagreb, Croatia

Background: Restless legs syndrome (RLS) has a prevalence of around 10% in the general population. Still, it is one of the most underdiagnosed neurological disorders. Non-idiopathic RLS is more frequently found in patients with anaemia. Recent transcranial sonography studies have shown that substantia nigra (SN) hypo-echogenicity appears to be a frequent finding in RLS, just as it is increased blood flow velocity in a. cerebri media (ACM), measured by TCCS, in anaemic patients. Aim of this study was to evaluate the usage of combined TCS/TCCS imaging in differential diagnosis of idiopathic and secondary RLS.

Patients and methods: 30 patients with RLS symptoms (diagnosis was made according to IRLSSG criteria), 20 patients with anaemia (haemoglobin values <12g/dl) and RLS symptoms, and 30 controls underwent neurological and sonographic examination.

Results: Bilateral mean SN area measured on TCS was significantly lower in idiopathic RLS patients versus controls (0.09±0.01cm² vs. 0.18±0.02 cm²; p<0.01). Values of mean blood flow velocity measured in ACM by TCCS were also higher in RLS patients (123.24±7.33 vs. 80.7±6.55; p<0.01) with normal finding of SN area.

Conclusion: TCCS in combination with TCS is a useful tool in diagnosing idiopathic RLS, just as it is in differentiating idiopathic from secondary RLS due to anaemia.

© 2012 EFNS European Journal of Neurology 19 (Suppl. 1), 90–457
P1581

**XCiDaBLE, a phase IV, prospective observational trial evaluating incobotulinumtoxinA (XEOMIN®) for cervical dystonia or blepharospasm: preliminary baseline data for subjects with blepharospasm**

M.S. LeDoux1, J. Jankovic2, K. Sethi3, A. Verma3, E.J. Pappert3, H.H. Fernandez4

1University of Tennessee Health Science Center, Memphis, TN, 2Baylor College of Medicine, Houston, TX, 3Merz Pharmaceuticals, LLC, Greensboro, NC, 4Cleveland Clinic, Cleveland, OH, USA

**Introduction:** While repeated injections of botulinum toxin-A are the established treatment for blepharospasm, there is a lack of prospectively acquired data on treatment outcomes in ‘real-world’ clinical practice.

**Methods:** XCiDaBLE is an open-label, prospective, observational US study. Subjects are followed for two cycles of incobotulinumtoxinA treatment with flexible dosing and injection intervals determined by the investigator. Subject-reported outcomes (recorded via Interactive Voice/Web Response) include the Jankovic Rating Scale (JRS). Investigators assess the baseline Clinical Global Impressions (CGI)-Severity. An employment questionnaire, work history and the SF-12v2 (0=worst, 100=best) are used to evaluate work productivity and quality of life (QoL).

**Results:** By 01 September 2011, 184 subjects with blepharospasm were enrolled (27.7% male, mean age 64.9 years, mean age at onset of blepharospasm 53.9 years, 97.8% previously treated with botulinum toxin). At baseline, subjects' CGI-Severity was: 32.8% normal-to-mild, 35.5% moderate, 22.4% marked, and 9.3% severe; mean JRS Sumscore was 5.0. Baseline mean SF-12v2 (0=worst, 100=best) are used to evaluate work productivity and quality of life (QoL).

**Conclusions:** Blepharospasm has a negative impact on QoL, employment status and work productivity. XCiDaBLE will provide valuable insight into the dosing and injection frequency of incobotulinumtoxinA in subjects with blepharospasm and treatment outcomes in ‘real-world’ clinical practice.

P1582

**Evaluating the efficacy of rasagiline on depressive symptoms in Parkinson’s disease patients without dementia: the ACCORDO study (ongoing clinical trial)**

P. Barone, for the ACCORDO Study Investigators

Centro per le Malattie Neurodegenerative, University of Salerno, Italy

**Objective:** In Parkinson’s disease (PD), the presence of depression is associated with worse cognitive function, functional ability, and patients’ quality of life. Accumulating evidence suggests that, in addition to its established motor benefits, treatment with rasagiline may also be beneficial in the management of certain non-motor symptoms of PD; however little is known about its effects on depression. This ongoing study aims to evaluate the efficacy of rasagiline on depression and explore the relationship between depressive symptoms and cognitive function in PD patients without dementia.

**Methods:** This is a multicenter, randomized, double-blind, placebo-controlled study, enrolling ~136 PD patients (Hoehn & Yahr I-III) with depression (Beck Depression Inventory (BDI-IA) score ≥15) but not dementia (MMSE <26). Patients are randomized (1:1) to rasagiline 1mg/day or placebo for 12 weeks; other anti-PD medications are permitted at a stable level. The primary efficacy measure is change from baseline to week 12 in BDI-IA total score. Secondary measures include a neuropsychiatric cognitive test battery, PD Quality of Life Questionnaire, Apathy Scale and Unified Parkinson’s Disease Rating Scale Parts II and III. Safety is assessed through adverse events (AEs).

**Results:** As of February 2012, 121 patients have been randomized. Mean age is 66.7 years and mean time from diagnosis is 4.3 years. So far, 4 patients have withdrawn early due to AEs (worsening of dyskinesia, vertigo, left trunk flexion due to PD, nausea).

**Conclusion:** ACCORDO is the first prospective study to evaluate the efficacy of rasagiline on depression. Full results are expected in Q4 2012.
**P1583**

**Quality of life in patients with different forms of primary dystonia**

N.S. Basurovic¹, M. Svetel², T. Pekmezovic³, V.S. Kostic²

¹Special Hospital for Cerebrovascular Diseases ‘St. Sava’, ²Institute for Neurology, Clinical Centre Serbia, ³Institute for Epidemiology, Clinical Centre Serbia, Belgrade, Serbia

**Introduction:** Dystonia is frequently associated with depression, anxiety, social phobia and poor quality of life.

**Aim:** Defining differences in quality of life in patients with primary focal and segmental dystonia.

**Patients and methods:** The study included 157 patients with primary focal dystonia (PFD) and 28 patients with primary segmental dystonia (PSD). Patients were treated at the Institute for Neurology KCS (1997-2008). All patients completed the Serbian translation of SF-36 which was used as an outcome measure for health-related quality of life (HR-Qol).

**Results:** The mean age at onset of dystonia in patients with PFD was 43.2±11.5 years, and in patients with PSD it was 43.3±17.3 years. The mean duration of disease in patients with PFD was 7.3 years, and in patients with PSD it was 9.9 years. The ratio man/women in the group with PFD was 64:9, and in group with PSD was 17:11. Patients with PSD scored significantly worse in bodily pain (PSD 30.6±28.2 vs. PFD 68.4±31.4) (p<0.01), role functioning emotional (PSD 38.1±44.2 vs. PFD 58.2±44.9) (p<0.01) and social functioning (PSD 50.0±13.6 vs. PFD 64.6±24.9) (p<0.05), while the same patient group scored significantly better in general health (PSD 64.6±15.7 vs. PFD 53.9±18.8) (p<0.05). There were no significant differences between the groups regarding physical functioning, role functioning physical, vitality and mental health.

**Conclusions:** The quality of life in patients with dystonia, has been defined by the complex interaction between distribution and/or severity of disease, characteristics of patient’s personality and the influence of social environment.

---

**P1584**

**Differentiation of parkinsonian disorders based on mineralization pattern of the deep grey matter by susceptibility-weighted magnetic resonance imaging**

M. Modi¹, S. Thakur²

¹Neurology, ²Radiodiagnosis, PGIMER, Chandigarh, India

**Objectives:** There are multiple causes of parkinsonism; idiopathic Parkinson’s disease (IPD) is most common (80-85%) and has to be differentiated from atypical parkinsonian disorders (APD), i.e., progressive supranuclear palsy (PSP), multiple system atrophy (MSA) and corticobasal denegation (CBD). The aim was to study mineralization pattern of the deep grey matter by susceptibility-weighted (SWI) magnetic resonance imaging to differentiate Parkinson’s disease and atypical parkinsonian disorders.

**Methods:** A total of 30 subjects was enrolled for the study of which 10 were in the control group and 20 patients presented with features of parkinsonism. MR imaging examinations were performed with a 18-channel 3.0T whole body imager (TIM MAGNETOM® Verio; Siemens). First, routine MR imaging of the brain including T1WI, T2WI and FLAIR sequences were done, followed by SWI. The hypo-intensity of post lateral putamen, red nucleus, substantia nigra, and dentate nucleus in all groups were measured in comparison with SI of the CSF and vein of Galen.

**Results:** In the conventional MRI, presence of midbrain atrophy, superior cerebellar peduncle signal changes and atrophy differentiated PSP patients from MSA-P and PD patients. The increased hypointensity scores of red nucleus on SWI in PSP patients differentiated it from PD and MSA-P. The increased hypointensity score of substantia nigra in PD patients supports the site of pathology and differentiated them from atypical parkinsonism patients.

**Conclusion:** Among the routine MRI techniques available to differentiate PD and APD patients, we observed SWI as a simple and advanced modality.
Does neuro-inflammation affect occurrence of dementia in patients with Parkinson’s disease?

I.-U. Song, J.-W. Park, K.-S. Lee, J.-S. Kim
Department of Neurology, The Catholic University of Korea, Seoul, Republic of Korea

Background and objective: The clinical value of high sensitivity C-reactive protein (hs-CRP) in patients with PD is poorly defined yet. Therefore, we conducted this study to analyze association between hs-CRP levels in PD and those in PD with dementia. hs-CRP is an exquisitely sensitive systemic marker of inflammation and tissue damage and increased level of hs-CRP is strongly associated with inflammatory reactions. Microglia-mediated neuroinflammation has been hypothesized to play an important role in the pathogenesis of idiopathic Parkinson’s disease (PD). Furthermore, many reports have suggested that high concentration of hs-CRP is associated with increased risk of cardiovascular disease, stroke, and cognitive impairment including dementia.

Methods: We examined 60 patients with PD without dementia and 40 patients with PD with dementia and 50 normal control subjects, and investigated differences of hs-CRP among these 3 groups.

Result: Comparing the 3 groups, there was no significant difference between PD and PDD groups for mean hs-CRP values, but these two groups demonstrated significantly higher mean hs-CRP values than the control group.

Conclusions: The pathogenesis of PD is currently unknown, but significant microglial inflammation is observed in the region of dopaminergic degeneration. Furthermore, it is known that inflammation plays a role in the pathogenesis of PD and dementia. However, we suggest in our study that, although neuroinflammation plays a role in neurodegenerative disease including PD and dementia, neuroinflammation did not contribute to the pathogenesis of PD with dementia.

Prevalence and characteristics of non-motor symptoms in Korean PD patients: study using a non-motor symptoms questionnaire

J.-Y. Kim
Neurology, Inje University Paik Hospital, Seoul, Republic of Korea

We investigated the frequencies and characteristics of non-motor symptoms (NMS) in Korean PD patients using a non-motor symptoms questionnaire (NMSQ). We performed a semistructured interview including NMSQ in 57 consecutive patients who visited the movement disorder clinic of Seoul Paik Hospital from May 2011 to October 2011. The demographic data, Hoehn and Yahr (HY) stage, and daily levodopa equivalent dose (LEDD) were also checked. Mean age and duration of disease were 70.8 and 4.6 years. Mean HY stage was 2.7 and LEDD was 793.4mg/day. We found that the mean number of NMS per patient was 14.3 and all patients had non-motor symptoms (range: 5-25). The most common items were: nocturia (87.7%), anxiety (73.7%), constipation (71.9%), remembering (70.2%), urgency (66.7%), and insomnia (66.7%). The most common domains were: the urinary (77.2%), depression/anxiety (65.7%), and sleep disorders (58.3%). The total number of NMS was correlated with HY stage but not with age and disease duration. In women, the mean number of NMS per patient was significantly high than in men (15.2 vs. 12.3, p=0.017). There was a marked difference in frequencies of sleep, depression/anxiety, and apathy/memory domains, which were significantly higher in women. We suggest that NMS is more prevalent in Korean PD patients compared with the results of other previous studies. Women might be more vulnerable to NMS than men especially in sleep, depression/ anxiety, and apathy/memory. Cultural differences might influence the frequencies or characteristics of NMS.
P1587

The examination of relationships between voice abnormalities and the respiratory functions in patients with Parkinson's disease

H. Nakamura¹,², E. Sugawara¹, M. Endou¹, T. Takahashi¹, Y. Kuroiwa²
¹Neurology, National Hospital Organization Yokohama Medical Center, ²Neurology, Yokohama City University, Yokohama, Japan

Introduction: Parkinson's disease (PD) is well known to exhibit voice impairments. The aim of this study is to evaluate objective changes in voice quality in patients with PD.

Methods: 32 PD patients (16 male and 16 female; mean age±SD: 70.8±9.01; Hoehn and Yahr: 2.34±0.70; Unified Parkinson's Disease Rating Scale (UPDRS) part III: 15.03±8.87) and control group (14 male and 15 female; mean age±SD: 69.8±7.58) were assessed. The analysed objective voice parameters were voice volume and maximum phonation time (MPT). All patients in the PD group were examined by respiratory function test (vital capacity and forced expiratory volume).

Results: There were significant differences in MPT which was significantly shorter in the PD group than in the control group (12.84 seconds and 17.58 seconds, respectively) and in voice volume, which was significantly smaller in the PD group than in the control group (91.99 and 98.60dB, respectively). In the PD group, %VC was 96.77±16.13 and FEV1% was 80.87±6.49. The correlations between the UPDRS motor score and the MPT, and between the UPDRS motor score and the voice volume were not significant at the 0.05 level.

Conclusion: The voice of PD patients is shorter and smaller than that of the control group. Voice abnormalities in PD patients are not correlated with respiratory function or motor function.

P1588

The functional interhemispheric asymmetry, clinical asymmetry and clinico-neuropsychological features in patients with Parkinson's disease

M.A. Bykanova, N.V. Pizova
Yaroslavl State Medical Academy, Yaroslavl, Russia

Purpose: To identify the relationship between clinical lateralization of Parkinson’s disease, individual profile of functional interhemispheric asymmetry (IPFA) and their influence on the neurophysiological features of patients with Parkinson’s disease (PD).

