



The *Movement Disorder Society*

17TH INTERNATIONAL CONGRESS OF PARKINSON'S DISEASE
AND MOVEMENT DISORDERS

LATE-BREAKING ABSTRACTS,
MDS STUDY GROUP ABSTRACTS AND
GUIDED POSTER TOUR INFORMATION

SYDNEY,
AUSTRALIA
JUNE 16-20, 2013



Late-Breaking Abstracts

LBA-1

A mir-153 binding site polymorphism in SNCA in a patient with Parkinson's disease

Authors: Han-Joon Kim MD, PhD¹, Gibeom Park MD², Beom S Jeon MD, PhD¹, Woong Yang Park MD, PhD², Young Eun Kim MD¹

¹Departments of Neurology and Movement Disorder Center, Parkinson Study Group, and Neuroscience Research Institute, Seoul National University College of Medicine, Seoul, Korea.

²Department of Biochemistry and Molecular Biology, Seoul National University College of Medicine, Seoul, Korea.

Background: Clinical and laboratory studies indicate that increased expression of α -synuclein is causally related to Parkinson disease (PD). Among the mechanisms by which the expression of α -synuclein is increased is alteration in microRNA-mediated post-transcriptional regulation, as evidenced by recent studies. Especially, polymorphism in the microRNA-binding site in the 3'UTR of α -synuclein gene (*SNCA*) can cause PD through increased expression of α -synuclein by reduced binding of microRNA

Objective: To analyze the polymorphism in the microRNA-binding site in the 3'UTR of *SNCA* in patients with PD and to examine its effect on *SNCA* expression.

Methods: In 262 PD patients, we sequenced the region containing two TargetScan-predicted microRNA binding sites, one for mir-7 and the other for mir-153, in the 3'UTR of *SNCA*. The effect of polymorphism at the microRNA binding site on *SNCA* expression was examined using Dual Luciferase assay.

Results: One patient was found to have polymorphism at the seed sequence of mir-153 binding site, *SNCA* 3'UTR 464C>A., which was not detected in 409 normal controls, 97 patients with familial PD, or 34 patients with multiple system atrophy. The minimum free energy change by *SNCA* 3'UTR 464C>A was from -18.7kcal/mol to -13.8kcal/mol. Luciferase assay showed that *SNCA* 3'UTR 464C>A attenuates, although not completely abolishes, the dose-dependent inhibition of gene expression by mir-153, indicating a defective modulation in α -synuclein expression by *SNCA* 3'UTR 464C>A.

Conclusions: Our result suggests that polymorphism in the microRNA binding site of *SNCA* can be the rare cause of PD.

Keywords up to six: Parkinson disease, microRNA, *SNCA*, microRNA binding site, polymorphism

Presenting author: Han-Joon Kim, MD, PhD

Department of Neurology, Seoul National University College of Medicine, Seoul, Korea

LBA-2

Specialist integrated rehabilitation for people with Parkinson's disease and carers: Short term outcomes from the SPIRiT study

Authors: Gage H, Grainger L, Ting S, Williams P, Chorley C, Carey G, Borg N, Bryan K, Castleton B, Trend P, Kaye J, and Wade D

Objective: To evaluate the clinical effectiveness of a domiciliary specialist multidisciplinary neurological rehabilitation service for people with Parkinson's and co-resident carers, compared to usual care (largely non specialist and non team-based).

Background: Parkinson's disease is complex with multiple symptoms. A collaborative multidisciplinary team (MDT) approach to rehabilitation is recommended to provide coordinated care to patients, and is accepted best-practice. However, the effectiveness of the MDT approach has not been widely researched.

Methods: A pragmatic randomised controlled trial set in contiguous communities in southern England. People with Parkinson's (any stage of the disease, without significant cognitive impairment) receiving the intervention were assessed and managed over a six week period (approximately nine hours of therapy input) in their own homes by a specialist MDT (Parkinson's nurse specialist, physiotherapist, occupational therapist, speech and language therapist) according to a care plan that was agreed amongst the professionals and with the patient and carer. Outcomes were independently assessed in the participant's home by a researcher blinded to group allocation using well validated scales within two weeks of completion of treatment. A per protocol analysis was undertaken. Short term effects of the MDT intervention were calculated within and between groups using change scores (post intervention minus baseline). Primary outcomes: Parkinson's Disease Disability Scale (patients), Modified Caregiver Strain Index (co-resident carers). Secondary outcomes included disease specific and generic health related quality of life, psychological wellbeing, self efficacy, mobility, posture, gait, speech and acceptability of the intervention.

Results: At baseline, 269 people with Parkinson's (155 co-resident carers) were analysed: 176 (102) received the MDT intervention; 93 (53) in the control group. Significant improvements from treatment arose for patients in disability, health-related quality of life, psychological wellbeing and speech, and for co-resident carers in psychological wellbeing. Over 80% of participants found the treatment very or extremely helpful; 90% said they had learnt a lot.

Conclusions: Domiciliary specialist multidisciplinary neurological rehabilitation service delivers short term benefits to people with Parkinson's and co-resident carers; longer term outcomes and cost effectiveness will be reported elsewhere.

This project was funded by the National Institute for Health Research Health Services and Delivery Research (NIHR HS&DR) programme (project number 08/1909/251). Visit the HS&DR website for more information.

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR HSDR programme or the Department of Health.

LBA-3

Visualising nigrosome loss as a novel MRI diagnostic in Parkinson's disease

Anna I Blazejewska¹, Stefan T Schwarz², Alain Pitiot³, Mary C Stephenson¹, James Lowe⁴, Nin Bajaj⁵, Richard Bowtell¹, Dorothee P Auer², and Penny A Gowland¹

¹SPMMRC, University of Nottingham, ²Division of Radiological and Imaging Sciences, University of Nottingham, ³School of Psychology, University of Nottingham, ⁴Division of Pathology, NUH NHS Trust, ⁵Division of Neurology, NUH NHS Trust

Objective: To investigate if (1) nigrosomes can be visualised directly *in vivo* (IV) by comparing IV and *post mortem* (PM) high field MRI and histochemical data; (2) nigrosome visualization in 7T and 3T MRI could provide a new diagnostic marker of PD.

Background: The pathological hallmark of PD is dopaminergic cell loss in the substantia nigra (SN). This cell loss is predominant in the nigrosomes, calbindin D_{28k} (CAL) [2] immunonegative substructures in the SN.

Methods: Two PM mid brains of healthy controls (HCs) and one of PD were scanned at 7T with a 3D FFE sequence (0.3mm isotropic). Perls', tyrosine hydroxylase (TH) and CAL stains of the adjacent transverse slices were co-registered to the MR data. Iron and neuromelanin (NM) of Perls' maps were separated using colour deconvolution [3], together with CAL and TH maps converted to grey scale and thresholded to produce masks of the iron+, NM+, TH+ or CAL+ overlaid on the T2*w images (Fig 1). 10 PD patients and 9 age-matched HCs were scanned at 7T using a 2D FFE sequence (0.35x0.35x1.0mm³, 10min). Two blinded neuroradiologists independently classified T2*w datasets based on the presence/absence of the hyperintense structure within the dorsal/posterior hypointense region according to the specific criteria. Eight HCs (33/11 y.o., 4F:4M) were scanned in 3T with similar T2*w sequence (0.43x0.43x1.5mm³, 10min).

Results: Comparison of PM histology and MRI for HC (Fig 1) revealed a CAL- region co-localised with dopaminergic cells (TH+) inside a larger CAL+ area; a region with such staining, size and approximate location was previously defined as nigrosome 1 [2]. This area was also iron-, NM+ and corresponded to the hyperintense substructure in the PM T2*w data. Perls' iron+ overlapped with T2*w hypointensity in the lateral part of the SN, but both neither overlapped with TH+ and NM+. In the PD PM sample although nigrosome 1 was still present as a CAL- region, it did not stain TH+ or NM+ indicating dopaminergic cell loss from nigrosome 1. A hyperintense substructure corresponding to nigrosome 1 was

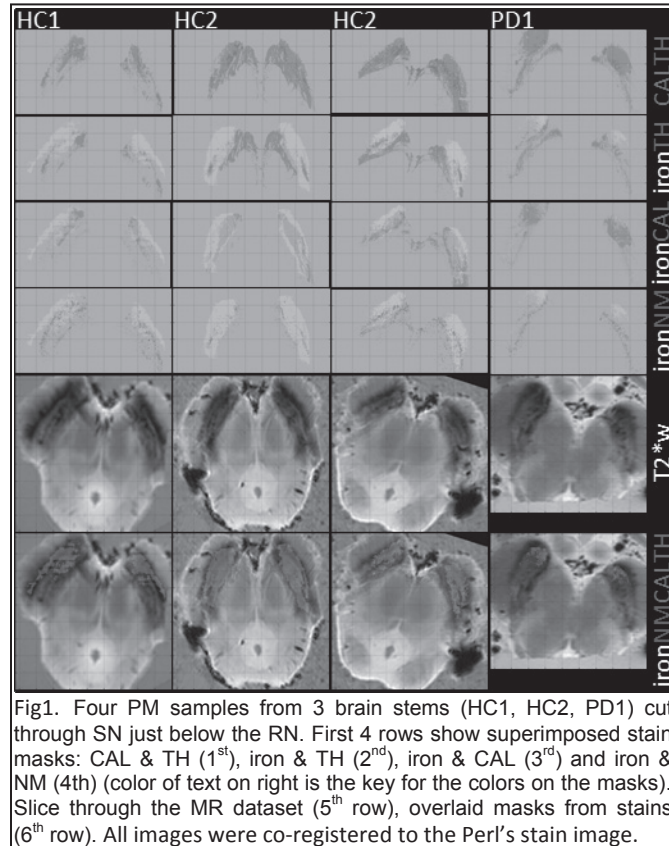


Fig1. Four PM samples from 3 brain stems (HC1, HC2, PD1) cut through SN just below the RN. First 4 rows show superimposed stain masks: CAL & TH (1st), iron & TH (2nd), iron & CAL (3rd) and iron & NM (4th) (color of text on right is the key for the colors on the masks). Slice through the MR dataset (5th row), overlaid masks from stains (6th row). All images were co-registered to the Perls' stain image.

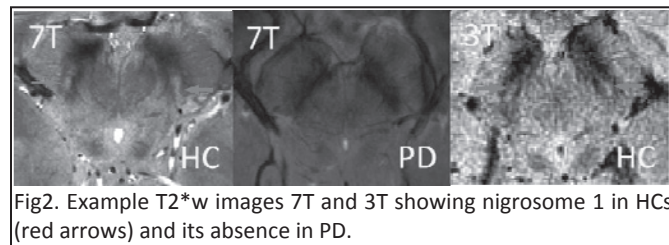


Fig2. Example T2*w images 7T and 3T showing nigrosome 1 in HCs (red arrows) and its absence in PD.

detected IV in HCs on 7T T2*w images (Fig 2). The neuroradiologists correctly classified 7/8 HC and 10/10 PD according to its presence/absence (sensitivity=100%, specificity=88%, inter-observer agreement $\kappa=1$). Preliminary scans at 3T also indicated presence of this feature, though less clearly (Fig 2).

Conclusions: We have identified the substructure of the SNpc, TH+, NM+, CAL-, iron-, and hypointense region on PM and IV T2*w images corresponding to nigrosome 1. Its absence on IV T2*w images is associated with PD, in agreement with a recent publication showing change in a T2*w hyperintense SN substructure in PD [4]. Moreover our preliminary data suggested that it will be possible to identify nigrosome 1 on more widely available 3T scanners, providing a new diagnostic marker of PD.

References : [1] Bajaj et al., *JNNP*. 2010, 81:1223-8; [2] Damier et al., *Brain* 1999, 122:1421-36; [3] Ruifrok et al., *Anal Quant Cytol Histol*, 2001, 23:291-9; [4] Kwon et al., *Ann of Neurol*, 2012, 71:267-77.

LBA-4

Involvement of p38 signaling in differential regulation by fucoidan of IFN- γ -induced NO and iNOS production in Glial cells and Macrophages

Eun-Soo Sohn,¹ Ye-Jin Kim², Taeseong Kim², Seon-A Jang², Hyun Jung Koo³, Jung-Eun Kwon³, Seung Namkoong⁴, Eun-Hwa Sohn², Se Chan Kang³

¹Division of Information Analysis Research, Korea Institute of Science and Technology Information, KISTI, Seoul 130-741, South Korea ²Department of Herbal Medicine Resources, Kangwon National University, Samcheok 245-710, South Korea ³Department of Life Science, Gachon University, Seongnam 461-701, South Korea ⁴Department of Physical Therapy, Kangwon National University, Samcheok 245-710, South Korea

Background: Neuroinflammation and the activation of inducible nitric oxide synthase (iNOS) have been proposed to play a role in the pathogenesis of Parkinson disease. In previous study, we found that fucoidan regulated TNF- α and IFN- γ -induced nitric oxide (NO) production differently in RAW264.7 macrophages and C6 glioma cells.

Objective: Accordingly, we here investigated the effects of fucoidan on iNOS/NO production and related molecular mechanisms induced by IFN- γ using two types of cells such as glia and macrophage.

Methods: This study examined the production of NO, iNOS and secreted TNF- α in IFN- γ -treated cells by fucoidan using RT-PCR, Western blotting and ELISA. We used inhibitors involved in JAK/STAT and p38 signaling pathways in order to reveal the mechanisms of fucoidan action.

Results: Our data demonstrates that fucoidan suppresses IFN- γ -induced iNOS/NO production in C6 glial cells via inhibition of JAK/STAT and p38 activation regulated positively. In contrast, with treatment of fucoidan, JAK/STAT is a positive regulator whereas p38 is a negative regulator of IFN- γ -induced NO/iNOS production in RAW264.7 cells.

Conclusions: IFN- γ -induced iNOS/NO production are affected differently by fucoidan in C6 glioma cells and RAW264.7 macrophages due to its different effects on p38 activation and TNF- α production in those cell types. These novel observations including selective and cell-type specific effects of fucoidan on IFN- γ -mediated signaling and iNOS expression raise the possibility that it alters the sensitivity of cells to the p38 activation.

LBA-5

Electrophysiologic evaluation of oropharyngeal dysphagia in patients with parkinson-plus syndromes

AHMET ACARER , LEYLA BAYSAL KIRAÇ, SEZİN ALPAYDIN, ZEYNEP TANRIVERDİ, ZAFER ÇOLAKOĞLU, İBRAHİM AYDOĞDU, CUMHUR ERTEKİN

EGE UNIVERSITY FACULTY OF MEDICINE NEUROLOGY AND NEUROPHYSIOLOGY DEPARTMENT, IZMIR, TURKIYE

Objective: Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP) are neurodegenerative diseases which have common properties at onset. Dysphagia is the most critical problem and is closely related to patient prognosis. Evaluation and appropriate treatment of dysphagia might prevent or delay complications such as aspiration pneumonia. In PSP and MSA swallowing abnormalities usually present earlier than PD. However ; only a few reports have been published on the oral or pharyngeal phase specific abnormalities in Parkinson-plus syndromes. The aim of this study was to assess oropharyngeal dysphagia through electrophysiological methods, to define the electrophysiologic characteristics and to improve our knowledge about the pathophysiologic mechanisms of dysphagia in Parkinson-plus syndromes.

Method: 44 patients with idiopathic PD, 22 patients with PSP, 18 patients with MSA-P and MSA-C and 41 healthy subjects were investigated by clinical and electrophysiological methods that measured the oropharyngeal phase of swallowing. Parkinson-plus patients fulfilled the criteria for probable or possible PSP and MSA according to the NINDS-SPSP (1996) and AAN-MSA (2008) diagnostic criteria. The laryngeal movements were recorded by a movement sensor . Submental EMG activity was monitored . Single bolus analysis, dysphagia limit and sequential water swallowing (SWS) of 100 ml of water tests were performed. The coordination of SWS and respiration was also studied .

Results: In Parkinson-plus group dysphagia was demonstrated in % 95 of all patients in whom dysphagia limit was abnormal. In single bolus analysis test, total oropharyngeal swallowing duration and triggering of the swallowing reflex were extremely prolonged and most of the patients had reflexive swallowing patterns. In addition dysphagia limit was significantly lower and aspiration was more frequently observed. Total duration and the number of swallows during SWS were significantly increased, and the capacity and speed of drinking reduced significantly. The regularity and rhythmicity of the swallowing pattern and coordination between SWS and respiration was disordered in nearly % 30 of the patients with MSA and PSP. In MSA group deterioration of dysphagia parameters were more marked than PSP.

Conclusion: In Parkinson-plus patients dysphagia is a more distinctive clinical and electrophysiologic finding. Reduced rate of swallowing and slowness of sequential movements are related with extrapyramidal system disorder . Features like severity in triggering of swallowing reflex and reflexive swallowing patterns suggested dysfunction in corticobulbar control of swallowing. Arrhythmic pattern of SWS which is demonstrated in some of the Parkinson-plus patients has not been observed in PD or healthy controls. Arrhythmical SWS can be related with dysfunction of central pattern generator at brain stem. Our electrophysiologic method can help in differential diagnosis of idiopathic PD and Parkinson-plus syndromes.