Methods and materials: To examine 70 patients (28 male and 42 female) from 1.5 to 3 stages of PD by using the following scales: UPDRS, HOEHN and YAHIR. The IPFA was defined using the special questionnaire with 48 jobs. 32 patients were examined using EEG study (Brain Loc).

Results: Left-sided onset was defined significantly more frequently in patients with mixed and left IPFA than in patients with the right IPFA (p<0.05). Right-sided onset was observed significantly more frequently in patients with right IPFA than in patients with mixed and left profile (p<0.05). Slow-wave activity in the form of generalized bilaterally synchronous bursts was observed in 27 persons (84.3%). The lateralization of abnormal slow-wave activity with a lack of response activation was identified in 21 (65.6%) patients. Generator of pathological activity in right-sided onset was detected predominantly in the left hemisphere, while left-sided debut - on the right hemisphere mainly at the thalamostrionigral structures. A clear lateralization EEG activity was observed in 18 (85.7%) from 21 patients with predominant involvement in the pathological process of the dominant hemisphere.

Conclusions: During the EEG study (Brain Loc) generator of pathological slow wave activity was detected on the opposite side of the affected limb, and a clear lateralization was observed with primary lesion of the dominant hemisphere.
P1589

Clinical correlates of depression and anxiety in patients with Parkinson’s disease

H. Tachibana1, T. Yamanishi1, M. Oguru1, K. Matsui1, M. Hashimoto1, K. Matsubara1, N. Takenaka1, S. Matsutani1, T. Oku1, D. Danno1, K. Kawabata1, B. Okuda2, K. Toda3, N. Oka4
1Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, 2Department of Neurology, Ehime Prefectural Central Hospital, Matsuyama, 3Toda Internal Medicine-Rehabilitation Clinic, Akashi, 4Department of Rehabilitation, NHO South Kyoto Hospital, Jouyou, Japan

Introduction: Although depression and anxiety are important determinants of quality of life (QOL) in patients with Parkinson’s disease (PD), it is unclear whether depression and anxiety are associated with similar demographic and clinical features.

Objective: To clarify whether depression and anxiety are similar in terms of their associations with other clinical variables.

Methods: 117 patients with PD participated in this study. Patients were associated clinically using assessment instruments comprising both neurologist-administered rating scales and self-administered questionnaires. The former assessments were the modified Hoehn and Yahr Scale (HY), the Unified Parkinson’s Disease Rating Scale (UPDRS), and the Mini-Mental State Examination (MMSE). The latter scales included State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), an apathy scale (AS), and 2 QOL instruments: the EuroQoL (EQ-5D) and the 39-item Parkinson’s disease questionnaire (PDQ-39).

Results: Anxiety (STAI ≥41 for men or ≥42 for women) was diagnosed in 52% of the patients and 55% were diagnosed to have depression (BDI ≥14). 14% of the total sample had anxiety without depression, whereas 17% had depression without anxiety. Both STAI and BDI scores were negatively correlated with 2 QOL scales and positively associated with AS score. BDI scores were associated with age at onset, duration of illness, HY stage, and UPDRS scores, whereas STAI scores were not associated with these variables.

Conclusions: These findings suggest that anxiety and depression may be separable in PD, although both are common in patients with PD and are associated with QOL.

P1590

Urinary and respiratory tract infections in people with Parkinson’s disease

A. Fisher1, J. English1, W. Gray2, G. Tan2, G. Idle2, R. Walker2
1Medical School, Newcastle University, Newcastle upon Tyne, 2Medicine, Northumbria Healthcare NHS Foundation Trust, North Shields, UK

Background: Bacterial infections can be a common complication in people with Parkinson’s disease (PD). Respiratory and urinary tract infections can result from non-motor symptoms such as impaired swallowing and urinary dysfunction. We aimed to audit patients’ urine and sputum culture results to investigate how common such infections are.

Methods: Within Northumbria Healthcare NHS Foundation Trust, UK, microbiology archives were used to locate PD patients with positive growth on culture during the ten year period from June 2001-June 2011. Organism was noted and the case notes were reviewed for clinical details.

Results: Of 643 eligible PD patients, only 12 (1.9%) had positive sputum growths. Of those who had positive sputum samples 75% were male and 58% were in early stage of disease (Hoehn and Yahr stage I). In contrast, there were 101 (15.7%) positive urine cultures, although 48% were asymptomatic. The most common urinary infections were E. Coli (33%) and Coliforms (29%).

Conclusions: Despite the fact that pneumonia is a common complication in people with PD, particularly in the later stage of disease, there were remarkably few positive sputum samples during the ten-year period. Interestingly, over half of the samples were in people with early stage of PD; this may reflect the difficulty of those in later stage disease to expectorate. Positive urine cultures were much more common, although this may reflect the relative ease of obtaining a sample. Whether these findings reflect the pattern of infection in people with PD is not clear. Comparison with the general population is required.
P1591

Epidemiology of restless legs syndrome in Croatia

M. Relja¹, V. Miletić²
¹Department Neurology, Medical School University of Zagreb, ²Department Neurology, Zagreb University, Zagreb, Croatia

Introduction: Restless legs syndrome (RLS) is a common and frequently underdiagnosed neurological disorder. RLS may be associated with sleep disturbances and may have a negative impact on quality of life. Reported prevalence estimate of RLS have varied widely (from 2.5 to 29%).

Aims of study: To estimate the prevalence and to evaluate the characteristics of RLS in Croatia.

Patients and methods: A cross-sectional survey included 1432 randomly chosen subjects aged 18 to 81 years. A neurologist and/or family physician conducted interviews using a questionnaire based on diagnostic criteria developed by the International Restless Legs Syndrome Study Group (IRLSSG).

Results: A total of 245 (17.6%) examinees answered positively, fulfilling minimal criteria for RLS. Idiopathic form of RLS was observed in 136 (55.5%) of 245 patients indicating the estimated prevalence of 9.5% in the Croatian population. Underlying conditions associated with secondary RLS were diabetes mellitus (50%), iron deficiency (37.5%) and use of medications (11.5% - SSRIs, antidepressants). The prevalence was higher in women and increased with age.

Conclusions: This is the first epidemiologic study of RLS in Croatia showing the 9.5% prevalence of idiopathic RLS. Only 4.5% complained of severe symptoms that needed treatment. The results found in this study are similar to the findings of other European countries.

Supported by the Croatian Ministry of Science

P1592

Ultrasonographic and clinical correlates in patients with idiopathic Parkinson’s disease: a prospective study

K. Lauckaitė¹, D. Rastenyte¹, D. Surkiene¹, A. Vaitkus¹, R. Gleizniene²
¹Neurological, ²Radiological, Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction: Among the new techniques, transcranial sonography (TCS) has been drawing attention as an easily accessible and inexpensive imaging method in Parkinson’s disease (PD), despite its value is still disputable.

Methods: The PD patients for prospective TCS investigation were referred from the Neurological Department of the Hospital of Lithuanian University of Health Sciences in 2011. A PA2-5 transducer on the ultrasound system Voluson 730 Expert (GE Healthcare, Austria) was used for TCS. A total of 113 patients were enrolled for further analysis, after excluding 19 (14.4%) with bilateral temporal insufficiency. Diagnosis was established according to the UK brain bank criteria. The clinical, demographic data, UPDRS-III, HAD, HamD scale results were collected.

Results: The mean age of PD patients (±SD) was 63.5±12.0yrs, UPDRS-III 12.8±5.4 points, and stage according to Hoehn-Yahr (H-Ys) 1.8±0.7. Tremor-dominant PD was diagnosed in 39 (34.5%), postural-instability-gait-disorder-dominant (PIGD) in 27 (23.9%), mixed type in 47 (41.6%). The subgroups did not differ according to age, sex, H-Ys. The biggest substantia nigra (SN) plots were in PIGD (Kruskal-Wallis Chi²=46.9, p<0.001). The significant correlations were detected between diameter of the third ventricle (V3) and age (Spearman r=0.5, p<0.001), V3 and H-Ys (r=0.2, p=0.05), HamD and H-Ys (r=0.6, p=0.003), PD subtype and SN plot (r=0.3, p=0.002), H-Ys and SN plot (r=0.3, p=0.004), UPDRS-III and SN plot on the left (r=-0.6, p=0.028), H-Ys and nuclei raphe changes (r=-0.2, p=0.049), H-Ys and lateral ventricles’ diameter (r=0.3, p=0.023).

Conclusions: Multiple correlates between ultrasonographic and clinical parameters were detected in PD patients, which add valuable clinical information.
P1593

Intravascular platelet activation in patients with hepatolenticular degeneration

M. Melnikova1, S. Lobzin1, T. Fedorova1, E. Panina1, L. Vedyukova1, G. Sisoeva1, L. Tarkovskaya2, T. Morozova2
1North-Western State Medical University named after I.I. Mechnikov, 2Russian Research Institute of Hematology and Transfusiology, Saint-Petersburg, Russia

Introduction: Hepatolenticular degeneration (HLD) is an autosomal recessive inherited disorder of copper metabolism, characterized by hepatic and neurological dysfunction. Accumulated amounts of copper produce angiotoxic and haemolytic effects, which can significantly influence haemostasis. However, the platelet morphofunctional characteristics in HLD were not investigated before.

Methods: Platelet count and intravascular platelet activation (IPA) were evaluated in 48 patients with HLD. 23 patients were examined before chelating therapy and 25 on different stages of treatment. All patients were divided into groups on the base of the prevalence of hepatic or neurological manifestations, and different severity of hepatic impairment. Severity of the disease was evaluated by the Unified Wilson’s Disease Rating Scale. A control group included 25 normal individuals.

Results: All patients had thrombocytopenia and significant increase of IPA parameters: total amount of active forms of platelets and number of platelets, involved in aggregation. Severity of the disease and degree of hepatic impairment influenced only the platelet count, but not IPA. Level of cytolysis and cholestasis did not influence IPA (p<0.05). In patients receiving chelating therapy parameters of IPA were reduced significantly, but remained higher than in controls.

Conclusion: In HLD patients, activation of platelet haemostasis is observed. Parameters of IPA remain high during the chelating therapy. Impairment of morphological and functional properties of platelets contributes to severity of chronic brain and liver diseases and requires treatment. Thus, some additional factors can modify the activation and aggregation of platelets in HLD and be the goal for further research.

P1594

Total numbers of neurons and glial cells in the basal ganglia of brains from patients with multiple system atrophy

B. Haugen1, K. Winge2-3, L. Salvesen1-2, T. Agander1-4, B. Pakkenberg1
1Research Laboratory for Stereology and Neuroscience, 2Bispebjerg Movement Disorders Biobank, 3Department of Neurology, Bispebjerg University Hospital, Copenhagen, 4Department of Pathology, Roskilde University Hospital, Roskilde, Denmark

Introduction: MSA is a sporadic, progressive neurodegenerative disorder characterized by varying severity of parkinsonism, cerebellar ataxia and autonomic failure. MSA is histopathologically characterized by glial cytoplasmic inclusions and selective neurodegeneration. The details on the pathogenesis are still unknown.

Material and methods: The material comprises 10 brains from patients with MSA and 10 control subjects. The total number of neurons and glial cells in Substantia Nigra, the Subthalamic Nucleus (StN) and the Red Nucleus (RN) of brains from patients with MSA were estimated using design based stereological methods providing quantitative data on brains affected by a neuronal loss. Data were analyzed using Sigma Stat 11.0, Systat Software Inc., San Jose, California, USA.

Results: The MSA brains were estimated to have about 40% fewer pigmented neurons in Substantia Nigra (40.1*10^4 versus 91.8*10^4, p<0.001). In the Subthalamic Nucleus and the Red Nucleus the total number of neurons, oligodendrocytes and astrocytes were the same in the two groups, whereas microglia were more abundant in the MSA brains in both StN (20.4*10^4 versus 82.6*10^4, p=0.026) and RN (10.2*10^4 versus 33, 1*10^4, p<0.001).

Conclusion: In terms of cell numbers the Subthalamic Nucleus and the Red Nucleus are not severely affected in patients with MSA compared to the control subjects. The increased microglia level could indicate inflammation in MSA. The high loss of neurons in Substantia Nigra supports the neurodegenerative nature of MSA.
P1595

A case of orthostatic tremor associated with Grave's disease

S. Mazzucchi, D. Frosini, M. Giuntini, E. Del Prete, R. Ceravolo

Department of Neuroscience, University of Pisa, Pisa, Italy

Introduction: Orthostatic tremor (OT) is a rare disorder characterized by high frequency lower limbs tremor and unsteadiness on standing with remission during sitting or lying.

A 70-year-old woman presented with a sense of unsteadiness and tremor in her legs mainly during standing and walking, which gradually worsened over a year without any benefit after clonazepam. Neurological exam showed tetrahyperreflexia, paraparetic gait and inability to perform tandem gait. She also reported intolerance of heat, excessive sweating and recent loss of weight with increased appetite, dysphagia and dysphonia.

Methods: Electromyographic recordings from vastus medialis and tibialis anterioris performed during standing showed a rhythmic contractile activity at about 8Hz. After prolonged supine rest, a rhythmic contractile activity at lower amplitude re-appeared in both lower legs. Due to atypical clinical and EMG activity and low frequency of tremor, a symptomatic origin was hypothesized. Brain and cervico-dorsal MRI and motor evoked potentials were normal. Her thyroid function exams revealed severe hyperthyroidism (thyroid stimulating hormone (TSH) <0.004µU/ml [0.400-4.000µU/ml], fT3 9.25pg/ml [1.80-4.80pg/ml], fT4 5.05ng/dl [0.80-1.80ng/dl]) and positivity of TSH receptor antibodies. A chest and neck CT scan revealed an increase in thyroid size involving the upper mediastinum and affecting the left side of the oesophagus.

Result: A diagnosis of Graves disease was performed and she was started on Carbimazole with dramatic improvement of tremor.

Conclusion: Graves syndrome has been recently described as a possible cause of OT, and should be taken into account mainly when OT presents with atypical phenotype.