LBA-6

Efficacy and safety of opicapone, a new COMT inhibitor, for the treatment of motor fluctuations in Parkinson's disease patients: A phase III, randomized, double-blind, placebo-controlled, parallel-group study (BIPARK II)

Andrew Lees¹, Joaquim J. Ferreira², Raquel Costa³, José Francisco Rocha³, Cristina Oliveira³, Nelson Lopes³, Teresa Nunes³, Patrício Soares-da-Silva^{3,4}

¹ National Hospital for Neurology and Neurosurgery, London, UK, ² Neurological Clinical Research Unit, Instituto de Medicina Molecular, Lisbon, Portugal; ³ Dept. Research & Development, BIAL – Portela & C^a – S.A., 4745-457 S. Mamede do Coronado, Portugal; ⁴ Dept. Pharmacology & Therapeutics, Faculty of Medicine, University Porto, Porto, Portugal.

Aims: To investigate the efficacy and safety of 2 different doses (25 and 50 mg) of opicapone (OPC) administered once a day, compared with placebo, in patients with Parkinson's Disease (PD) on levodopa treatment and with end-of-dose motor fluctuations.

Methods: This was a multinational, multicentre, double-blind (DB), placebo-controlled and parallel-group study. Subjects were randomized to placebo (n = 135), 25 mg OPC (n = 125) or 50 mg OPC (n = 147). The DB phase lasted between 14 to 15 weeks. The primary efficacy variable was the mean change from baseline in absolute OFF-time, based on patient diaries. Secondary endpoints include proportion of responders, course of OFF/ON-time, UPDRS III, quality of life (PDQ-39) NMSS, PDSS, tolerability and safety (including mMIDI, C-SSRS and clinical laboratory tests) assessments.

Results: The mean reduction in absolute OFF-time in both the 25 and 50 mg OPC groups was considerably greater than in the placebo arm (1.7, 2.0 and 1.1 h, respectively). Despite the high placebo response, 50 mg OPC was significantly better than placebo (p=0.0084), but 25 mg OPC missed statistical significance by only 0.1 h (95%CI: -1.35, 0.11). Significantly more patients receiving either 25 or 50 mg OPC achieved the OFF-time responder endpoint than occurred with placebo (62.4% [p=0.0405], 66.0% [p=0.0088] and 50.4%, respectively) and they also achieved greater OFF-time reductions (11.0% [p=0.0297], 12.1% [p=0.0044] and 6.7% respectively). Furthermore, the mean increase in absolute ON-time without or with non-troublesome dyskinesias was considerably greater in both the 25 and 50 mg OPC groups than in the placebo arm (1.4h, 1.43h and 0.8h, respectively). Significant differences were observed for both 25 and 50 mg OPC groups for the sum of all ON-times compared with placebo (p=0.0209 and p=0.0051, respectively). Opicapone was safe and well tolerated at both tested doses.

Conclusion: OPC once-daily was safe, well tolerated, and effective in reducing the OFF-time in patients with PD on levodopa treatment and with motor fluctuations.

LBA-7

Reliability and validity of the Turkish version of the MoCA scale in Parkinson's disease

Betul Ozdilek, Gulay Kenangil
Erenkoy Research and Training Hospital for Neurologic and Psychiatric Disorders,
Department of Neurology, Istanbul, Turkey

Background: Due to the high prevalence of cognitive impairment in Parkinson's disease (PD), cognitive screening is important for the optimal management of patients with PD. It is reported that the Montreal Cognitive Assessment (MoCA) is more sensitive than the commonly used Mini-Mental State Examination (MMSE) in detecting mild cognitive assessment (MCI) and dementia in elderly population and patients

with PD. The aim of the present study is to examine the reliability and validity of the Turkish version of the MoCA (MoCA-TR) scale in patients with PD.

Methods: 45 patients with PD and 20 age and education matched healthy controls were included in this study. Both patients and controls have at least for 5 years of education and received 17 points or less in the Beck depression scale. MoCA-TR, MMSE-TR, and a neuropsychological battery with operationalized criteria for cognitive deficits were administered to Parkinson patients within a month and MoCA-TR and MMSE-TR were administered to controls. The discriminant validity of the MoCA and MMSE as screening and diagnostic instruments was ascertained. Concurrent and criterion validity, test-retest reliability, internal consistency of the MoCA-TR and MMSE-TR were examined and clinical observations were made.

Results: Approximately half of the sample met diagnostic criteria for a cognitive disorder (22% PDD and 20% MCI). Mean (SD) MoCA-TR and MMSE-TR scores in patients were 21.7 (4.7) and 26.1 (3.1), respectively. The Cronbach's alpha of MoCA-TR as an index of internal consistency was 0.73. The test-retest reliability of MoCA-TR, using intraclass correlation coefficient between the scores at baseline survey and follow-up survey one month later was 0.88 ($P < 0.001$). MoCA-TR total scores was highly correlated with MMSE-TR total scores ($r = 0.77$, $P < 0.001$). The overall discriminant validity for detection of any cognitive disorder was similar for the MoCA-TR and the MMSE-TR (receiver operating characteristic area under the curve [95% confidence interval]): MoCA-TR (0.71 [0.584, 0.837]) and MMSE-TR (0.71 [0.585, 0.835]). The sensitivity and specificity of the MoCA-TR were 62% and 40%, respectively, with a cut-off score of 24 points.

Conclusion: The present results indicate that the MoCA-TR maintains its core diagnostic properties rendering it a valid and reliable scale for the cognitive screening among Turkish patients with PD.

Key words: Parkinson's disease, cognitive impairment, MoCA-TR, validity

LBA-8

Evaluation of sleep disorders in Parkinson's disease: History taking in comparison to self-administered questionnaires

Sontaya Jongwanasiri, M.D., Wattanachai Chotinaiwattarakul, M.D., Naraporn Prayoonwiwat, M.D., Apichart Pisarnpong, M.D., Prachaya Srivanitchapoom, M.D., Chotipat Danchaivijit, M.D.
Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, THAILAND

Background: Sleep disorders are more common in patients with Parkinson's disease (PD) and still be underestimated by the general practitioners. The unrecognition and delaying treatment of sleep disorders may provide an unfavorable outcome. The sleep questionnaires have become a popular and more practical tool for creating the possibility to early detect sleep problems in PD.

Objective: To determine whether sleep questionnaires could diagnose sleep disorders in patients with PD in comparison to those diagnosed by physicians based on clinical symptoms.

Methods: Patients with PD in movement disorders clinic at Siriraj hospital were recruited in this prospective cross-sectional study. Participants completed multiple types of sleep questionnaires including Simplified sleep questionnaire (SSQ), Modified Parkinson's Disease Sleep Scale (MPDSS), Epworth Sleepiness Scale (ESS), Scales for Outcomes in Parkinson's disease-Sleep Scale (SCOPA), and Thai Berlin questionnaire (Th-BQ). All participants were also evaluated by sleep medicine specialist for specific sleep problems.

Results: One-hundred and twenty participants were included in the study. Males were 73 (60.8%). Mean age was 61.48 ± 12.02 years. Body mass index (BMI) was 22.69 ± 3.47 kg/m² (BMI ≥ 30 kg/m² in

1.67%). Simplified sleep questionnaire were able to detect sleep problems in 86.7% of patients, whereas a clinical evaluation was able to detect only 59.2%. ($p < 0.05$) The results were comparable to various standard sleep questionnaires e.g. 81.7% in MPDSS, 29.2% with ESS > 10 and 28.3% was high risk on Th-BQ.

Conclusion: Sleep disorders are common in patients with PD. Questionnaires are superior to clinical evaluation in detecting these conditions. However, these problems are still underestimated due to two main reasons. Firstly, lacking of awareness of sleep problems in patients with PD and secondly, screening of sleep problems are not routinely performed in general clinical practice. In conclusion, this study demonstrated the benefit of sleep questionnaires and the efficacy for detecting common sleep disorders in patients with PD is superiority to routine history interviewing by physicians.

LBA-9

Efficacy, safety, and tolerability of AFQ056 for the treatment of chorea in patients with Huntington's disease

Reilmann, R.*, Rouzade-Dominguez, M-L., Saft, C., Süßmuth, S.D., Priller, J., Rosser, A., Rickards, H., Schöls, L., Pezous, N., Gasparini, F., Landwehrmeyer, B.G., Johns, D., Gomez-Mancilla B.
*Münster, Germany

Objective: To assess anti-choreatic efficacy, safety, and tolerability of AFQ056 (Mavoglurant) in Huntington's disease (HD).

Background: Treatments of chorea in patients with HD have limited efficacy and side-effects. AFQ056, a selective metabotropic glutamate receptor-5 antagonist shown to reduce levodopa-induced dyskinesia in Parkinson's disease, was hypothesized to reduce chorea in HD.

Methods: This was a 32-day randomized, double-blind, parallel-group, placebo (pbo)-controlled, proof-of-concept study. Patients were 30–85 years old, with HD (CAG ≥ 36) in clinical stage I–III, and maximal chorea sum score >10 in the Unified HD Rating Scale-Total Motor Score (UHDRS-TMS). Patients were randomized (1:1) to AFQ056 (Days 1–12, titration 25–150mg twice daily [bid]; Days 13–28, 150mg bid; Days 29–32, 50mg bid) or pbo. Primary objectives were to assess efficacy of AFQ056 vs pbo at Day 28 on UHDRS-TMS maximal chorea sum score and orientation index (non-dominant hand) from quantitative-motor (Q-Motor) grasping task and to assess safety and tolerability of AFQ056. Key secondary efficacy assessments included total UHDRS-TMS, UHDRS-TMS Luria score, UHDRS-TMS finger taps, and additional Q-Motor measures.

Results: Overall 42 patients (mean age 55.2 years, HD duration 6.6 years) were randomized. At Day 28, there were no significant improvements on UHDRS-TMS maximal chorea sum score ($p=0.155$) or orientation index (non-dominant hand, $p=0.626$) in AFQ056-treated patients vs pbo. A significant reduction in Q-Motor speeded-tapping variability was observed favoring AFQ056 vs pbo ($p=0.011$) and reverting at study end; this was accompanied by UHDRS-TMS finger-tapping scores showing a trend towards improvement. No significant treatment effects were observed at Day 28 on other key secondary endpoints. Adverse events were reported by 14 and 12 AFQ056- and pbo-treated patients, respectively.

Conclusions: AFQ056 did not reduce involuntary choreatic movements in HD. The Q-Motor findings in speeded-tapping may reflect an improvement in fine motor coordination, but their clinical relevance is unknown. Overall, AFQ056 was well tolerated.

STUDY SUPPORTED BY: Novartis Pharma AG, Basel, Switzerland

Keywords:

- 1) Huntington's disease
- 2) Chorea
- 3) AFQ056
- 4) mGluR5 antagonist
- 5) Quantitative motor

Disclosure information: RR has received consulting fees and/or research support from Novartis, Siena Biotech, Neurosearch Inc., Ipsen, Teva, Lundbeck, Medivation/Pfizer, Wyeth, ISIS Pharma, Link Medicine, Prana Biotechnology, the Cure Huntington's Disease Initiative Foundation, MEDA Pharma, Temmler Pharma GmbH, AOP Orphan Pharmaceuticals AG, the High-Q-Foundation, the Deutsche Forschungsgemeinschaft and the European Huntington's Disease Network.

CS has received consulting fees from Temmler Pharma GmbH and Co.KG and research support from Neurosearch, Novartis, Siena Biotech, Teva Pharma GmbH and the Cure Huntington's Disease Initiative Foundation.

JP has provided consulting services and/or lectures for: Actelion, Neurimmune, Bayer. He is Lead Facilitator of the Symptomatic Research and Treatment Working Group of EHDN. Dr. Priller has received grant support from the Huntington Society of Canada/Huntington Study Group, DFG and BMBF. AR has received consulting fees from CIRM and research support from Novartis and Siena Biotech.

HR has received research support from Siena Biotech.

LS has received grant support from the Deutsche Forschungsgemeinschaft, the German Research Council to Leukonet and mitoNET, EUROSCAR, NeurOmics and the HSP-Selbsthilfegruppe Deutschland eV.

GBL has received consulting fees from Siena Biotech S.P.A., AOP Orphan, TEVA, GlaxoSmithKline, Bayer Pharma AG, IPSEN and research support from the European Commission, CHDI Foundation, Medivation, NeuroSearch, Novartis, Medesis and Amarin.

LBA-10**Effects of Rivastigmine on balance control in Parkinson's disease dementia**

Emmanuelle Pourcher^{1,2}, Alexandra Nadeau³, Jaime McDonald³, Philippe Corbeil^{3,4}

⁽¹⁾ Clinique Sainte-Anne « Mémoire et Mouvement », Québec, Canada.

⁽²⁾ Faculty of Medicine, Laval University, Québec, Canada.

⁽³⁾ Groupe de recherche en analyse du mouvement et ergonomie, Faculté de médecine, kinésiologie, Université Laval, Québec, Canada.

⁽⁴⁾ Vieillissement, Centre de recherche FRSQ du centre hospitalier affilié universitaire de Québec, Québec, Canada.

Introduction: Postural Instability is considered a significant step in the functional deterioration of Parkinson's disease, possibly based on extra-nigral, non dopaminergic progression of degeneration. Impaired attention predicts falling in Parkinsonian patients (Allcock et al., 2009). 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 platform 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.

LBA-11

Progressive Supranuclear Palsy: Diagnosis through skin biopsy

Authors:

Ildefonso Rodriguez-Leyva, Md¹ and Jose Renan-Perez, Md¹. ¹Neurology, Central Hospital "Dr. Ignacio Morones Prieto", San Luis Potosi, Mexico, Mexico.

Objective: To assess the skin biopsy as a supportive method to evaluate a patient with parkinsonism.

Background: Nowadays the diagnosis of neurodegenerative parkinsonism is difficult and time consuming, and the only definitive diagnosis is made by mostmortem studies. Exploring the terminal nerve endings could yield a good assessment method for neurodegenerative disorders, since it has been described in Parkinson's Disease and it is an area of active research in Alzheimer's disease.

Methods: We report a Mexican male patient presented with frequent falls at age of 59, 4 years ago presented slurred speech. 2 years ago the patient became rigid, mostly in trunk, emotionally labile, with bursts of crying or laughing without objective stimuli, excessive drooling, dysphagia. Exam showed a low cognitive score (15/30 MMSE), vertical gaze palsy, optokinetic nistagmus absent, slow pursuit movements, dysphagia, dysphonia, parkinsonism, snouting, glabellar and grasping reflexes, cog-wheel rigidity and axial dominant rigidity with a tendency to put back his head while walking, severe bradikinesia, with apraxia of the upper left extremity, dysmetric and disidiadokinetic. MRI showed severe atrophy within cerebellar peduncles, humming bird sign and morning glory sign, cortical and subcortical atrophy. Patient fulfilled the mandatory PSP diagnostic criteria and all the supportive criteria.

Method: With the patient and patient's caregivers authorization we underwent skin biopsy, staining for immunoreactive Tau protein, then exploring the biopsies with single microscopy and confocal microscopy.

Results: We observed immunoreactive Tau-positive inclusions in the terminal nerve endings.

Conclusions: There are no previous studies showing such pattern, and the utility and feasibility of a skin biopsy could help the clinician to get PSP definitive diagnosis "in vivo". PSP subtypes tend to be clinically misdiagnosed.

LBA-12

Subjective memory complaints predict future cognitive decline in cognitively normal patients with Parkinson's disease

Jin Yong Hong¹, Mun Kyung Sunwoo², Jee Hyun Ham², Ji E. Lee², Young H. Sohn², Phil Hyu Lee^{2,3}.

Department of Neurology, Yonsei University Wonju College of Medicine, Wonju, Korea
Department of Neurology and Brain Research Institute, Yonsei University College of Medicine, Seoul, Korea²
Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul, Korea³

Background: Growing evidences suggest that subjective memory complaints (SMC) are predictive factor for future dementia. We recruited the Parkinson's disease (PD) patients with normal cognition, and followed up average of 2.4 years to investigate whether the SMC are predictable for future cognitive decline.

Methods: A total of 46 cognitively normal PD patients were selected using comprehensive neuropsychological test, and classified depend on presence (PD-SMC⁺, n=25) or absence of SMC (PD-SMC⁻, n=21). After average 2.4 years, the subjects were reevaluated their cognitive status.

Results: The clinical characteristics and cognitive performance at baseline were comparable between two groups. Fourteen of PD-SMC⁺ and 4 of PD-SMC⁻ group were diagnosed with mild cognitive impairment (MCI) at follow-up assessment, and PD-SMC⁺ patients showed more rapid decline in visuospatial memory and semantic fluency task than PD-SMC⁻ did. The multivariate logistic regression model revealed that the SMC was a significant risk factor for incident MCI after adjusted for age, K-MMSE score, and severity of motor symptom (OR=5.25, 95% CI, 1.28-21.56).

Conclusion: Our study shows that the SMC in cognitively normal PD patients are independent risk factor for incident MCI, which suggests that the feeling of memory decline may be associated with actual cognitive deterioration.

LBA-13

Apomorphine: A potential modifier of amyloid deposition in Parkinson's disease?

Alison J Yarnall, MRCP¹, Tammarny Lashley, PhD², Helen Ling, MRCP², Andrew Lees, MD, FRCP, FMedSci², Tamas Revesz, MD, FRCPATH², David J Burn, MA, MD, FRCP¹

¹Institute for Ageing and Health, Newcastle University, Newcastle, UK

²Queen Square Brain Bank, Department of Molecular Neuroscience, University College London, UK

Objective: To determine whether ante-mortem exposure to apomorphine is associated with lower levels of amyloid- β (A β) in brain tissue.