P1596

Study of osteoprotegerin concentrations and level of 25(OH)D in blood serum of patients with Parkinson's disease, ischemic stroke and other neurological diseases

U. Fiszer, M. Piaścik-Gromada, B. Parafinqu, G. Korczak-Kowalska, K. Bocian, T. Szatanowski

1Medical Center of Postgraduate Education, 2The Children's Memorial Health Institute, 3University of Warsaw, Poland

Osteoporosis and decrease of the level of vitamin 25(OH)D was described in patients with PD. Concentration of osteoprotegerin (OPG) has been associated with the risk of osteoporosis and vascular pathology, however, it has not yet been examined in PD patients.

Methods: The study group included 95 patients, within this group 45 suffered from PD. A - with initial PD (20 persons), B - with advanced PD >5 years (25 persons), C - with stroke (30 persons), D - with other neurological disease (OND) (20 persons). Osteoprotegerin concentration measured by the sandwich ELISA, and the level of 25(OH)D in blood serum was obtained by the automatic chemiluminescence method.

Results: Osteoprotegerin concentration in serum was (mean): A - 5.50pg/ml, B - 6.80pg/ml, C - 7.59pg/ml, D - 5.68pg/ml. The results demonstrate an increased osteoprotegerin concentration in stroke patients (C v A, U Mann Whitney test p<0.03). The mean level of 25(OH)D in groups was: A - 15.45ng/ml, B - 13.80ng/ml, C - 11.12ng/ml, D - 17.48ng/ml. The results demonstrate an increased osteoprotegerin concentration in stroke patients (C v A, U Mann Whitney test p<0.03). The mean level of 25(OH)D in groups was: A - 15.45ng/ml, B - 13.80ng/ml, C - 11.12ng/ml, D - 17.48ng/ml. Normal level of 25(OH)D in adults is between 30 and 80ng/ml. Results showed decrease of level of 25(OH)D in patients with initial and advanced PD. It was also seen in patients with OND, and particularly with ischemic stroke (C v D, p<0.03, t-Student test).

Conclusion: No increase of OPG in initial PD was found, as opposed to stroke patients. The results also showed insufficient supply of vitamin D in patients with different neurological diseases.
P1597

Chronic pain in Parkinson’s disease - characteristics and association with bone mineral density

H.-J. Jung¹, S.-M. Choi¹, E.-S. Park², S.-Y. Lee², B.-H. Cho², B.-C. Kim², M.-K. Kim², M.-S. Park², S.-H. Lee²
¹Neurology, Chonnam National University Hwasun Hospital, Hwasun-gun, ²Neurology, Chonnam National University Hospital, Gwangju, Republic of Korea

Background and purpose: Chronic pain and low bone mineral density (BMD) in Parkinson’s disease (PD) are increasingly recognized as a major cause of reduced health-related quality of life. But, there have been few studies concerning chronic pain and relationship between osteoporosis in PD, even though patients with PD have a high incidence of falls. The aim of this study was to investigate the prevalence and the characteristics of chronic pain and its associations with BMD in patients with PD.

Patients and methods: 91 patients diagnosed with idiopathic PD were interviewed with semi-structured pain questionnaire. The severity of PD judged using Unified PD Rating Scale, Hoehn and Yahr staging. BMD in the lumbar spine and proximal femur were evaluated by dual X-ray absorptiometry. Patients were divided into three groups according to chronic pain, acute pain and no pain. We then investigated the clinical correlation between severity of PD and BMD.

Results: 73 (80.2%) out of 91 patients reported pain and 68 (74.7%) patients had chronic pain. Patients with chronic pain were more prevalent in females (p=0.02) and old age (p=0.042) and higher UPDRS II (p=0.016), NMSAS (p=0.028), and the Gait and Falls questionnaire (p=0.01). BMD in patients with chronic pain were significantly lower femur BMD.

Conclusions: Pain is common in patients with PD and associated with poor ADL, higher frequency of falling and lower BMD. Patients with chronic pain should be carefully examined and screened for osteoporosis to prevent bone loss and associated disability due to falling.

P1598

Motor phenotype of LRRK2-associated Parkinson’s disease: a longitudinal study

F. Nabli, S. Ben Sassi, E. Hentati, I. Lakhdhar, H. Nahdi, R. Amouri, F. Hentati
National Institute of Neurology, Tunis, Tunisia

Background and aims: Mutations in the Leucine-rich repeat kinase 2 gene (LRRK2) showed to be a significant cause of autosomal dominant forms of Parkinson’s disease (PD). In order to determine the motor characteristics of LRRK2-related disease, we conducted a longitudinal study of 58 LRRK2-associated PD patients and compared them with idiopathic PD patients.

Patients and methods: 58 patients diagnosed with PD-related LRRK2 G2019S mutation were included in the study and compared to 59 sporadic PD patients with negative tests for LRRK2 G2019S, PINK1, SNCA, PRKN et DJ1 mutations. Patients were assessed at baseline and after a follow-up period of six years. Collected data included the Movement Disorder Society-unified Parkinson’s Disease rating scale (MDS-UPDRS), the Hoehn and Yahr stage and the Schwab and England scale.

Results: The LRRK2-associated PD patients had a mean age at baseline of 68.45±11.82 years, a mean age of onset of 56.25±12.05 years and in most cases (61%) a PIGD phenotype. The mean annual decline in the UDRS motor score and the Hoehn and Yahr staging were of 1.3% and 2%, respectively. Motor severity correlated with disease duration and PIGD phenotype, and tremor dominant phenotype predicted slower progression of motor impairment. PD motor phenotype and motor scores were similar in the LRRK2-associated PD group and in the idiopathic PD group with no significant differences in the progression rate of motor impairment.

Conclusion: Motor phenotype seems to be similar in LRRK2-related PD and idiopathic PD.
Is the nigrostriatal dysfunction a possible predictive marker of visual hallucinations in Parkinson’s disease? Evidence from a 123I-FP-CIT SPECT study

L. Kiferle, R. Ceravolo, V. Nicoletti, P. De Feo, D. Volterrani, U. Bonuccelli
Department of Neuroscience, University of Pisa, Italy

Introduction: The pathogenesis of visual hallucinations (VH) in Parkinson’s disease (PD) has been considered multifactorial. In the pathophysiology of VH, a combination of impaired visual processing and attention was reported. Imaging studies evidenced a role of the primary visual system and visual association areas as well as a dysfunctional activation of frontal areas. Moreover, longitudinal neuropsychological studies showed an association of VH with baseline frontal dysfunction, suggesting verbal fluency as a potential predictor of VH within 2 years. Due to the functional connections between basal ganglia and frontal areas, a role of basal ganglia and of the frontostriatal circuits in the pathogenesis of VH may be postulated.

Objective: To unveil whether a worse nigrostriatal dysfunction at baseline may predict the development of VH in PD.

Methods: 16 non-demented VHPD and 14 non-demented non-VHPD patients, matched for age of onset of disease, disease duration and severity, levodopa equivalent dose, underwent a 123I-FP-CIT SPECT at disease onset. Striatal uptake values in the two groups were investigated.

Results: The group of VH had a significant reduction (p<0.05) of right caudate uptake values at baseline when compared with non-VHPD. No significant differences were present between groups in left caudate and putaminal uptake values.

Conclusions: The frontal impairment reported in VHPD may be due to a right caudate dysfunction, as it is connected to the frontal brain areas via neuronal loops. Our data could suggest the early caudate dysfunction as a potential predictive marker of VH in PD.

Glucocerebrosidase L444P mutation confers a genetic risk factor for Parkinson’s disease in central China

N. Xiong, Y. Wang, C. Chen, J. Huang, T. Wang
Department of Neurology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Introduction: Mutations of the glucocerebrosidase (GBA) gene have been reportedly associated with various ethnic Parkinson’s disease (PD) populations. However, whether or not there is any association of different sequence variants of GBA with PD in central China remains unknown. The agriculture-related central China area should be drawn particular attention to, as recent epidemiological studies suggest an association of environmental toxins such as rotenone and other pesticides with the higher incidence of sporadic PD in rural areas.

Methods: Here, we conducted a case control study in a cohort of 208 central Chinese PD patients and 298 control subjects for three GBA mutations (L444P, N370S and R120W) by Polymerase chain reaction-restriction fragment length polymorphism and DNA sequence.

Results: Our data suggested a significant higher frequency of L444P mutation in GBA gene of PD cases (3.4%) compared with the controls (0.3%) (p=0.007, OR=10.34, 95% CI=1.26-84.71). As for gender, there was no significant difference between mutation carriers and non-carriers. Additionally, the average age at onset of PD carriers showed no significant difference between mutation carriers and non-carriers. Specifically, the frequency of L444P mutation was higher in late onset PD (LOPD) cases compared with that in control subjects. The N370S and R120W mutations experienced no difference between the PD group and the control group.

Conclusions: Our observations demonstrated that the GBA L444P mutation confers a potential risk factor for PD, especially LOPD, in the central China area.
**P1601**

**Is the “cold hands” sign useful in differentiating multiple system atrophy from Parkinson’s disease?**

M. Asahina¹, D.A. Low², C.J. Mathias², Y. Fujinuma¹, A. Katagiri¹, Y. Yamanaka¹, J. Shimada¹, A. Poudel¹, S. Kuwabara¹

¹Neurology, Chiba University School of Medicine, Chiba, Japan. ²Autonomic & Neurovascular Medicine Unit, Imperial College London at St. Mary’s Hospital, London, UK

**Aim:** A previous study on a small number of patients showed that low skin temperature of the hands with skin colour changes, the so-called “cold hands sign”, may be useful for distinguishing multiple system atrophy (MSA) from Parkinson’s disease (PD). Therefore, low skin temperature of the hand may be a characteristic of MSA rather than PD. We evaluated the skin colour and temperature of the hand in a larger number of MSA and PD patients.

**Methods:** Skin temperature on the centre of the palm was measured in 50 MSA patients (age, 64.4±6.0 years; duration, 2.9±1.7 years), 50 PD patients (67.5±7.7 years; 8.1±7.6 years), and 25 healthy subjects (age, 64.7±11.4 years). All participants were Japanese by ethnicity.

**Results:** Temperatures of <28°C were observed in 3 MSA patients (6%) and none of the PD patients and controls. We could not find any skin colour changes on the hand, such as dusky and violaceous, in any participants. Palm skin temperature was significantly lower in MSA patients (32.0±2.7°C) than in controls (34.1±0.9°C, p=0.0002), but was not different compared with the PD group (32.9±1.8°C, p=0.06). There was no significant difference between the PD and control groups.

**Conclusions:** Measurement of skin temperature is easy and non-invasive and the “cold hands (<28°C)” sign may be useful for distinguishing MSA from PD. However, the sensitivity appears to be low.

---

**P1602**

**Reasons for discontinuation of botulinum-toxin treatment of focal hand dystonia**

M. Balaz¹, T. Gajda³, M. Bares¹

¹Department of Neurology, Masaryk University, St Anne’s University Hospital, ²CEITEC - Central European Institute of Technology, MU Brno, ³Medical Faculty, Masaryk University, Brno, Czech Republic

**Objective:** The goal of the study was to assess the reasons for discontinuation of long-term treatment of writer’s cramp in patients treated with botulinum toxin (BTX). We also observed the long-term BTX treatment outcomes.

**Introduction:** Botulinum toxin A is considered to be an effective treatment for the patients suffering from focal hand dystonia (such as writer’s cramp) but its long-term usefulness may be limited by frequent discontinuation of the treatment for various reasons.

**Methods:** We reviewed the records of 54 patients who had more than 400 applications of BTX. We also conducted surveys via mail or telephone interviews with the patients who were lost to regular follow-up.

**Results:** Each patient had at least 2 application sessions, median treatment duration was 82 months. 83% of treated patients reported at least a partial improvement of their condition. There were no serious adverse events. Most frequent side effect was the weakness of muscles adjacent to the injection site. Altogether 30 (55%) patients chose to discontinue the treatment.

**Conclusions:** A high proportion of the patients chose to discontinue the treatment with BTX. Main reasons for discontinuation were side effects (33%), low efficacy (30%), relocation (6.5%), change of writing habits (6.5%), new symptoms and change of treatment (6.5%), other and unknown reasons (17.5%). While BTX remains an effective treatment, drop-out rate may be higher than in other focal dystonias, especially due to the side effects and subjectively assessed low efficacy in some patients.
P1603

Association between falls and urinary disturbance in Parkinson’s disease

K. Sakushima1, S. Yamazaki2, Y. Hayashino2, S. Fukuhara2, I. Yabe1, H. Sasaki1
1Department of Neurology, Hokkaido University Graduate School of Medicine, Sapporo, 2Department of Healthcare Epidemiology, Graduate School of Medicine and Public Health, Kyoto, Japan

Introduction: Falling is one of the most common and serious incidents among public health problems. It can cause injuries such as sprains and fractures. Hospitalization may be required when it is a serious injury. Patients with Parkinson’s disease have a higher risk of falls. Urinary incontinence is also known as a risk factor of falls for the elderly. However, the risk of falling associated with other symptoms of urinary disturbance is unclear. The purpose of this study is to identify the association between falls and urinary disturbance in Parkinson’s disease.

Methods: A prospective cohort study at a single institution with six months observation period was conducted. Subjects were ambulatory patients with Parkinson’s disease. Assessment included patient demographics, disease severity measured by Hoehn and Yahr Scale, and urinary disturbance measured by overactive bladder symptom score (OABSS). Falls were reported by a self-documented falls record.

Results: A total of 86 patients (33 males, 53 females) were included. Mean age was 71.0±7.5. Hoehn and Yahr Scale was 2.6±1.1. 39 patients (45%) had at least one fall (faller) and 28 patients (33%) had two or more falls in six months. In OABSS, urinary urgency and urgency incontinence were more common in fallers than in non-fallers (55% vs. 30% and 58% vs. 35%, respectively). However, daytime frequency and night-time frequency is not associated with falls.

Conclusion: Falls in patients with Parkinson’s disease were not associated with urinary frequency but associate with urinary urgency and incontinence.

P1604

Pain and its clinical types in Parkinson’s disease

J. Harsany1, M. Hanakova1, P. Valkovic1,2
1Second Department of Neurology, School of Medicine, Comenius University, 2Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovak Republic

Introduction: Pain is an important and distressing symptom in Parkinson’s disease (PD). A frequently overlooked clinical feature of PD, pain may be severe enough to overshadow the motor symptoms of the disorder. Aim of this study was to determine frequency and types of pain in patients with PD. Moreover, we correlated pain characteristics with demographic data, quality of life, and depression.

Methods: This is a single-centre cross-sectional study. 35 consecutive subjects with PD participated. Demographic data, severity and types of pain were assessed using structured questionnaire and Beck Depression Inventory, respectively. Pain was divided based on Fords’ classification (Mov Disord. 2010;25 Suppl 1:S98-103): musculoskeletal, dystonic, central parkinsonian, low back/radicular, and not-classified pain. Severity of average pain during the last week was rated on 10-point visual analogous scale.

Results: In our set of PD subjects, the presence of pain types was as follows: musculoskeletal pain 34.3%, dystonic pain 8.6%, central parkinsonian pain 17.1%, low back /radicular 54.3%, and not-classified pain 14.3%. No pain referred 20% of patients, one type 48.8%, two types 20.0%, three types, 5.7%, and four types 5.7%. A significant correlation was found between PD duration and number of pain types (rho=0.53018, p=0.0011), and number of pain types and average pain severity (rho=0.63984, p<0.0001)

Conclusion: Pain in PD is present in 80% of patients. The most frequent type of pain is the low/back radicular pain. Our results stress the importance of pain type determination because of different treatment approaches.
P1605
Non-motor symptoms in Parkinson's disease: a correlation with depression and quality of life
M. Hanakova1, J. Harsany1, P. Valkovic1,2
1Second Department of Neurology, School of Medicine, Comenius University, 2Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovak Republic

Introduction: Non-motor symptoms (NMS) of Parkinson's disease (PD) are not well recognized in clinical practice, and are frequently missed during routine. Aim of this study was to determine frequency and severity of NMS in patients with PD. Moreover, we correlated NMS scores with demographic data, quality of life, and depression.

Methods: This is a single-centre cross-sectional study. NMS severity was determined by using the Non-Motor Symptom assessment scale for PD (NMSS; Chaudhuri KR, et al. Mov Disord. 2007;22(13):1901-11.) and self-completed NMS-Questionnaire for PD (the NMSQuest; Chaudhuri KR, et al. Mov Disord. 2006;21(7):916-23.). Quality of life was assessed by PDQ-8 questionnaire, and depression was scored by means of Beck Depression Inventory (BDI).

Results: Data from 35 consecutive patients, mean age 65.2±7.8 years, duration of disease 5.5±4.5 years, and all stages of PD were collected. The mean NMSS score was 39.6±24.6 (range: 9-110). The mean NMSQuest score was 10.5±4.7 (range: 2-22). We found significant correlation between NMSS score and NMSQuest score (rho 0.71; p<0.0001), NMSQuest and duration of PD (rho=0.55; p=0.0007), NMSQuest and BDI (rho 0.69; p<0.0001), NMSS and BDI (rho 0.56; p=0.0005), and PDQ-8 score and BDI (rho=0.51, p=0.0017).

Conclusion: NMS are significantly frequent across all stages of PD. This study proves the efficiency of screening questionnaire the NMS-Quest, as well as of NMSS. Scores of both instruments highly correlate. Moreover, NMS correlate with depression that correlates with quality of life in PD. Our results stress the importance for active detection of NMS in PD patients.

P1606
Defective iron-handling and altered cellular oxidative status in skin fibroblasts from pantothenate kinase associated neurodegeneration patients
S. Levi1,2, A. Campanella1, D. Privitera1, M. Guaraldo1, C. Barzaghi3, A. Cozzi2, P. Santambrogio2, B. Garavaglia1
1Vita-Salute San Raffaele University, 2Division of Neuroscience, San Raffaele Scientific Institute, 3Fondazione IRCCS-Istituto Neurologico Carlo Besta, Milan, Italy

Introduction: Pantothenate Kinase Associated Neurodegeneration (PKAN) is the most prevalent form of neurodegeneration involving iron accumulation in the brain. It is characterized by progressive impairments in movement, speech and cognition. The disease is inherited in a recessive manner due to mutations in the Pantothenate Kinase-2 (PANK2) gene that encodes a mitochondrial protein involved in Co-enzyme A synthesis.

Aim: To elucidate the molecular mechanism leading to iron homeostasis dysfunction in Pank2 gene defect cells.

Patients and methods: We analyzed, in primary skin fibroblasts from three PKAN patients and three unaffected subjects, the oxidative status and their ability to respond to iron.

Results: In basal conditions, PKAN fibroblasts show an increase in carbonylated proteins and altered expression of antioxidant enzymes with respect to the controls. After iron supplementation, the PKAN fibroblasts had a defective response to the additional iron. Under these conditions, ferritins were up-regulated and Transferrin Receptor 1 (TfR1) was down-regulated to a minor extent in patients compared to the controls. Analysis of Iron Regulatory Proteins (IRPs) reveals that, with respect to the controls, PKAN fibroblasts have a reduced amount of membrane-associated mRNA-bound IRP1, which responds imperfectly to iron. This accounts for the defective expression of ferritin and TfR1 in patients' cells. The inaccurate quantity of these proteins produced a higher bioactive labile iron pool and consequently increased iron-dependent ROS formation.

Conclusions: Our results suggest that Pank2 deficiency promotes an increased oxidative status that is further enhanced by the addition of iron, potentially causing damage in cells.
P1607

Fatigue in Parkinson’s disease

T. Torgan
Perin State Medical Academy, Perm, Russia

Introduction: It is not clear whether fatigue in patients with Parkinson’s disease is the primary or the secondary symptom.

Objective: To investigate whether fatigue is associated with depression, autonomic disturbances, the severity of movement disorders and sleep disturbance in patients with Parkinson’s disease.

Methods: The Unified Parkinson’s Disease Rating Scale, Hoehn and Yahr scale, the Multidimensional Fatigue Inventory (MFI-20), the Hospital Anxiety and Depression Scale (HADS), the Epworth Sleepiness Scale (ESS), Veyn Questionnaire for autonomic disturbances were used.

Results: 55 patients (16 males, 39 female) with Parkinson’s disease without dementia were studied. Mean age was 64 (60-70) years, the duration of the disease was 5 (2-5) years. Patients received different dopaminergic therapy and were examined in “off” period. The control group consisted of 19 persons of the same age and sex. The mean rate of fatigue in patients with Parkinson’s disease (37; 25-46 points) was higher (p=0.000) than in the control group (15; 9-19 points). It did not depend on sex and age of the patients. 38 patients had more than 36 points on MFI-20. The rate of fatigue in this group did not correlate with the duration (R=-0.11, p=0.644) and the severity of the disease (R=0.23, p=0.308), the severity of motor disorders (R=-0.11, p=0.642) and depression (R=-0.02, p=0.924). The autonomic (R=-0.41, p=0.070) and sleep disturbances (R=0.02, p=0.093) did not influence the fatigue.

Conclusion: Fatigue in patients with Parkinson’s disease is not the secondary symptom due to depression or sleep disturbances, but is a primary phenomenon with its own pathogenesis.

P1608

Montreal cognitive assessment as a new screening tool for dementia in Huntington’s disease: a validation study

P. Moskal1, K. Banaszkiewicz2, E.M. Klimiec1, A. Starowicz3, M. Blaz1, A. Szczudlik1

1Department of Neurology, Jagiellonian University Medical College, 2Krakowska Akademia Neurologii, 3Department of Medical Psychology, Jagiellonian University Medical College, Krakow, Poland

Background and aims: Cognitive disturbances are often the first manifestation of Huntington’s disease (HD) and are an important factor contributing to patients’ disability. Neuropsychological assessment is the most relevant, but time consuming, method of cognitive evaluation. The Montreal Cognitive Assessment (MoCA) is a new screening instrument which detects early cognitive impairment. However, MoCA has not been compared with neuropsychological tests in HD. The aim of this study was to find a cut-off for MoCA that sensitively screens for dementia in HD patients.

Patients and methods: 22 HD patients were examined with MoCA and a battery of neuropsychological tests which assessed 5 cognitive domains: Stroop Test and Perception and Attention Test for attention; Benton Visual Retention Test for memory; Trail Making Test, Wisconsin Card Sorting Test and Similarities from Wechsler Adult Intelligence Scale (WAIS) for executive functions; Verbal Fluency Test for language; Block Design from WAIS for visuospatial abilities. Dementia was defined as an impairment in at least two cognitive domains. Receiver operating characteristics analysis was used to find a sensitive cut-off in MoCA to diagnose dementia.

Results: According to neuropsychological assessment 15 patients had dementia. The most sensitive MoCA cut-off score was 26, with 100% sensitivity and 71% specificity. Another 2 patients were impaired in only one cognitive domain and scored ≤26 on MoCA, the other 5 patients without any cognitive disturbances scored >26.

Conclusion: MoCA cut-off score ≤26 allows for sensitive screening for dementia in HD.
**P1609**

**Spasticity and "spastic" gait in children with hereditary spastic paraplegias**

I.U. Isaias¹², A. Marzegan¹, E. Todeschini¹, P. Cavallari¹, J. Volkman², P. Crenna¹

¹Dipartimento di Fisiologia Umana, Laboratorio per l’Analisi del Movimento (LAMB) P. & L. Mariani, Università degli Studi di Milano, Italy, ²Neurologische Klinik und Poliklinik, Universitätsklinik Würzburg, Germany

**Introduction:** Hereditary spastic paraplegias (HSPs) are a clinically and genetically heterogeneous group of conditions characterized by the presence of lower limb spasticity and pyramidal weakness. We aimed to address spastic muscle behaviour under dynamic conditions (unperturbed overground walking) in children with HSP.

**Patients and methods:** 10 children (3 male; age range: 4-13 years) were enrolled in the study and evaluated clinically and by means of brain MRI, BAER, SSEP and MEP. Spastic muscle (soleus) behaviour was quantitatively characterized by the level of current EMG activity as a function of the muscle lengthening velocity (muscle kinematics was estimated by geometrical models).

**Results:** Four different patterns of spastic muscle behaviour were described. Pattern-I was defined by the presence of hyper-synchronous activity in the post heel-contact phase with equal or higher amplitude with respect to the following push-off phase (and no activity pause between these two phases). We classified pattern-II or -III when the hyper-synchronous activity in the post heel-contact phase (as in pattern-I) was paused by "Post Synchronous Discharge Silent Periods (PSDSPs)" >70ms (pattern-III if PSDSPs were >3). Pattern-IV was characterized by hyper-synchronous activity also in the swing phase. Each child showed a different combination of these patterns. Overall, pattern-II was the most frequent (30%) followed by pattern-I (14.5%) and pattern-III and -IV (< 10%).

**Conclusion:** A dynamic evaluation allowed a detailed profiling of spasticity in children with HSP. This might be useful to determine functional severity of lower limb spasticity at follow-ups and for proper medical treatment.

---

**P1610**

**The impact of non-motor symptoms on health-related quality of life in patients with atypical parkinsonism**

S.-B. Koh, C.-N. Lee

Neurology, Korea University College of Medicine, Seoul, Republic of Korea

**Background:** Atypical parkinsonism is less common and has more severe symptoms than Parkinson’s disease. Relatively little is known about the characteristics of non-motor symptoms (NMS), which could affect to health related quality of life (QoL) in multiple systemic atrophy (MSA) and progressive supranuclear palsy (PSP). We report the characteristics of NMS and the impact of NMS on health-related QoL of MSA and PSP.

**Methods:** Out of 58 patients with a diagnosis of atypical parkinsonism, 32 patients had multiple systemic atrophy parkinsonian subtype (MSA-P), 14 patients had multiple systemic atrophy cerebellar dysfunction subtype (MSA-C), 12 patients had PSP. We assessed the Unified Parkinson’s Disease Rating Scale part III (UPDRS-III), the modified Hoehn & Yahr scale (H&Y), the Parkinson’s Disease Questionnaire (PDQ-39) and the non-motor symptom scale (NMSS).

**Results:** There were no differences of sex ratio, disease duration, UPDRS-III score, and H&Y stage in the three groups. In the MSA-P, MSA-C and PSP group, PDQ-39 scores are correlated with NMSS scores, not UPDRS-III scores. Concerning the correlations of domains in NMSS scores and PDQ-39 scores, PDQ-39 scores of MSA-P group are correlated with domains of mood/cognition, cardiovascular inducing falls, and urinary dysfunction. In MSA-C group, PDQ-39 scores are correlated with domains of sleep/fatigue, mood/cognition, urinary dysfunction. In PSP group, PDQ-39 scores are correlated with domain of mood/cognition.

**Conclusion:** Non-motor symptoms are associated with QoL in the three groups, and the mood/cognition domain is a very important part of NMS. When we treat MSA, PSP patients, we must consider non-motor symptoms, especially mood/cognition.
P1611

White matter lesions and depression in patients with Parkinson’s disease

V. Marković1, I. Petrović1, E. Stefanova1, D. Kozic2, R. Semnic2, V. Kostić1
1Movement Disorders Department, Neurology Clinic Clinical Center of Serbia, Belgrade, 2Diagnostic Imaging Center, Institute of Oncology, Sremska Kamenica, Serbia

Introduction: The incidence of Parkinson’s disease (PD) increases with age, and white matter changes (WMHs) present as signal hyperintensities on T2W MRI studies are commonly observed in older adults. Severity of deep WMHs was also correlated with depression.

Objective: To investigate whether WMHs were associated with depression in PD patients.

Methods: We included 34 patients with (PD-D) and 25 without depression (PD-nD) with PD onset above 60yrs, and 30 healthy controls. Diagnosis of depression was established via Structured Clinical Interview for DSM-IV Axis I disorders and quantified using Hamilton Depression Rating Scale (HDRS). Patients underwent brain 1.5-T MRI. WMHs were rated using T2W images and classified using the semiquantitative visual rating scale of Scheltens.