Background: Dementia affects up to 80% of people with PD (PDD). Although the precise cause of PDD is unknown, evidence from clinical and pathological studies suggests a role for both α -synuclein and A β . A recent study demonstrated an improvement in memory and reduced A β burden in transgenic murine Alzheimer (AD) models given subcutaneous apomorphine injections. We therefore investigated the effect of apomorphine on A β plaque load in a clinicopathological study of PD subjects with and without PDD.

Methods: The case notes of donors with pathologically proven PD who had (n=36; Apo+) and had not received apomorphine (n=43; Apo-) during life for motor complications were reviewed to determine

presence (CI) or absence (CN) of cognitive impairment. The severity of A β mature/diffuse plaque load was established together with the severity of AD development (Mirra 1991, Thal 2002). Cerebral amyloid angiopathy (CAA) was determined based on a 4-tier grading system. Tau pathology was assessed according to Braak and Braak. α -synuclein pathology was classified using the Braak and McKeith staging systems. ApoE genotype was established in 25 Apo+ and all Apo- cases.

Results: 20 Apo+CN, 16 Apo+CI, 16 Apo-CN and 27 Apo-CI cases were assessed. A trend towards reduced diffuse plaque load and overall A β plaque burden was found in Apo+CN when compared with the Apo-CN groups (mean Diffuse plaque_{sum} scores 2.20 vs 4.81, p=0.077; Plaque_{sum} + Diffuse plaque_{sum} 3.15 vs 7.00, p=0.083). When the CN group were dichotomised into those who had not and had received apomorphine doses greater than the median value, there was significantly less A β peptide deposition in those who had received high dose apomorphine (Plaque_{sum} 0.11 vs 2.04, p=0.047; Diffuse plaque_{sum} 4.31 vs 0.67, p=0.005; Plaque_{sum} + Diffuse plaque_{sum} 6.35 vs 0.78, p=0.005). No significant difference in plaque burden was found between the Apo+CI and Apo-CI groups.

Conclusions: This work in progress suggests that apomorphine may have a modifying effect on amyloid deposition in non-demented PD cases. Apomorphine may therefore represent a possible therapeutic target to reduce the burden of cognitive impairment in PD.

Mirra et al. Neurology 41:479-86, 1991
Thal et al. Neurology 58:1791-80, 2002

LBA-14

Normalization of basal ganglia D2 but not D1 receptors, in L-DOPA-treated parkinsonian monkeys following a chronic treatment with the mGlu5 receptor antagonist 2-methyl-6-(phenylethynyl)pyridine (MPEP)

Nicolas Morin, B.Pharm., M.Sc.^{1,2}, Vincent Jourdain, M.Sc.^{1,2}, Marc Morissette, PhD¹, Laurent Grégoire, B. Sc.¹ and Thérèse Di Paolo, PhD^{1,2}.

¹ Neuroscience Research Unit, Centre de recherche du CHU de Québec, Quebec City, QC, Canada, G1V 4G2;

² Faculty of Pharmacy, Laval University, Quebec City, QC, Canada, G1V 0A6

Objective: The aim of this study was to investigate the long-term effect of the prototypal metabotropic glutamate 5 (mGlu5) receptor antagonist 2-methyl-6-(phenylethynyl)pyridine (MPEP) with L-3,4-dihydroxyphenylalanine (L-DOPA) on D1 and D2 dopamine (DA) receptors in monkeys lesioned with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).

Background: In the long term, the majority of Parkinson's disease (PD) patients treated with L-DOPA will develop L-DOPA-induced dyskinesias (LID). Brain glutamate overactivity is well documented in PD and ant glutamatergic drugs are proposed to relieve PD symptoms and decrease LID. mGlu5 receptor antagonists reduce LID in PD. The effects of long-term treatment with these drugs are yet to be characterized.

Methods: MPTP monkeys were treated for one month with L-DOPA and developed dyskinesias while those treated with L-DOPA and MPEP (10 mg/kg) developed significantly less LID. Normal control and saline-treated MPTP monkeys were also included for biochemical analysis.

Results: [³H]SCH-23390 specific binding to D1 receptors in the caudate nucleus, putamen, internal (GPI) and external (GPe) globus pallidus was decreased in all MPTP monkeys compared to controls and no difference was observed between saline, L-DOPA and L-DOPA+MPEP-treated monkeys. In the caudate nucleus and putamen D1 receptor mRNA levels remained unchanged for all experimental groups.

[³H]raclopride specific binding to D2 receptors in the caudate nucleus, putamen, GPi and GPe was increased in saline and L-DOPA+MPEP-treated monkeys as compared to control and L-DOPA-treated monkeys, no difference between the latter groups was observed. In the caudate nucleus and putamen, the same pattern of changes as [³H]raclopride specific binding was observed for D2 receptor mRNA levels with a positive correlation between them. D1 receptor mRNA levels in the caudate nucleus and putamen did not correlate with D1 receptor specific binding. D1 and D2 receptors mRNA levels were low in the GPi and GPe and no change in the experimental groups was measured.

Conclusions: A chronic treatment with MPEP reduced the development of LID and was associated with a normalization of striatal D2 receptors while D1 receptors remained unchanged.

LBA-15

Effectiveness of the NINTENDO® WII BALANCE BOARD in rehabilitating patients with severe Parkinson's disease

Peppe A., Piermaria J., Tramontano M., Marchetti F., Caltagirone C.I.R.C.C.S. Fondazione Santa Lucia, Via ardeatina, 309, Roma Italy

Objective: We set out to demonstrate the effectiveness of Nintendo's Wii Fit Balance Board in rehabilitating balance in patients with Parkinson's disease and reducing the risk of falling.

Background: It is now well documented that most people with Parkinson's disease (PD) have a serious balance deficit linked to a higher risk of falling. Design: In addition to neurological motor therapy, patients also took part in a daily rehabilitation session consisting of 20 min. on the Wii balance board, 20 min. on a treadmill and 20 min. on a cyclette.

Subjects and Methods: Twelve patients with the following characteristics were enrolled in the study: Akinetic-rigid form of idiopathic Parkinson's disease, Hoehn & Yahr's scale score of 3-3.5, disease duration of 11.75 years (range 1-26 years) with complicated response (Wearing Off, Abnormal Involuntary Movements to pick of LD response and predictable OFF status) to pharmacological treatment. Enrolled patients were submitted to neurological motor therapy and rehabilitation with the Wii balance board. All patients were evaluated using the UPDRS (II, III part), the GMT, Tinetti's scale, the PDQ – 39 and the 6MWT.

Results: Statistical analysis showed that the means of Student's T and the Wilcoxon-Mann-Whitney test were significantly different after rehabilitation.

Limits: Limitations of the study include small sample size and lack of a control group.

Conclusions: Improved balance obtained on the scale was linked to use of the Wii Fit Balance Board. The latter seems to be a good tool that can compete with other devices for use in innovative complementary rehabilitation of Parkinson's disease patients.

LBA-16

Continuous apomorphine infusion in advanced Parkinson's disease: A seven-year experience with 143 patients

Sesar A, Ares B, Rivas MT*, Castro A

Movement Disorder Unit. Hospital Clínico Santiago de Compostela. Spain. *Servicio de Neurología. Complejo Hospitalario de Orense. Spain

Objective: We evaluate treatment with continuous subcutaneous apomorphine infusion (APO) in patients with advanced Parkinson's disease (PD).

Background: APO is one of the therapies available for advanced PD. We present our experience in treating 143 patients throughout 7 years.

Patients and methods: 143 patients with advanced PD were treated with APO. Main indications were lack of criteria for deep brain stimulation (DBS), transient therapy before DBS, suboptimal DBS outcome or patient's refusal of DBS. We have analyzed the motor situation, change in levodopa (LD) and dopamine agonists (DA), and PD complications of 55 patients currently on APO before and after this therapy. 4 patients on APO less than 3 months were excluded. We have also examined the causes of withdrawal for 84 patients in which APO was stopped. The APO pump was placed in the outpatient clinic in all cases. No major complications were observed with this procedure.

Results: 55 subjects (28 males, 27 females) have been on APO for at least 3 months. Mean age was 71.09 (± 8.42), mean disease duration 15.79 (± 7.04) and mean duration of APO 33.00 (± 22.51) months. After APO, daily off hours showed a considerable reduction from 5.59 (± 2.21) to 1.16 (± 1.16), $p < 0.0000$. Daily dose of LD also significantly decreased from 1149.07 (± 359.04) to 859.72 (± 376.81), $p < 0.0000$. DA were stopped or significantly reduced. A significant decrease in intensity of dyskinesias was found, $p < 0.0000$. Balance also improved, $p < 0.0000$. Hallucinations did not significantly change. Cognitive dysfunction moderately worsened in patients with APO. 84 patients (42 males, 42 females) stopped APO after mean treatment duration of 20.59 (± 20.30) months. Main causes for withdrawal were side effects (21), DBS (17), death from an unrelated cause (12), patient's decision (7), lack of effect (6), lack of family support (6), loss of effect (5).