Results: Comparing controls and PD patients as a group there were no differences in WMHs in any examined region. However, PD-D group had significantly higher WMHs scores for total deep WM and BG regions when compared to controls as well as for frontal deep WM and total periventricular regions WMHs comparing with the PD-nD group. There were no differences in WMHs between PD-nD patients and controls in any of the examined regions. The multivariate linear regression analysis was carried out with HDRS score as a dependent variable and lobar (frontal, temporal, parietal, occipital), periventricular and BG WMHs, age, education and cerebrovascular risk factors as independent variables. Significance was only shown for periventricular WMHs total score (p=0.04), explaining the 39% of the variance in the HDRS.

Conclusion: Our study confirms the role of WMHs in depression associated with PD.

P1612

MAPT rs242562 and GSK3β rs334558 are associated with Parkinson’s disease in a central Chinese cohort

N. Xiong, L. Yu, J. Xiong, J. Huang, T. Wang
Department of Neurology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Background: MAPT is a neuronal protein involved in the pathogenesis of several neurodegenerative diseases including PD. GSK3β catalyzes phosphorylation in multiple sites of tau protein. These results have driven out a research hotspot which is about the gene-gene interaction between MAPT gene and GSK3β gene and their respective links in several diseases. Previous data have indicated that the genetic alteration of GSK3β and its interaction with MAPT haplotype are collectively related to PD morbidity rate in a Greek cohort. However, the association among the GSK3β gene alteration, MAPT haplotype and PD have not been explored previously in the Chinese population.

Methods: Here, we performed a case-control association study in a Chinese cohort of 211 PD patients and 279 matched controls from central China by Polymerase chain reaction-restriction fragment length polymorphism.

Results: Our data showed that allele frequency of MAPT rs242562 G/G polymorphism was significant higher in controls than that in PD patients while G/A genotype of MAPT rs242562 revealed higher frequency in PD subjects compared to controls. The genotype frequency of GSK3β rs334558 C/C was over-represented in matched female controls compared to female PD patients. Compared with female PD patients, the genotype frequency of GSK3β rs334558 T/T polymorphism was higher in male PD patients.

Conclusions: We conclude that G/G genotype of MAPT rs242562 and C/C genotype of GSK3β rs334558 are associated with PD and may serve as protective genetic factor for PD in the central Chinese population.
P1613
The mechanisms of movement control and time estimation in cervical dystonia patients: a behavioural study
P. Filip1,2, I. Husárová1, M. Bareš1,2
1First Department of Neurology, Faculty of Medicine Masaryk University and St. Anne’s Teaching Hospital, 2Central European Institute of Technology, CEITEC MU, Brno, Czech Republic

Introduction: The pathophysiology of cervical dystonia is still relatively unknown. The functional imbalance of respective muscle groups is thought to be caused by neurochemical abnormalities in basal ganglia and recently, there has been emerging substantial evidence of considerable cerebellar involvement. This project aims to affirm the function of the above mentioned structures in precise movement timing.

Methods: The participants were asked to perform a series of simple computer tasks where the parameters of a moving object (speed, acceleration, partially the movement direction) were generated randomly. As the object moved on the computer screen from left to right, the participant had to press a button in an optimal time window to launch a “fireball” from the bottom of the screen that was supposed to hit the moving target. The “fireball” travelled with a constant speed and trajectory. However, as the speed was not sufficient to ignore the launch-interception time, anticipatory reaction according to changing parameters of the object was essential. We evaluated the hit ratio and percentage of early and late errors. The results were compared to the healthy subjects’ data.

Results: The overall hit ratio in the healthy subjects was significantly higher than in the cervical dystonia group (42.07%±9.18% versus 34.91%±8.23%). Also the reaction time in cervical dystonia patients was significantly longer.

Conclusions: Our data suggest that cervical dystonia patients have a substantial problem with predictive motor timing. The results imply that cerebellum and basal ganglia participate in the integration of visual information with motor output.

P1614
Predictors of quality of life of patients with Parkinson’s disease
M. Gomez-Gallego, S. Oliveira, M. Leon, C. Albert
Catholic University of Murcia, Spain

Introduction: Current treatments for Parkinson’s disease are mainly symptomatic and aimed at improving patients’ quality of life (QoL). The objective of this study is to determine which clinical factors are the most relevant for patients’ QoL.

Methods: 39 PD patients were administered the QoL scale PDQ-39. A complete neurological examination, including the Hoehn & Yahr Scale (H-Y), the Barthel Index (BI), and both part I and part III of Unified Parkinson’s Disease Rating Scale (UPDRS) was performed. The associations between sociodemographic and clinical variables (years of disease, treatment, H-Y stage, BI and UPDRS domains scores) with PDQ-39 domains were tested using ANOVA tests and correlational analyses. Multiple regression analyses were carried out for each domain of PDQ-39.

Results: PDQ-39 total score was significantly associated with marital status, UPDRS part I score, BI, postural tremor score, axial function score, and both left and right bradykinesia scores. BI and UPDRS part I scores explained 63% of the model variance. Higher BI scores and taking L-DOPA predicted lower PDQ-mobility scores (R2=70.2). The predictors of PDQ-activities of daily living were BI, axial function score and H-Y stage (R2=66). PDQ-39-communication was predicted only by BI (R2 =15.4); PDQ-39-cognition by UPDRS part I score (R2=25.8); PDQ-39-bodily comfort by rigidity score (R2 =14.4); and PDQ-39-emotional well-being by UPDRS-part I score (R2=18.8).

Conclusions: Disability is the strongest predictor of QoL in PD. Treatment for PD should include strategies to improve functional independence.
P1615

CSF levels of chromogranin-A in the early stage of Parkinson’s disease

M. Kaiserová1, K. Mensikova1, D. Stejskal1, P. Kanovsky1
1Department of Neurology, Palacký University and University Hospital, Olomouc, 2Center of Laboratory Medicine, Prostějov, Czech Republic

Background: Chromogranin-A levels in the cerebrospinal fluid have been shown to be significantly reduced in late stages of Parkinson’s disease (PD). There are only few data referring to its level in the early disease stage; its significance as a potential marker in the differential diagnoses of PD could not be established yet.

Objectives: To establish the level of chromogranin-A in a pilot cohort of early stage, treatment-naïve PD patients.

Methods: 10 patients (4 males, 6 females) and 10 gender- and age-matched controls have been examined for the levels of chromogranin-A in the cerebrospinal fluid; the control subjects were those patients suffering from either low back pain or tension-type headache.

Results: The mean CSF level of chromogranin-A in PD patients was 74.8 (range 41.9 - 123.8) µg/l, in the control group it was 143.9 (range 116 - 181.3) µg/l. The statistical analysis showed a difference at the significance level of p≤0.005.

Conclusions: Our pilot study showed that chromogranin-A levels in CSF of early stage PD patients is significantly reduced; it probably deserves further research with regard to its role as a potential biomarker in the differential diagnosis of PD.

P1616

Quality of life in Huntington’s disease and its association with psychopathology

J. Fernandes1, I. Moreira1, S. Cavaco1,2, J. Damásio3, R. Loureiro3, M. Magalhães3
1Unidade Multidisciplinar de Investigação Biomédica, Instituto de Ciências Biomédicas da Universidade do Porto (UMIB, ICBAS-UP), 2Unidade de Neuropsicologia, 3Serviço de Neurologia, Centro Hospitalar do Porto (CHP), Porto, Portugal

Introduction: Huntington’s disease (HD) is a hereditary and neurodegenerative disorder without cure or treatments that can alter the course of disease progression. Health-related quality of life (QoL) in HD patients is an important target of clinical intervention.

Aim: To explore the association between HD patients’ QoL and their demographic, clinical, and psychopathologic characteristics.

Method: The Short Form Health Survey (SF-36) was used to assess QoL in 24 HD patients (9 males, 15 females; mean age of 48.8±13.3 yrs; 5.6±2.2 yrs of education; mean disease duration of 6.2±4.5 yrs; mean CAG repeat of 43.6±4.7) and 24 demographically-matched healthy subjects. The Unified Huntington Disease Rating Scale (UHDRS), Hamilton Rating Scale for Depression (HRSD), Beck Depression Inventory (BDI) and Dementia Rating Scale-2 were also applied to HD patients. Mann-Whitney and Pearson’s correlations were used for data analyzes.

Results: Statistically significant reductions in HD patients’ QoL were observed in all SF-36 dimensions (Physical Functioning, p=0.008; Role Functioning-Physical, p=0.006; General Health, p=0.001; Vitality, p=0.008; Social Functioning, p=0.018; Role Functioning-Emotional, p=0.002; Mental Health, p=0.018), except Bodily Pain. Among HD patients, females had worse SF-36 Role Functioning-Physical (p=0.014) and Vitality (p=0.003). The decrease in QoL (all except Body Pain) was significantly related (r=-0.42 to -0.73) to severity of psychopathological symptoms (UHDRS Behaviour Subscale, BDI, and HRSD). Relatively modest associations were found with other demographic and clinical variables.

Conclusion: These results point to the importance of depressive symptoms in HD patients’ QoL and reinforce the need for an integrated and multidisciplinary clinical approach in HD.
P1617

Cognitive functions, autonomic and sensorial involvements in patients with essential tremor

M. Korkmaz¹, Y. Kütükçü¹, M.A. Dikililer², M. Yücel¹, H. Akgün¹, M.T. Kaşıkçı¹, Z. Odabaşı¹
¹Department of Neurology, Gülhane Medical Academy, ²Department of Family Medicine, Şırnak Military Hospital, Ankara, Turkey

Introduction: Essential tremor (ET) is one of the most frequent movement disorders in neurology practice. In recent years, there are many discussions about ET being a neurodegenerative disease.

Aim: Neurodegenerative diseases appear with an insidious onset and are usually progressive. Their incidence increases parallel to age. Neuronal loss frequently is seen in pathological materials. These characteristic features are also valid for essential tremor. Therefore ET may be accepted as a neurodegenerative disease. To research this hypothesis we aimed to evaluate cognitive functions, autonomic and sensorial affects in patients with ET.

Methods: 60 patients diagnosed with essential tremor according to Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) Essential Tremor Diagnose Criteria were included in our study. Patients are separated in two groups as severe and mild according to results of performance subscale of Essential Tremor Rating Assessment Scale (TETRAS).

Results: No difference was seen in Sympathetic Skin Response and R-R intervals between groups. Lower standard mini mental test scores, longer cortical somatosensory evoked potentials latencies and higher serum total copper levels were observed in the severe group compared to the mild group.

Conclusion: We also observed cognitive and sensorial involvement in electrophysiological tests. In addition, high levels of serum total copper were correlated with disease severity. Detailed investigation about copper metabolism in more patients should be made to uncover this functional correlation.

P1618

Selegiline rescues gait deficits and dopaminergic cells in a subacute MPTP mouse model of Parkinson’s disease

Q. Zhao¹, Y. Bai¹, D. Cai²
¹Department of Neurology, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, ²Department of Integrative Medicine, Zhongshan Hospital, Fudan University, Shanghai, China

Monoamine oxidase type-B (MAO-B) inhibitors have been often recommended as the first-line Parkinson’s disease treatment. Clinical studies showed that they had limited symptomatic improvements which seem to be associated with enhancement of neurotransmission. Besides selective inhibition of MAO-B activity and elevating endogenous dopamine concentration many experiments found that they possessed neuroprotective effects and a potential of disease-modification in PD. It may be one of the significant strategies for supporting neuronal survival in PD to augment neurotrophic factor activity, especially glial cell line-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF). In this study, we investigated the effects of selegiline on rescuing motor dysfunction and dopaminergic function in 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP)-lesioned mice. We found that oral administration of selegiline (1.0mg/kg/day for 14 days) to MPTP-treated mice, commencing after impairment of the nigrostriatal system, suppressed the reduction of nigral dopaminergic neurons and striatal fibres of MPTP-lesioned animals (p<0.001). At the 7th and 14th days of low dose selegiline-treatment, the gait disorder showed obvious improvement. Furthermore there was a significant elevation in expression of GDNF and BDNF mRNA (2.10 and 2.75-fold) and proteins (143.53% and 157.05%) in selegiline-treated mice compared with saline-treated MPTP-lesioned mice. In addition, the Bax/Bcl-2 ratio of gene and protein in MPTP-lesioned mice obviously increased, and this effect could be reversed by selegiline. Correlation analysis revealed that both the gait measurement and GDNF/BDNF were positively correlated with the number of dopaminergic neurons. These findings demonstrate that selegiline has neurorescue effects probably associated with induction of NTFs and anti-apoptotics.
P1619

The evolution of complexity in transcranial magnetic stimulation induced surface EMG: a possible illustration of plasticity-like changes

M. Cukic1,2, A. Kalauzi3, M. Ljubisavljevic4, N. Jorgovanovic2, V. Kostic1
1Institute for Neurology, Belgrade University, Belgrade, 2Department for Signals, Systems and Automatic Control, University of Novi Sad, Novi Sad, 3Institute for Multidisciplinary Studies, University of Belgrade, Serbia, 4Department of Physiology, Faculty of Medicine and Health Sciences, UAE University, Al Ain, United Arab Emirates

Introduction: The aim of this study was to determine whether a single-pulse TMS induces changes in complexity of surface EMG immediately after the stimulation.

Methods: We analyzed changes in Fractal Dimension (FD) in FDI muscle of the dominant hand in 9 healthy subjects, while exerting three intensities of voluntary activation weak (<30% of MVC), medium (30-60%) and strong (>60%); control group were 5 healthy volunteers sustaining the same three levels of contraction without presentation of TMS. FD was calculated using Higuchi’s algorithm, of EMG immediately after a TMS-induced silent period and compared with those calculated from preceding TMS EMG sections; FD with moving window was used to depict the curves of complexity changes, and then we performed FFT of the data. All analysis were performed in response to three intensities of TMS stimulation set at 1.1 x MT, 1.2 x MT and 1.3 x MT. Ten single TMS stimuli were delivered in each series using a figure-of-eight coil positioned over the optimal spot on the skull to elicit MEP from FDI muscle.

Results: The FD of the EMG after TMS fell in the majority of examined series of recordings (in 72 out of 90 series), and cyclic-like changes were observed in all the curves constructed. Statistically significant changes in FD of series ‘before’ and ‘after’ were more prominent for recordings during sustaining mild and medium MVC, than in strong MVC (p<0.05).

Conclusion: It appears that single pulse TMS of the motor cortex induces plasticity-like changes in the voluntary EMG signal.

P1620

Does brain degeneration in Wilson’s disease involve not only copper but also iron accumulation?

M. Skowronska1, T. Litwin1, K. Dzieżyc1, A. Wierzchowska1, A. Czlonkowska1,2
12nd Department of Neurology, Institute of Psychiatry and Neurology, 2Department of Experimental and Clinical Pharmacology, Medical University of Warsaw, Poland

Introduction: Wilson’s disease (WD) is an autosomal recessive inherited disorder of copper metabolism. Clinical manifestations of WD include neurologic, hepatic and psychiatric symptoms. Changed MR results are observed in most WD patients with the neuropsychiatric form, and in some with the hepatic and presymptomatic forms. In previous studies showed that T2* and susceptibility-weighted imaging (SWI) are highly sensitive to brain iron accumulation, which causes decreased signal intensity. Brain abnormalities in WD patients have been also demonstrated with transcranial sonography (TCS).

Aim: Our aim was to investigate whether Wilson’s disease patients have MR changes typical of neurodegeneration with brain iron accumulation, using T2* and blood oxygenation level dependent imaging protocols. We also investigated TCS lesions in basal ganglia in WD patients.

Methods: MRI with established protocol and TCS was performed in admitted, clinically stable, and treated patients.

Results: Hypo-intensity in the lenticular nucleus (LN) was observed on T2* images of 78% neurologic, 50% presymptomatic, and no hepatic patients (p<0.05) In SWI images we found hypointense signal in LN in all neurologic, 83% presymptomatic, and 46% hepatic patients. No acoustic window was found in 2 patients. Hyperechogenicity in TCS in LN was found in 87.5% neurologic, 83% presymptomatic and 75% hepatic patients. SWI is more sensitive in detecting a paramagnetic signal than conventional T2 and T2* sequences, especially for Wilson’s disease hepatic patients.

Conclusions: Magnetic resonance data suggests brain iron accumulation in Wilson’s disease. TCS is also a valid tool for detection of basal ganglia metal accumulation in WD patients.
P1621

Progressive supranuclear palsy-like syndrome as a relatively common feature of different neurodegenerations

R. Matěj, R. Rusina
1Pathology and Molecular Medicine, 2Neurology, Thomayer Hospital, 3Neurology, Institute for Postgraduate Education in Medicine, Praha, Czech Republic

Introduction: Progressive supranuclear palsy (PSP) is characterized by early gait disturbances and falls, axial rigidity, vertical gaze palsy, and subcortical dementia. PSP is considered to be a tauopathy; however, a PSP-like syndrome has been associated with different neurodegenerative entities. We present a series of 10 patients with a clinical presentation evoking PSP and neuropathological findings of different neurodegenerative entities.

Methods: Patients fulfilling the clinical and radiological diagnostic criteria for possible or probable PSP were post mortem neuropathologically examined. The detailed histopathological assessment included immunohistochemical analysis using a spectrum of antibodies against different proteins associated with neurodegenerations.

Results: We found in 5 patients frontotemporal lobar degeneration (FTLD-TDP); 2 patients had a synucleinopathy (multiple system atrophy and diffuse Lewy body disease, respectively), 1 case was neuropathologically closed as a genetic form of Creutzfeldt-Jakob disease and 2 cases were Alzheimer’s disease.

Conclusion: Our observations support previous data suggesting that the clinical picture of PSP-like syndrome seems to be related to preferential localization of pathogenetic inclusions and neuronal cell loss rather than to specific pathological mechanisms of the disease itself. Moreover, our observation confirms the importance of neuropathological verification in patients clinically diagnosed as atypical PSP.

Acknowledgement: This study was supported by grant IGA NT12094-5/2011 from the Czech Ministry of Health.

P1622

International studies on Huntington’s diseases in Poland

D. Zielonka
Poznan University of Medical Sciences Poland, Poznan, Poland

Introduction: Huntington’s disease (HD) is a progressive neurodegenerative disorder where the conditioning factor is a dynamic mutation in HTT gene. Being rare, it is difficult to collect a large enough cohort for significant interventional and environmental studies.

Materials and methods: Conducted in Poland, HD research initiatives were reviewed in an archive of the HD research Coordination Centre for Poland located at the Department of Social Medicine of Poznan University of Medical Sciences in Poland, Clinical Trials - a service of the U.S. National Institutes of Health (www.clinicaltrials.gov), EMBASE database, and the U.S. National Library of Medicine National Institutes of Health (PubMed).

Results: Two observational and three clinical studies regarding HD were conducted in Poland. The core study for such research initiatives is REGISTRY; a prospective, observational, longitudinal study on the rate of HD progression collecting a large number of data on patients during annual visits. Participants of the HD studies as well as number of cross-sectional and clinical studies increased quickly in the last years. Based on REGISTRY and other studies, database as well as HD patients’ association participants are easily and quickly collected for any other studies. 643 participants underwent all HD studies in Poland up to date.

Conclusions: Due to its large population Poland has become a target country for rare diseases research. REGISTRY was formed as a novel approach, to overcome difficulties in patient collection for Huntington’s disease interventional and environmental studies, to effectively increase the number of enrolled study participants.
P1623

Normal 0 21 primary episodic lingual protrusion dystonia

R. Manso-Calderón
Neurology, Hospital Universitario de Salamanca, Salamanca, Spain

Introduction: Lingual protrusion dystonia (LPD) is a disabling form of cranial dystonia which varies from repetitive and/or episodic to sustained tongue protrusion, and can also be action-induced with speaking or eating. LPD often occurs in association with oromandibular dystonia but can be isolated. Both idiopathic and secondary cases exist. Secondary causes include tardive dystonia, head injury, electrical injury, heredodegenerative diseases (neuroacanthocytosis, pantothenate kinase-associated neurodegeneration, neuroferritinopathy, Wilson’s disease) or varicella infection. However, primary episodic LPD is rare.

Methods: A 17-year-old woman presented with a one-year history of episodic tightening of her tongue while speaking and eating, causing difficulty in articulation and swallowing. Each attack lasted less than 1 minute. This symptom started after experiencing a cervical spine trauma. There was no family history of neurological disorders. She did not take neuroleptics or other medications. On examination she had episodic speech-induced tongue protrusion associated with mild dysarthria. The remainder of the neurological and general examination was normal.

Results: Routine haematological and biochemical evaluation were completely normal, as well as thyroid function, copper and ceruloplasmin, number of acanthocytes, autoimmune screen and serologies. Magnetic resonance imaging of the brain and cervical spine was normal. EEG recorded during an episode of tongue spasm was normal. Interictal EMG of the tongue showed no evidence of denervation or myokymia. Two trials of treatment with clonazepam and carbamazepine were ineffective. The patient refused further trials of medication.

Conclusion: In contrast to most other paroxysmal movement disorders, episodic LPD does not appear responsive to anti-epileptic drugs.

P1624

Cerebral amyloid and hypertensive angiopathy as the cause of diminished level of consciousness and complex movement disorders

Neurology, Fundación Jiménez Díaz, Madrid, Spain

Introduction: Amyloid and hypertensive angiopathies can infrequently cause transient focal neurological episodes. These episodes use to be sensitive (paresthesias), motor seizure-like episodes or visual disturbances.

Patient: A 84-year-old woman, with a chronic respiratory condition and a chronic renal insufficiency due to hypertension, previously treated with two courses of antibiotics for a respiratory infection, developed a pneumonia. She was treated with iv cefepime. 24 hours after admission, she started to be unresponsive. 48 hours later, left upper limb choreic and ballistic movements, together with lower limb ballistic movements and generalized myoclonias appeared. The CT scan showed an extensive chronic microangiopathic angiopathy. The CSF exam did not disclose any sign of infection or haemorrhage. The EEG exam demonstrated a diffuse encephalopathy with no signs of epileptic activity. We started treatment with iv valproic acid and tiapride. The antibiotic therapy was adapted to the renal insufficiency. An MRI was performed showing an extensive and severe microangiopathic angiopathy. Several haemosiderin deposits related with past microbleedings were seen both in supratentorial and infratentorial locations. There were no signs of acute haemorrhage or ischaemia. After 4 days with the new antibiotic scheme and under valproic acid and tiapride, the patient started to improve. First, the fever and the movement disorders disappeared. Then, the level of consciousness returned to normal. She was discharged 27 days after admission with no signs of neurological impairment.

Discussion: We present a very infrequent case of acute multifocal choreic, myoclonic and ballistic related to amyloid and hypertensive angiopathy.
**P1625**

**Improvement of tremor in a Parkinson's case after thalamic infarction**

A. Köksal¹, M. Öztürk¹, N.H. Sütpideler Köksal², B. Mutluay¹, A. Ceyhan Dirican³, F. Aysal¹, S. Baybaş¹

¹Neurology, Bakırköy Training and Research Hospital for Mental Health and Neurological Sciences, ²Neurosurgery, Istanbul Educational and Research Hospital, Istanbul, Turkey

**Introduction:** The medical treatment of Parkinson’s disease includes dopamin agonists, enzyme inhibitors and neuroprotective agents together with L-dopa. These drugs are all symptomatic and do not affect the course of the disease and motor complications may arise during medical treatment. Thus, surgery is also performed for the symptomatic treatment of this disease. Surgery is observed to be more effective on tremor rather than the bradykinesia and rigidity of Parkinson’s disease.

**Case report:** A 76-year-old male Parkinson’s patient is followed in our outpatient clinic since 2003. He had right side dominant bradykinesia, rigidity and resting tremor. He was Hoehn&Yahr Stage 2 and had a UPDRS score of 16 points. His symptoms were partially under control with a combination of L-dopa, benserazide and entacapone. The patient was admitted to our emergency clinic in May 2007 with difficulty in speaking and right-sided weakness. Neurological examination revealed dysarthria and slight right-sided hemiparesis involving the face. Diffusion-weighted cranial MRI showed an acute infarction at the ventromedial part of the thalamus.

**Results:** On the 15th and 30th day, neurological examination revealed a complete recovery of dysarthria and hemiparesis as well as the tremor of Parkinson’s disease. Bradykinesia and rigidity were unaffected.

**Conclusion:** Though the possibility of recovery of tremor in Parkinson’s disease after a thalamic infarction is theoretically known, it is a very rare clinical entity. We aimed to present this rare case with thalamotomy-like effects of thalamic infarction and also to discuss surgery in Parkinson’s disease in the light of this case.

---

**P1626**

**Effects of Nigella sativa oil on haloperidol induced movement deficits in a rat model**

T. Malik¹, D.J. Haleem¹, S. Pervez², S. Hasan², T. Fatima³

¹Neurochemistry & Biochemical Neuropharmacology Unit, Biochemistry Department, The University of Karachi, Karachi, ²Department of Pathology and Microbiology, ³Department of Biological Biomedical Sciences, The Aga Khan University Hospital, Karachi, Pakistan

The neuropathological status of haloperidol (HP) induced extrapyramidal symptoms (EPS) remains unclear, but several lines of evidence suggest that persistent neuronal alterations in the basal ganglia cause EPS by HP provoked oxidative stress. The objective of this study was to evaluate the possible protective effects of the antioxidative agent “Nigella sativa (NS)” oil on HP induced neuropathological alterations and related motor symptoms in the rodent striatum.

**Methods:** HP was administered alone and with NS oil. EPS was monitored in the HP treated groups and the animals treated with NS only and placebo.

**Results:** The HP treated group displayed a high degree of motor impairment (p<0.00) shown on rota rod experiment, vacuous chewing movement (p<0.00) shown grossly disturbed the large fraction of the cytoarchitectonic pattern (p<0.05), histopathology with nerve cell depletion concomitant shrunken cytoplasm, nuclear membrane breakdown and chromatin disorganization. Scarring was also a prominent feature owing profusion of astrogliosis in the dorso- and ventrolateral regions of the caudate putamen and in the core of nucleus accumbens. Moderate levels of halo and pyknotic neurons were also observed in HP treated rodents. The morphological HP induced neuronal changes were almost absent in the HP plus NS treated groups (p<0.00). However minor astrogliosis was observed with no obvious indication of cell loss and 82% normal neuronal densities were observed using a quantitative, analytic approach in the NS plus HP treated striatum. We conclude that NS therapy has preventive effects on HP induced neuronal degeneration in the striatum.
P1627
Cardiovascular factors in hospitalized patients with idiopathic Parkinson's disease: a retrospective analysis
K. Lauckaite¹, G. Zemgulyte², I. Sniokaite², D. Surkiene¹, D. Rastenyte¹, A. Vaitkus¹
¹Neurological, ²Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction: Evidence suggests that cardiovascular abnormalities, co-morbid presence of white matter lesions (WML) may exacerbate or contribute to some motor and cognitive deficits in Parkinson’s disease (PD).

Methods: A retrospective study was carried out at the Hospital of the Lithuanian University of Health Sciences. We have analyzed case histories of 129 (55 males, 74 females) PD patients hospitalized in 2011. Diagnosis was established according to the UK brain bank criteria. The clinical, demographic data, computed tomography (CT), electrocardiogram, carotid ultrasound (ECCS), Barthel index (BI), MMSE results were collected.

Results: The mean age of PD patients (±SD) was 68.6±8.9yrs, and stage according to Hoehn-Yahr (H-Ys) 2.2±0.9. Tremor-dominant PD (TD) was diagnosed in 39 (30.2%), postural-instability-gait-disorder-dominant (PIGD) in 58 (45%), mixed type (MT) in 25 (19.4%), 7 (5.4%) were unclassified. The most advanced H-Ys (p=0.027) and the lowest MMSE points (p=0.099) were in MT and PIGD groups. Mostly TP accounted for the urgent admission (37.5%, Chi2=9.1, p=0.028). H-Ys correlated negatively with BI (r=-0.4, p=0.001), systolic BP (r=-0.2, p=0.03) and QRS interval (r=-0.3, p=0.014). Brain CT was performed in 43 (33.3%), with WML detected in 22 (51.2%). The highest rate of WML was in PIGD (Chi²=8.3, p=0.004) and in the elderly (p=0.002). Linear velocities on ECCS (n=46, 35.7%) were lower in common or external carotid arteries at stages ≥2 vs. 1 (p=0.05).