Conclusions: Continuous apomorphine infusion is an effective and safe treatment for advanced PD, with a significant decrease in off hours and LD daily dose. This improvement is sustained over years in many cases. Placing the infusion system and training the patient and family may be carried out safely in the outpatient clinic.

LBA-17

A phase I study of intranasal glutathione in Parkinson's disease

Mischley LK, Standish LJ, Leverenz J, Samii A

Objective: To evaluate the safety and tolerability of intranasally-administered reduced glutathione, (in)GSH.

Background: Glutathione is a primary antioxidant defense system of the central nervous system. Decreases in glutathione concentrations are among the earliest reported biochemical events to occur in the Parkinsonian substantia nigra and the reduction has been associated with both disease severity and progression. Glutathione augmentation has been proposed as a therapeutic strategy in PD.

Methods: A double blind, placebo-controlled phase I study of (in)GSH was conducted in 30 individuals with Parkinson disease (PD). Individuals were randomized to administer 1 ml three times daily of placebo (sterile saline), 100, 200 mg/ml GSH, or a watchful waiting arm. Safety outcome measures included laboratory values (CBC, ALT, AST, BUN, creatinine, uric acid, and urinalysis), clinical assessment (Monitoring of Side Effect Scale, Sino-nasal Outcome Test for sinusitis, Sensonics Smell Identification Test for hyposmia, Unified Parkinson Disease Rating Scale (UPDRS), and Montreal Cognitive Assessment (MoCA)). Tolerability was measured by frequency and severity of reported adverse events, study drug compliance, and withdrawals from the study.

Results: Of the 30 participants who initiated the study, one withdrew due to adverse reaction; a female the 100mg/ml group reported an immediate exacerbation of pre-existing, chronic pruritus that had been several months quiescent. There were few differences between groups in all laboratory measures, sinusitis scores, UPDRS, MoCA, or Hoehn & Yahr. Average side effect scores decreased slightly across all groups. Smell test scores improved by 20% for the 200mg/ml group, but stayed constant for the others. All groups used more than 80% of the prescribed dose. The glutathione remained stable during the study, retaining 89% of its potency 30 days after being issued.

Conclusion: After 3 months, there were no differences between groups in the number of adverse events reported or observed among all safety measures assessed. Compliance targets were met in all groups. These data support the safety and tolerability of this novel method of glutathione augmentation; Future studies should evaluate the therapeutic potential of (in)GSH as a neuroprotective agent and as a treatment for hyposmia.

FUNDING: NIH 5K01AT004404

LBA-18

Alexithymia is an independent risk factor for impulsive-compulsive disorders in Parkinson's disease

Authors: (presenting author) Katharina S Goerlich, Catharina Probst, Karsten Witt, Günther Deuschl, Thilo van Eimeren

Affiliation: Department of Neurology, Christian-Albrechts University, Kiel, Germany

Objective: We aimed to identify alexithymia (a – *lack*, lexis – *word*, thymos – *emotion*) as a risk factor for impulsive-compulsive disorders (ICDs) in Parkinson's disease (PD).

Background: ICDs are frequent side effects of dopaminergic medication in PD. Previous research indicates that such disorders are linked to impulsive, novelty seeking personality traits and to symptoms of anxiety and depression. Alexithymia, a personality trait characterized by difficulties identifying and describing one's feelings and an externally oriented thinking style, has been linked to a number of disorders characterized by poor impulse control in the general population. However, whether alexithymia is associated with ICDs in PD is currently unknown.

Methods: Using the Toronto Alexithymia Scale (TAS-20) and the Questionnaire for ICDs in PD - rating scale (QUIP-RS), we assessed ICDs and alexithymia in a sample of 91 patients with PD, along with other self-report questionnaires measuring impulsivity, depression, anxiety, behavioral inhibition/approach, and emotion regulation strategies.

Results: We found that alexithymia, particularly difficulty identifying and describing feelings was significantly correlated with impulsive-compulsive disorders in PD patients, even when controlling simultaneously for impulsivity, anxiety, and depression.

Conclusions: This study identifies alexithymia as an independent risk factor for ICDs in PD. This is new and important information for the neuropsychiatric assessment of patients with PD and for cognitive behavioral therapy in PD patients with ICDs.

LBA-19

A mathematical model of long-term outcomes in Parkinson's disease

Boris Hayete¹, Jason Laramie¹, Jadwiga Bienkowska², Shirley Eberly³, Iya Kahil¹, Anthony Lang⁴, Kenneth Marek⁵, David Oakes³, Ira Shoulson⁶, Andrew Singleton⁷, Tao Song², Ajay Verma², Matthew Wien², Bernard Ravina^{2*}

¹GNS Healthcare, Cambridge, MA; ²Biogen Idec, Cambridge, MA; ³University of Rochester, Rochester, NY; ⁴The University of Toronto, Toronto, ON; ⁵Institute for Neurodegenerative Disorders, New Haven, CT; ⁶Georgetown University, Washington, DC; ⁷National Institute on Aging, NIH, Bethesda, MD

*Corresponding Author: Bernard.ravina@biogenidec.com

Objective: To build a mathematical model of Parkinson's disease (PD) to aid in the identification of predictors of long-term motor and cognitive function.

Background: Long-term follow-up is necessary to determine the prognostic value of baseline clinical features and biomarkers. The LABS-PD study acquired demographic, clinical, laboratory, genetic, and dopamine transporter imaging data in a cohort of de novo PD subjects. We report on the modeling of predictors of outcomes in years 4-7 of follow-up in 244 subjects with complete data.

Methods: Primary measures of motor and cognitive progression were the Unified Parkinson's Disease Rating Scale (UPDRS) and Montreal Cognitive Assessment (MoCA). DAT imaging was conducted with [¹²³I][β]-CIT and SPECT. Genetic data included 25 SNPs covering 15 risk genes, including microtubule-associated protein tau (MAPT), alpha-synuclein (SNCA) and ApoE isoforms. We adjusted for levodopa equivalents at the time of outcome assessment. We used the super computer enabled software platform Reverse Engineering and Forward Simulation (REFS™) to construct a dynamic Bayesian graphical model of predictors of outcome and progression. A billion variable interactions were scored and were assembled into the most-likely ensemble of Bayesian graphical network models given the LABS-PD data. Simulations then varied baseline variables between their 5th and 95th quantiles, of the training dataset, and the output variable's response was measured. A permutation test, with power analysis, was used to determine which baseline variables strongly influenced outcomes.

Results: We found several significant predictors of long-term UPDRS and MoCA. The most consistent predictor of UPDRS parts III (motor) was baseline UPDRS part I(mental) and II (ADL) with p values ranging from p<0.001 to p<.07 (earlier to later time points) . There were several predictors of MoCA annual outcomes and rate of change. The most robust and consistent over time included older age, baseline UPDRS parts I and II, Schwab and England ADL, striatal DAT binding, especially in the caudate, and the SNP rs11724635. The SNP rs11724635 is located in the gene bone marrow stromal cell antigen 1 (BST1) gene, named for its role in B cell maturation. BST-1 is involved in calcium signaling in endoplasmic reticulum. We did not observe an influence of SNPs in MAPT or SNCA on motor or cognitive function.

Conclusion: We built a unified dynamic mathematical model of long term outcomes in PD based on baseline clinical, genetic, and DAT imaging data. Baseline functional status and age were drivers of motor and cognitive outcomes at multiple time points, consistent with prior reports. We confirmed DAT imaging as predicting long-term cognitive outcomes. We identified a SNP in the gene BST-1 as having a potential influence on cognitive outcomes and rate of progression.

LBA-20

A pilot comparison study comparing bilateral STN DBS using the ANS Libra DBS System with 8 channel lead vs. the ANS Libra DBS System with 4 channel leads in PD

Elena Moro,^{1,2} Christos Sidiropoulos,^{2,3} Yu-Yan Poon², Mateusz Zurowski,⁴ Melanie Cohn,⁵ Sarah Duff-Canning,⁵ Julie So,² Susan H Fox,² William D Hutchison,⁶ Melanie Fallis,² Mojgan Hodaie⁶

¹ Division of Neurology, Grenoble University Hospital, Grenoble, France

² Movement Disorders Center, TWH, University Health Network, University of Toronto, Toronto, Canada

³ Parkinson's Disease and Movement Disorders Program, Henry Ford Hospital, West Bloomfield, Michigan, USA

⁴ Department of Psychiatry, TWH, University Health Network, University of Toronto, Canada

⁵ Neuropsychology Center, TWH, University of Toronto, Toronto, Canada

⁶ Division of Neurosurgery, TWH, University Health Network, University of Toronto, Toronto, Canada

Background: Bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) is an effective surgical treatment for Parkinson's disease (PD). It induces motor and non-motor effects that largely depend on the current spreading inside and outside the STN. Increased specificity of stimulation may achieve better motor results while minimizing possible side effects.