Conclusions: WML were associated with an age and PIGD PD. The highest motor and cognitive impairment was detected in MT and PIGD. According to cardiovascular factors, stage 2 and later is an advanced disease.

P1628
Social isolation and quality of life in Parkinson's disease
J.Y. You
Neurology, Hanil General Hospital, Seoul, Republic of Korea

Background: Parkinson patients have many difficulties in mobility, cognition and psychiatric symptoms such as depression, anxiety and suicidal idea. Of course many physical problems disable patients, but recent progress including medication and surgical methods have improved progressively. So physical disabilities improved rapidly. But psychosocial disabilities have been undertreated and missed. So this study aims to find other psychosocial support that can change the QoL of Parkinson patient.

Method: 20 Parkinson patients who live alone or with an old spouse were selected. Inclusion criteria were no regular job and social club. So socially isolated patient were selected. The patients’ QoL was measured and assessed by the Parkinsons disease quality of life (PDQL) and the Beck Depression inventory (BDI). We divided this group. One group (N=12) is newly attending the day care unit or rehabilitation center providing the physical activity and cognitive rehabilitation. The other group (N=8) is socially isolated, as before. Baseline, 3 months, 6 months PDQL and BDI were checked.

Result: The first group who newly joined social activities showed improvement in BDI and PDQL. The improvement difference gap is increased to time.

Conclusion: Socially isolated state due to physical activity, depression or other socio-economic state aggravated Parkinson patient’s QoL. So physicians must consider the social isolation. If physicians consider this problem, the family and social support will be increased. Recently in Korea, government supporting social nursing insurance is started. And this system is expected to improve the Parkinson patient’s QoL in aspects of social isolation.
P1629

Parkinson’s disease (PD) epidemiology and clinical presentation in Lugansk, eastern Ukraine

I. Pepenina

Out-Patient, Hospital N10, Lugansk, Ukraine

PD is a common extrapyramidal disorder in Ukraine which is vastly misdiagnosed. Low awareness of PD differential diagnosis, as well as low access to drugs and neurosurgical interventions seriously affect management efficiency.

Study objective: To analyze PD prevalence in Lugansk (Eastern Ukraine).

Methods: The retrospective follow-up study of PD prevalence in the region has been performed. Diagnosis of PD was based on Hughes et al. criteria (1992), for staging Hoehn-Yahr scale (1967) was used.

Results: Prevalence of PD in different age groups varies significantly from 4.8 per 100,000 at the age below 55 to 178.0 per 100,000 in older patients. Clinical disease peculiarities have been analyzed in 71 cases. Patients in stages 2-4 predominated (21 males, 28 females). Tremor prevailed in 22 patients (8 males, 14 females), akinetic-rigid syndrome in 21 patients (13 males, 8 females), mixed symptoms were found in 28 patients (14 males, 14 females). Right-side onset was established in 42 cases (18 males, 24 females), left-side in 29 (17 males, 12 females). Rapid progression was more frequent in 29 cases (16 males, 13 females), whereas moderate and slow type were detected in 19 cases (11 males, 8 females) and 18 cases (7 males, 11 females), respectively. In the disease management mostly L-dopa, NMDA-antagonists, and dopamine-receptor agonists are being used (in 56, 34 and 27 cases, respectively). 6 patients use MAO-B inhibitors.

Conclusion: PD in Lugansk is being mostly detected in advanced stage seriously hampering the life quality in older patients.

P1630

High intake of folate provides anti-parkinsonism effects: no role for plasma level of homocysteine

H. Haghdooest-Yazdi1, N. Fraidouni2, A. Faraji1, M. Sarookhani1

1Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, 2Tarbiat Moalem University, Tehran, Iran

Several lines of evidence show that homocysteine (Hcy) levels are increased in blood and CSF of patients with Parkinson’s disease. Folate is necessary for Hcy metabolism and there is generally an inverse relationship between plasma folate and Hcy levels. In the present study, effect of folate supplementation on the severity of 6-hydroxydopamine (6-OHDA)-induced parkinsonism was investigated. Rats were nourished with different doses of folate supplements from 1 month before stereotaxic injection of 6-OHDA to the end of experiments. Plasma Hcy was measured at the end of experiments to identify its association with parkinsonism. Our results indicate that folate supplementation attenuates severity of parkinsonism. The best effect was seen in rats receiving folic acid at 10-folds of normal MEM (minimum essential medium). In this group, number of apomorphine-induced rotations in the post-surgery tests was more than 60% lower than that in the control group. These rats also showed significant better performances in rotarod test and had learning patterns similar to healthy rats. 5-fold supplementation of folate also remarkably improved the rotarod performances but had modest effect on the rotational behaviour. 2-fold supplementation had no effect. The levels of Hcy in rats receiving moderate and low doses of folate supplementations were near to that in the control group. However, in rats treated by high dose of folate, Hcy was significantly higher than that in the control group. Our results indicate that folate supplementation provides anti-parkinsonism effect, in a dose dependent manner, but this effect is not mediated by lowering plasma Hcy.
P1631
Rasagiline for the treatment of gait disturbances in patients with Parkinson’s disease (PD): an open label study

N. Van Blercom, G. Linazasoro
Centro Investigación Parkinson Policlinica Gipuzkoa, San Sebastian, Spain

Background: Gait disturbances are a major cause of disability in patients with advanced PD. Their management is difficult and the classical dopaminergic treatment is often unsuccessful. Rasagiline has shown some beneficial effects against gait disorders.

Aim: To study the symptomatic effect of rasagiline 1mg/day on gait and mobility in advanced PD.

Methodology: 15 non-demented PD patients (mean age 74.6±5.8 y.o; mean PD duration 9.3±6.1 years; mean Hoehn & Yahr stage 3.14±0.8) were included in this prospective, open study of 8 weeks duration. They showed clinically significant gait disturbances as determined by the Timed Up and Go test (TUaG), (TUaG >10 seconds in ON and 14 in OFF). They were receiving a stable dose of antiparkinsonian medications. Besides TUaG (primary variable), patients were assessed by using the UPDRS, freezing of gait and new freezing of gait questionnaires (FOG-Q and NFOG-Q) and PDQ-39.

Results: 4 patients were withdrawn due to early mild side effects. TUaG was significantly improved (basal 26.6±18.7, final 20±14; p<0.05). UPDRS, PDQ39, FOG and NFOG questionnaires remained unchanged though a trend towards improvement in the last two questionnaires was observed.

Conclusion: Rasagiline improved some parameters related to gait performance, mainly TUaG. Rasagiline is a therapeutic option in this clinical situation.

The study was sponsored by Lundbeck.

P1632
The role of the activity of NO-system in the development of depression in Parkinson’s disease

R.J. Matmurodov, K.M. Khalimova, M.M. Raimova
Tashkent Medical Academy, Tashkent, Uzbekistan

Some non-motorized manifestations such as disorders of smell, constipation, depression, pain syndromes occur before the development of the classic motor symptoms of Parkinson’s disease (PD).

Objective: To study the role of the activity of NO-system in the development of depression in patients with PD.

Methods: A total of 58 (35 of them with depression and 23 non-depressed) patients with PD. The average age was 54.3±4.5 years. For the estimation of NO-system studied in the concentration of red blood cells NOx, the activity of NADPH-dependent NO, the level of peroxynitrite (ONOO-), the activity of NO-synthase (NOS). The level of depression was determined using the Zung scale.

Results: The results of this analysis showed that the NO-system parameters in patients without depression comprise: NO 22.7±0.55mmol/l, eNOS 13.9±0.26mol/min/l, NADPH-HP 1.02±0.03mmol/min/l, ONOO- 0.08±0.005mmol/l. In patients with mild depression up: NO 30.8±0.34, eNOS- 9.71±0.13, NADPH-NR-1.46±0.02, ONOO- 0.021±0.003. In patients with depression of moderate severity parameters of NO up: NO 38.5±0.45mmol/l, eNOS 8.3±0.3mol/min/l, NADPH-HP 1.79±0.1mmol/min/l and ONOO- 0.35±0.02mmol/l. Our data indicate that the degree of growth depression in PD is accompanied by a worsening imbalance of the NO-system and the progression of the clinical course.

Conclusion: Thus, the degree of depression in PD depends on the activity of the NO-parameter system. In this connection, the imbalance in the NO-system can be considered as a factor in the progression of depression in PD.
P1633

Parkinson's syndrome in chronic neuroborreliosis

N.S. Baranova, M.A. Bykanova
Yaroslavl State Medical Academy, Yaroslavl, Russia

Purpose: To identify the occurrence of Parkinson's syndrome (PS) in patients with chronic neuroborreliosis (CNB).

Materials and methods: We explored 164 patients (115 female and 49 male) with diagnosis of CNB, average age 49.6±16.27 years. CNB was diagnosed by the criteria: the presence of neurologic symptoms within 6 months from the appearance of erythema migrans and/or a tick bite or symptoms persisting for more than 6 months; the presence in serum or CSF of diagnostically significant elevated titres of antibodies to Borrelia burgdorferi; the presence of clinical improvement from specific antibiotic therapy and/or decrease in antibody titres to Borrelia burgdorferi in the dynamic study of blood serum; the exclusion of other causes, which could explain development of existing symptoms. They also used the Diagnostic criteria UK Parkinson's disease (PD) Society Brain Bank (1992), Schwab and England scale, MRI.

Results: PS was diagnosed in 5 (3%) patients with CNB. The combination of PD and CNB was observed in 3 (1.8%) patients (1 male and 2 female). Slight deterioration was noted (no more than 10% of Schwab and England) and the persistence of symptoms of PD after antibiotic treatment of neuroborreliosis. PS due to CNB was defined in 2 (1.2%) female. Symptoms of PS due to CNB significantly decreased after antibiotic therapy. Levodopa, dopamine agonists were not effective.

Conclusion: PS as a manifestation of neuroborreliosis occurred in 1 patient from 82 cases of CNB. Antibiotic therapy significantly reduced the severity of parkinsonian symptoms.

P1634

Muscle testing and loss of ambulation in Friedreich's ataxia

C. Mignard-Moydelacroix1, A. Boufferet2, L. Bonnet2, D. Mignard-Moydelacroix2, Centre de Référence Maladies Neurologiques Rares
CHR de La Reunion, 2Neurologie-Maladies Rares, CHU de La Reunion, Saint-Pierre, Reunion

Many genetic diseases are observed in Reunion Island, a French island in the Indian Ocean. Late-onset Friedreich’s ataxias are frequent. Many adult people are walking yet in our experience.

Aims: The neurological disorder affected mainly the cerebellar tracts. Initially, the muscles are not weak. The muscle testing changes over time were compared with the walking status to clarify the cause of the loss of ambulation.

Materials and methods: 44 patients for 12 years were classified into three categories: walkers (16), standing (11) and non-walkers (17). 175 muscle testings were achieved since 2008: The average score showed muscle damage for each muscle group. Next, in six patients who lost the ability to walk (6) since 2008: the testing done before, during and after the loss of ambulation were reviewed.

Results: The “walkers” had a mean score between 4 and 5 for all muscle groups; the “standing up” had poorer outcomes (between 3 and 4) with elective involvement (3/5) on three muscle groups, (psoas, gluteus and adductors); “non-walkers” scores showed the same involvement. In the 6 patients who lost ambulation since 2008, 6 months before the loss of ambulation, no patient had a wholesome muscle score (all<5). Three muscle groups were more impaired than others (3/5): the gluteus, psoas and adductors.

Conclusion: The loss of ambulation in patients with Friedreich’s ataxia is correlated markedly and significantly with muscle weakness of psoas, gluteus and adductors. Preventive muscle strengthening on these muscles, could delay the disease progression.
P1635

Exposure of multiple system atrophy (MSA) patients with or without orthostatic hypotension (OH) to potentially hypotensive drugs

S. Perez-Lloret¹, M.V. Rey¹, A. Pavy-Le Traon², W. Meissner³, F. Ory-Magne², C. Brefel-Courbon², N. Fabre², F. Tison³, O. Rascol¹
¹Clinical Pharmacology, ²Neurology, CHU Toulouse, ³Neurology, CHU Bordeaux, France

Background: OH is a hallmark of MSA.
Objective: To assess the exposure of MSA patients with or without OH to drugs that can potentially induce OH.
Methods: Patients were assessed at the French MSA reference Centers between 2008 and 2011. Blood pressure (BP) was measured 5 min after lying down and every min during 10 min after standing up. According to Gilman’s criteria, OH was defined as systolic/diastolic BP fall ≥30/15mmHg during the first 3 min after standing. Exposure to drugs commonly associated with OH, such as insulin, antihypertensives of any class, peripheral vasodilators, drugs for heart-disease, alpha1-adrenergic receptor antagonists, dopaminergic drugs and antidepressants, was recorded.
Results: 131 MSA patients were included in the study (age 64.7±0.7, 50% males, 61% MSA-P, UMSARS II score 25.3±0.7). OH was detected in 76 (58%) patients. 84% of patients were exposed to at least 1 potentially hypotensive drug. These patients were exposed to a mean of 2±1 potentially hypotensive drugs. Patients with OH were less frequently exposed to antihypertensives (16% vs. 31%, p<0.01), levodopa (58% vs. 78%, p<0.01) or dopamine agonists (9% vs. 36%, p<0.01). Results remained significant after adjusting for demographic or disease-related factors by logistic regression analysis.
Conclusion: Our study showed that patients with OH were less frequently exposed to antihypertensives, levodopa or dopamine agonists. As it is possible that treating physicians may have avoided exposing MSA patients to these drugs, drug exposure may not be a major factor connected with OH in MSA.

P1636

Medication use in patients with multiple system atrophy or Parkinson’s disease compared to a group of patients consulting a general practitioner

S. Perez-Lloret¹, M.V. Rey¹, A. Pavy-Le Traon², W. Meissner³, F. Ory-Magne², C. Brefel-Courbon², N. Fabre³, F. Tison³, O. Rascol¹
¹Clinical Pharmacology, ²Neurology, CHU Toulouse, ³Neurology, CHU Bordeaux, France

Objective: To compare drug utilization between MSA, Parkinson’s disease (PD) patients or unselected patients consulting a general practitioner (GP).
Methods: 147 MSA patients (according to Gilman criteria) were assessed at the MSA reference Center between 2008 and 2011. 653 PD patients (according to UKPDSBB criteria) and 98 patients visiting a GP for reasons not related to PD or MSA were recruited from the same geographical area. Data were analyzed by chi-square test followed by pair wise comparisons by bonferroni-adjusted z-test for proportions.
Results: MSA patients were younger than PD or GP patients (65±1 vs. 68±1 and 71±1 years p<0.001). Proportion of males was similar in the 3 groups (MSA: 50% vs. PD: 49% and 46%, p=0.9). MSA patients were more frequently exposed to drugs for bowel disorders (MSA: 19% vs. PD: 6% and GP: 10% p<0.01), to urinary antispasmodics (MSA: 18% vs. PD: 2% and GP: 1% p<0.01) to drugs used for orthostatic hypotension such as midodrine or fludrocortisone (MSA: 42% vs. PD: 3% vs. GP: 0%, p<0.01) to antihypertensives (MSA: 22% vs. PD: 40% vs. GP: 58% p<0.001). MSA patients were less frequently on antiparkinsonians as compared to PD (73% vs. 88% p<0.05). Finally, MSA patients were more frequently on antidepressants (MSA: 48% vs. PD: 18% and GP: 10% p<0.001).
Conclusions: Medication use patterns differ in patients with MSA, PD and those visiting a GP.
P1637

Medication use in the patients of the French multiple system atrophy (MSA) reference center

M.V. Rey¹, S. Perez-Lloret¹, A. Pavy-Le Traon², W. Meissner¹, F. Ory-Magne², C. Brefel-Courbon², N. Fabre², F. Tison³, O. Rascol¹
¹Clinical Pharmacology, ²Neurology, CHU Toulouse, ³Neurology, CHU Bordeaux, France

Objective: To describe medication use in MSA patients and to relate it with different characteristics of the disease.

Methods: Patients were assessed at the French MSA reference Center. The following variables were collected: MSA diagnosis (“probable” vs. “possible” according to Gilman criteria), disease duration, autonomic dysfunction (SCOPA-Aut), clinical subtype (MSA-P vs. MSA-C) and any medication use (coded by ATC). Data were analyzed by chi-square test; only significant differences are reported.

Results: 147 MSA patients were recruited (mean age 65.3±0.7; 50% males, 61% MSA-P; 82% “probable” MSA; mean UMSARS-score 48.9±1.3; mean disease duration 5.1±0.2). Overall, MSA patients received 8.2±0.4 medications. 73% of patients received at least one antiparkinsonian (mainly levodopa: 67%), 33% midodrine and 10% fludrocortisone. More severely affected patients (UMSARS>47) more frequently received antithrombotics (27% vs. 14%; p<0.05) antidepressants (61% vs. 38%; p<0.01) or drugs for bowel disorders (30% vs. 10%; p<0.01). More patients with MSA-P (versus -C) received antiparkinsonian (mainly levodopa: 67%), 33% midodrine and 10% fludrocortisone. More severely affected patients (UMSARS>47) more frequently received antithrombotics (27% vs. 14%; p<0.05) antidepressants (61% vs. 38%; p<0.01) or drugs for bowel disorders (30% vs. 10%; p<0.01). More patients with MSA-P (versus -C) received antiparkinsonian (90% vs. 46%; p<0.01), antihypertensive (28% vs. 12%; p<0.05) or analgesic (19% vs. 4%; p<0.01) medications. More patients with “probable” MSA (versus “possible”) received midodrine (39% vs. 7%; p<0.01) and less alpha-blockers (5% vs. 19%; p<0.02). Patients with SCOPA-Aut score >22 were more frequently on fludrocortisone (18% vs. 3%; p<0.01) or antidepressants (57% vs. 41%; p<0.04). Patients with disease duration >5 years were more frequently on alpha-adrenergic blockers for urinary problems (14% vs. 3%; p<0.01).

Conclusion: In MSA, medication use significantly differs according to disease characteristics.

P1638

Features of the basal metabolism in patients with Parkinson's disease

R. Bogdanov¹, A. Bogdanov², E. Manannikova¹, B. Kaganov², S. Kotov¹
¹Department of Neurology, Moscow Regional Scientific Research Clinical Institute n.a. M. F. Vladimirsky, ²The Institute of Nutrition Russian Academy of Medical Science, Moscow, Russia

Aim: To study basal metabolic rate in patients with Parkinson’s disease.

Material and method: 30 patients with a diagnosis of Parkinson’s disease were examined and compared with 30 control subjects. None of the patients were receiving any anti-parkinsonian treatment before the examination. We studied basal metabolic rate and oxidation rates of macronutrients (protein, fat and carbohydrates) by indirect respiratory calorimetry in all patients.

Results: The average basal metabolic rate was defined. It was increased by 33.9% in the patients with Parkinson’s disease compared to the control group. The separated analysis of the average rate of oxidation of the macronutrients in patients with Parkinson’s disease showed that the average rate of oxidation of the fats was increased by 94%, average rate of oxidation of the carbohydrates was increased by 8.6%, and there were no statistical significant changes for proteins, compared to the control group.

Conclusion: Our results show that the increased basal metabolic rate of patient’s with Parkinson’s disease, in the first place, was caused by increased basal oxidation of the fats, and in the second place it was caused by increased basal oxidation of the carbohydrates. This result may be used for diet therapy optimization of patients with Parkinson’s disease.
P1639

Using an endophenotype to evaluate the effect of environmental factors in disease penetrance of adult onset primary torsion dystonia

A. Molloy1, O. Kimmich1, D. Bradley1, R. Reilly2, S. O’ Riordan1, M. Hutchinson1
1St Vincent’s University Hospital, 2Trinity Centre for Bioengineering, Trinity College Dublin, Ireland

Objective: We aim to investigate whether significant differences exist in environmental exposures among manifesting individuals with adult onset primary torsion dystonia (AOPTD) and their unaffected first degree relatives with abnormal temporal discrimination, indicating abnormal gene carriage, to determine reasons for the reduced penetrance of AOPTD.

Background: AOPTD is a poorly penetrant autosomal dominant disorder. Most (85-90%) gene carriers for AOPTD are non-manifesting despite having reached an adequate age for penetrance. The temporal discrimination threshold (TDT) is abnormal in patients with AOPTD and 50% of their unaffected first degree relatives. An abnormal TDT is a mediational endophenotype indicating gene carriage in unaffected relatives. It is hypothesized that genetic, epigenetic and environmental factors may exert protective or deleterious effects affecting penetrance of AOPTD. By examining environmental exposure history in both AOPTD patients and their similarly aged unaffected siblings with abnormal TDTs we may determine the role of the environment in disease penetrance.

Methods: This is a case-control single centre prospective study that will be performed using a standardised questionnaire. The questionnaire will collect information on demographics and on a range of past environmental exposures in patients with AOPTD and their unaffected siblings. A total of 60 AOPTD probands with cervical dystonia and one or more of their unaffected siblings with abnormal TDTs will be recruited. All unaffected siblings will be over 40 years of age, and age and gender matched to the proband.

Results: Results of this study will be available at the congress.

P1640

Drug-induced parkinsonism treated with Yokukansan in elderly patients

Department of Cardiovascular & Neurologic Diseases, College of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea

Introduction: Drug-induced parkinsonism (DIP) is a common cause of parkinsonism in elderly people. Many different types of medication, not only neuroepileptics, may induce or exacerbate parkinsonism. Older people are more exposed to developing DIP, because they are on multiple medications for chronic senile diseases. DIP is considered to be reversible after stopping the offending drugs within 4 months. However in some cases, it may persist. The management with anticholinergic agents or dopaminergic drugs seemed to have additional drug side effects especially in elderly people. Yokukansan (YKS) is a herbal formula used to treat Parkinson’s disease in oriental medicine. We introduce cases of DIP treated with Yokukansan in old patients.

Case report: We describe 4 cases of DIP possibly caused by medication for common senile diseases, which were dibenzodiazepine, SSRIs for depression, flunarizine for vertigo, and levosulpiride for dyspepsia. All patients were female and above 70 years of age. They presented postural upper limb tremor and bradykinesia about 5 months after the initiation of offending drugs. 2 of them concurrently had oral-buccal dyskinesia.

Results: Symptoms completely improved several weeks or months after discontinuing the causative drugs and being treated with YKS. None of the patients suffered from any side effects attributable to YKS.

Conclusions: DIP adversely affects the quality of life in older patients. Through careful medication history taking and avoidance of any potentially offending medication, it can be often reversible. Furthermore, we propose that YKS might be helpful to the management of DIP.
P1641
Non-motor disturbances in patients with Parkinson’s disease
S.B. Sattarova¹, Y.N. Madjidova², D.B. Sattarova²
¹Tashkent State University, Nezami, ²Tashkent Medical Academy, Tashkent, Uzbekistan

P1642
Hemifacial spasm due to posterior fossa lipoma: a case report
S. Nazarbaghi
Neurology Department, URMIA University of Medical Sciences, Urmia, Iran

P1643
Apomorphine in treatment of Parkinson’s disease: initiation without discontinuation or reduction of dopaminergic therapy
M.F. Oztekin¹, N. Oztekin², F. Ak²
¹Neurology, MOH Ankara Yildirim Beyazit Education and Research Hospital, ²Neurology, MOH Ankara Numune Education and Research Hospital, Ankara, Turkey

P1644
Subjective evaluation of emotional visual stimuli in patients with Parkinson’s disease: a pilot study
Department of Neurology, University Medical Centre Ljubljana, Slovenia

P1645
Life quality improvement in Parkinson’s disease treated with foetal stem cells
N. Sych, M. Klunyky, O. Ivankova
Embryonic Tissues Center EmCell, Kiev, Ukraine

P1646
Strategy of starting levodopa treatment in Parkinson’s disease patients in Armenia
Z. Tavadyan¹,², H. Bakunts³
¹Department of Angioneurology, Yerevan State Medical University after Mkhitar Heratsi, ²'Somnus’ Sleep and Movement Disorders Clinic, Yerevan, Armenia

P1647
The effect of homocystein and MTHFR gene mutation in Parkinson’s disease treatment
P. Nurkan¹, H.A. Idrisoglu², A. Sazci², N. Polat²
¹Merid Company, ²Department of Neurology, Medical Faculty of Istanbul, Turkey

P1648
Association of Parkinson’s disease and essential tremor
V. Razdorskaya, G. Yudina, O. Voskresenskaya
Saratov State Medical University, Saratov, Russia

P1649
Development and validation of a quality of life measure for carers of people with Parkinson’s disease
C. Jenkins, S. Dummett
University of Oxford, Health Services Research Unit, UK

P1650
The combination of SPECT-CT and functional MR imaging in the diagnosis of neuro-acanthocytosis: a case report
N. Xiong, Q. Zhu, Z. Liang, C. Liu
Department of Neurology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

P1651
Aphasia as primary symptom in corticobasal degeneration
C. Balla, J.L. Pepin
CHR Citadelle, Liège, Belgium

P1652
Overnight switching from pramipexole to ropinirole CR in patients with Parkinson’s disease: an open preliminary trial in Korea
M.Y. Park, H.J. Park
Neurology, Yeungnam University College of Medicine, Daegu, Republic of Korea
P1653
Treatment of patients with writer’s cramp by injections of botulinum toxin-A
V. Zmachynskaya, S. Likhachev, T. Charnukha
Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

P1654
Comorbidities of fatigue syndrome in patients with Parkinson’s disease
V. Datieva, O. Levin
Russian Medical Academy of Postgraduate Education, Moscow, Russia

P1655
Investigation of the prevalence of essential tremor in individuals aged 18-60 in Erzurum
L. Özel¹, R. Demir¹, G. Özdemir¹, E. Özyıldırım², U. Avşar¹, H. Ulvi¹, R. Aygül¹
¹Department of Neurology, ²Department of Public Health, Family Medicine, Medical School of Atatürk University, Erzurum, Turkey

P1656
The heterogeneity of hypersomnia in Parkinson’s disease
M. Nodel, N.N. Yakhno
Neurology, Moscow Medical Academy, Moscow, Russia

P1657
Recently diagnosed chronic liver disease presenting with parkinsonian symptoms
T. Kasikci¹, S. Bek², E. Tokgoz², Y. Kutukcu², Z. Odabasi²
¹Neurology, ²Gülhane Medical Faculty, Ankara, Turkey

P1658
Post-infectious cerebellar atrophy
C. Silva, D. Neutel, M. Coelho, L. Albuquerque
Hospital Santa Maria, Lisbon, Portugal

P1659
Paroxistic non-kinesiogenic and hipnogenic dyskinesia (Lugaresi disease): a case report
M.A. Sierra-Beltrán¹, C.M. Hernández-Cárdenas², H. Senties-Madrid³
¹CIDyT, Mèdica Sur, ²Critical Care Medicine, ³Neurology Department, INCMNSZ, Mexico City, Mexico

P1660
New approach to gait disorders therapy in late stages of Parkinson’s disease
I. Litvinenko¹, L. Krasakov¹-², R. Khalimov¹, A. Trufanov¹
¹Department and Clinic of Neurology, Military Medical Academy named after S.M. Kirov, Saint-Petersburg, ²The Center of Extrapyramidal Disorders, The Nikiforov Russian Center of Emergency and Radiation Medicine, Saint Petersburg, Russia

P1661
The effectiveness of cognitive & reflexive saccade measures in discriminating Huntington’s disease from healthy controls
E.A. Toh¹-², M.R. MacAskill¹-², J.C. Dalrymple-Alford¹-²-³, D.J. Myall², L. Livingston¹-², J. Ross², T.J. Anderson¹-²
¹Department of Medicine, University of Otago, ²New Zealand Brain Research Institute, ³Department of Psychology, University of Canterbury, Christchurch, New Zealand