Objective: To compare safety and effects of bilateral STN DBS using the ANS Libra DBS System with 4-channel lead and 8-channel lead for reducing some of the symptoms of advanced LD-responsive PD.

Methods: This was a prospective, single center, randomized 2 arms (1:1 ratio; 4 channel lead vs. 8 channel lead), 6-month postoperative study. UPDRS (motor UPDRS from a blinded rater), neuropsychological and psychiatric scales, quality of life, clinical diaries, surgical complications and side effects, LEDD, parameters of stimulation, time for programming and number of visits were recorded before and at 2, 4 and 6 months after surgery.

Results: Ten PD patients (9 M, 1 F) were enrolled. Age and PD duration at surgery were 60 ± 6.1 and 13 ± 3.8 years, respectively. Five patients had bilateral 4-channel lead and 5 patients bilateral 8-channel lead implants. At the 6-month end point, the motor improvement was significant in both groups (from 35.1 ± 11.8 to 20 ± 6.6 , and from 27.3 ± 12 to 14.6 ± 5.4), without intergroup difference. No significant differences were found between groups in the other clinical outcomes. Surgical complications were more frequent in the 8-channel lead group (2 small hemorrhages without neurological sequelae and one extension fracture).

Conclusions: No clear clinical advantages were found by using a 8-channel lead vs. a 4-channel lead by targeting the STN in PD patients.

LBA-21

Nocturnal manifestations in Parkinson's disease: Prevalence, manifestations, the relationship to daytime symptoms and their impact on caregivers. The evidence from NIGHT-PD study (NCT01662427)

Roongroj Bhidayasiri, MD, FRCP¹, Pawut Mekawichai, MD², Lalita Kaewwilai, RN¹, Onanong Jitkriksadakul, MD¹, Sitthi Petchrutchatachart, MD¹, Pattamon Panyakew, MD¹, Priya Jagota, MD¹, Suwanna Setthawatcharawanich, MD³.

¹Chulalongkorn Center of Excellence on Parkinson's Disease & Related Disorders, Chulalongkorn University, Bangkok; ²Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, ³Songklanagarind Hospital, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand.

Objective: To determine the prevalence, manifestations of nocturnal problems in PD and the relationship to daytime symptoms and their impact on caregivers.

Background: Many PD patients are distressed during the night but nocturnal symptoms in PD are often overlooked. In addition to sleep-related problems, PD patients may experience a range of motoric and psychiatric symptoms during the night which may have profound effect on caregivers.

Methods: Employing a multidisciplinary approach, a set of questionnaires including Modified PD Sleep Scale (MPDSS), Nocturnal Akinesia Dystonia and Cramp Score (NADCS), PD Questionnaire (PDQ-8), Non Motor Questionnaire (NMSQuest), and Wearing Off Questionnaire (WOQ-9) were administered to 280 PD patients at various H&Y stages (2.19 ± 0.82) from three main medical centers in Thailand. The Zarit burden interview and Hospital Anxiety and Depression Scale (HADS) were completed by 94 caregivers. Descriptive statistics were used and the correlation analyses of these scales on H&Y, and disease duration were performed with the Spearman's rank test. The statistical significant was set at α 0.05.

Results: 74.3% of PD patients (46.7% in H&Y 2) reported at least one nocturnal motor symptom with nocturnal cramp (45.3%) being the most frequent manifestation, followed by nocturnal akinesia (44.9%). In patients who rated their symptom in $MPDSS < 6$, the most frequent problem was nocturia (55.2%), followed by snoring or breathing problem (42.1%), tiredness after waking up (41.2%), and difficulty staying asleep (41%) respectively. NMS were reported in 38.5% of patients with nocturia being the most common symptom (78%), followed by constipation (67.3%). There was a correlation between the severity of nocturnal akinesia and higher H&Y ($0.42, p < 0.001$) as well as longer disease duration ($0.34, p < 0.001$). A correlation was observed between nocturnal parameters and WOQ-9 (both motor and NMS) as well as NMS from NMSQuest (Table 1).

	Motor – WOQ9	NMS – WOQ9	NMS (NMSQuest)
Nocturnal akinesia	.40***	.40***	.36***
Nocturnal dystonia	.33***	.24***	.13*
Nocturnal cramp	.20**	.06	.01
MPDSS total	-.33***	-.34***	-.60***

Similar correlation was also demonstrated between nocturnal parameters and Zarit scale (Table 2).

	PDQ-8	Zarit
Nocturnal akinesia	.48***	.38***
Nocturnal dystonia	.18**	.18
Nocturnal cramp	.15*	.10
MPDSS total	-.51***	-.30

Conclusions: Over 70% of our PD patients experienced at least one nocturnal motor symptom with almost 50% of early PD patients reported similar problem. The presence of daytime wearing-off (both motor and non-motor) and daytime NMS may indicate similar symptoms at nighttime. Nocturnal symptoms among PD patients increase caregiver burden.

LBA-22

The PROSPERA study: A randomized, placebo-controlled, single center trial to evaluate the safety and efficacy of rasagiline in progressive supranuclear palsy

Georg Nübling¹, Sabine Paul¹, Mira Hensler¹, Carina Abright², Alexander Crispin³, Stefan Lorenzl¹.

¹Department of Neurology, University of Munich, LMU; ²Neurological Hospital Bad Aibling; ³Department of Biomathematics, University of Munich, LMU

Objective: To evaluate safety and efficacy of rasagiline treatment in progressive supranuclear palsy (PSP).

Background: PSP is a progressive tauopathy comprising clinical features of Parkinsonian disorders. To date, no pharmacological treatment has demonstrated a significant long term effect on symptom control or disease progression of PSP.

Methods: From 1/2010 to 7/2012, 44 of the 129 screened patients with PSP were included in the PROSPERA trial and treated with either 1mg/d rasagiline (n = 22) or placebo (n = 22) for one year. Study visits took place every three months, and additional telephone visits were included between study visits. The combined primary endpoint consisted of disease progression as determined by the integral of PSP rating scale (PSPRS) scores over time and differences in the requirement of rescue medication (L-dopa). For safety analysis, severe adverse events, blood samples and ECG recordings were documented at every visit. Secondary endpoints included number of falls, postural stability as measured by posturography, and development of depression and dementia.

Results: The PROSPERA study failed to achieve the aimed-at number of 120 participants mostly due to an abundant use of the study drug by patients. Testing the 44 patients for the combined endpoint yielded a non-significant result (p = 0.61). The mean PSPRS increase over 1 year was 12.1 (95% CI: 9.2 to 14.9) in the rasagiline group and 10.6 (95% CI: 7.2 to 14.0) in the placebo group. The relative risk of a levodopa dose increase in rasagiline vs. placebo patients was 1.13 (95% CI: 0.79 to 1.63). Safety analysis and analyses of secondary endpoints were not available at the time of abstract submission.

Conclusion: The analysis of the primary endpoints of the trial on the limited number of patients recruited failed to provide evidence for an impact of rasagiline on PSP progression.

LBA-23

A pilot feasibility study of telemedicine in Huntington's disease

Authors: Michael Bull, BS, BA; Kristin Darwin, BS; Vinayak Venkataraman, BS; Joseph Wagner; E. Ray Dorsey, MD, MBA; Kevin M. Biglan, MD, MPH

Objective: To evaluate the feasibility and reliability of performing Huntington disease (HD) clinical assessments remotely using telemedicine via web-based video conferencing.

Background: Access to care for individuals with neurodegenerative conditions can be limited by distance, disability, and number of doctors available. Using technology to provide access to specialty involvement could be important for clinical care and clinical research.

Methods: Individuals with mild to moderate HD were recruited locally and at the Huntington Disease Society of America annual meeting. Participants underwent in-person assessments, including the motor portion of the Unified Huntington's Disease Rating Scale (UHDRS) (all done by one investigator, KMB)

and a survey of current care for HD. Participants were then randomized to have remote assessments conducted via web-based video conferencing by one of two investigators (KMB or ERD) three times over the ensuing four months. A modified motor portion of the UHDRS (mUHDRS) lacking rigidity and pull tests was conducted during the telemedicine visits, resulting in a modified Total Motor Score (mTMS).

Results: Thirteen individuals from ten states enrolled in the study. Participants' mean age at baseline was 56 years, 92% were Caucasian and 54% were female. A total of 33 visits were completed via telemedicine. 6 visits were not completed as 2 participants were lost to follow up prior to conducting any telemedicine visits. Of those with at least one telemedicine visit, 81.8% of the telemedicine visits were completed as scheduled (n=33). Moreover, 87.9% of mUHDRS were scored completely and 98.6% of all motor items (n=957) were scored over those visits. The mTMS in-person compared with the mTMS conducted via telemedicine demonstrated good reliability (ICC of 0.79; n=11). The test-retest reliability of mTMS conducted via telemedicine was excellent (ICC of 0.90; n=11). Participants reported traveling, on average, a total of 227 miles (SD=299) for 237 minutes (SD=277) in order to receive their usual care for HD. Average total time spent on telemedicine visits, including set up and time with the physician was 37 minutes (SD=25).

Conclusion: This study demonstrates that telemedicine is a feasible and reliable means of evaluating individuals with HD. Telemedicine may allow for a reduction in time and costs associated with traditional in-person care and could help improve access to care and facilitate participation in clinical research.

This research was funded by a research grant from Lundbeck Inc., Deerfield, IL

LBA-24

Cognition in early Parkinson's disease and the effect of laterality of Motor Symptoms

Ravi Yadav¹, Sikandar Adwani¹, S R Chandra¹, Keshav Kumar J², Pramod Kumar Pal¹

¹Department of Neurology and ²Clinical Psychology,

National Institute of Mental Health and Neurosciences, Bangalore, India. 560029

Background: Cognitive dysfunction in Parkinson's disease (PD) is seen in executive, memory and visuospatial domains. Studies show that right side onset (RPD) patients perform poorly on verbally mediated tasks, whereas left onset (LPD) patients perform worse on visuospatial tasks. Few studies have addressed this issue in patients with early PD.

Objective: The present study was conducted to know the cognitive profile of patients with early PD and to assess the effect of laterality of motor symptoms on cognition.

Methods: It was a prospective case control study conducted at department of Neurology and Clinical psychology of National Institute of Mental Health and Neurosciences (NIMHANS) a tertiary care centre situated in Bangalore, India from October 2011 to December 2012. The patients with PD were diagnosed as per United Kingdom PD Society Brain Bank Diagnostic Criteria (UKPDS). Those with a disease duration of < 5 years or Hoehn and Yahr stage of <2, with no past history of cognitive decline, Mini mental status score of > 24, age < 65 years and a formal education of > 7 years were included. The patients were evaluated using various standard scales (Unified PD rating scale, Hamilton depression and anxiety rating scale, Modified Edinburgh handedness inventory) and a comprehensive neuropsychological battery devised at NIMHANS was used.

Results: A total of 50 patients (25 RPD; 25 LPD) and 50 age, gender and education matched controls were enrolled in the study. The mean age of patients was 50.4 ± 8.2 years, (range: 35-65:males (M):females(F)- 37:13). The mean age, age of onset, years of education and duration of PD in patients with RPD was 52.24±7.96 years; 49.72±8.4 years; 12.32±2.9 years; 2.31±1.28 years and in LPD was 48.44±8.07 years; 46.04±8.22 years; 12.52±3.22 years and 2.58±1.48 years. The patients performed poorly on the memory task, executive functions, attention and psychomotor speed as compared to

controls ($p < 0.05$). No difference in the neuropsychological scores was seen between RPD and LPD versus controls and also between RPD and LPD groups ($p > 0.05$).

Conclusions: Memory, executive functions and attention impairment is common in the early stage of PD. Side of onset of symptoms do not influence cognition in early PD.

LBA-25

Quantitative assessment of non-motor fluctuations in advanced Parkinson's disease using the modified NMSS

Alexander Storch, M.D.^{1,2,*}, Per Odin, M.D., Ph.D.^{3,4}, Gerd Fuchs, M.D.⁵, Wolfgang H. Jost, M.D.⁶, K. Ray Chaudhuri, D.Sc., M.D.⁷, Heinz Reichmann, M.D., Ph.D.⁸, Georg Ebersbach, M.D.⁹, for the NoMoFlu-PD study group

Objective: To validate the modified Non-Motor Symptoms Scale (NMSS) for the comprehensive assessment of NMS fluctuations in advanced Parkinson's disease (PD) patients.

Background: NMS fluctuations have a great impact on patients with PD, but their patterns are heterogeneous and complex, and they do not correlate with demographic parameters or motor function. Although a quantitative assessment tool is thus of great importance for the management of advanced PD, a validated score for NMS fluctuations is not available. The NMSS is an instrument specifically designed for the comprehensive assessment of NMS but without addressing NMS fluctuations.

Methods: Multicenter cross-sectional study using the modified NMSS assessing NMS in motor On (NMSS_{On}) and Off state (NMSS_{Off}) combined with clinical NMS scoring (visual analogue scale, VAS) and motor investigations in advanced PD patients. Δ NMSS_{On/Off} was defined as the differences of NMSS scores between On and Off.

Results: 100 patients with fluctuating PD, 54% men, were recruited. Mean age was 68.4 ± 9.7 years, mean disease duration was 11.3 ± 6.2 years. Total NMSS_{On} score was 41.5 ± 37.6 points, while total NMSS_{Off} score was 76.0 ± 42.0 ($p < 0.001$, Wilcoxon rang test). The scores were higher in Off compared to On state for all domains except for the domain "Perceptual problems/Hallucinations" (Wilcoxon rang test). The scale was free of floor or ceiling effects in both motor states. For domains, the Cronbach α coefficient ranged from 0.23 to 0.94 in On and 0.23 to 0.84 in Off state. In terms of validity, NMSS_{On}, NMSS_{Off} and Δ NMSS_{On/Off} showed modest correlations with indicators of motor symptom severity and with other measures of NMS (NMSQuest), depression (BDI) and health-related quality of life (PDQ-8), but not with measures of disease progression or demographics (Spearman's rank correlation test). Correlations of NMSS items/domains with independent measures of related constructs were modest.

Conclusions: The modified NMSS is an acceptable and valid assessment instrument for NMS fluctuations in advanced PD.

Complete affiliations:

¹ Division of Neurodegenerative Diseases, Department of Neurology, Dresden University of Technology, 01307 Dresden, Germany

² German Center for Neurodegenerative Diseases (DZNE) Dresden, 01307 Dresden, Germany

³ Department of Neurology, Klinikum Bremerhaven, 27574 Bremerhaven, Germany

⁴ Department of Neurology, University Hospital, SE-221 85 Lund, Sweden

⁵ Parkinson Clinic Wolfach, 77709 Wolfach, Germany

⁶ Department of Neurology, Deutsche Klinik für Diagnostik, 65191 Wiesbaden, Germany

⁷ National Parkinson Foundation Centre of Excellence, Kings College Hospital and Kings College London and Biomedical Research Centre, Kings College London.

⁸ Department of Neurology, Dresden University of Technology, 01307 Dresden, Germany

⁹ Movement Disorders Clinic, 14547 Beelitz-Heilstätten, Germany

***Corresponding Author:**

Alexander Storch, M.D.
Division of Neurodegenerative Diseases, Department of Neurology
Dresden University of Technology
Fetscherstrasse 74, 01307 Dresden, Germany
Phone: ++49-351-458-2532; Fax: ++49-351-458-4352
e-mail: alexander.storch@neuro.med.tu-dresden.de

Funding: This study was supported in part by an unrestricted research grant from Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany. The financial sponsors of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had the final responsibility for the decision to submit for publication.

LBA-26

ND0612, a novel formulation of Levodopa/Carbidopa for continuous, subcutaneous administration, achieves steady-state Levodopa plasma concentrations in Parkinson's disease patients

Authors: Y. Caraco¹, S. Oren⁴, O. Yacoby-Zeevi⁴, P. LeWitt², **N. Giladi**³

Institutions: ¹Clinical Pharmacology Unit, Hadassah University Hospital, Jerusalem, Israel; ²Neurology, Wayne State University and Henry Ford Hospital, West Bloomfield, Michigan, USA; ³Neurology, Tel Aviv Medical Center and Sackler School of Medicine, Tel-Aviv University, Tel Aviv, Israel, ⁴NeuroDerm, Ltd, Ness Ziona, Israel

Objectives: To determine in Parkinson's disease (PD) subjects the safety and pharmacokinetics of continuous 24-hr subcutaneous (SC) administration of a novel levodopa (LD)/carbidopa (CD) solution (ND0612) combined with oral LD/CD/entacapone (Stalevo 100).

Background: Achieving steady-state LD plasma concentration has been long-standing goal for improving LD therapy. Two common problems in managing advanced PD, "off" states and dyskinesias, can be linked to fluctuating plasma LD concentration. Sustained-release oral LD and inhibitors of COMT and MAO-B provide only limited benefits. An invasive approach, maintaining constant plasma LD concentration through intra-duodenal infusion, has only limited applicability. Previous ND0612 studies in healthy volunteers showed that this drug, given subcutaneously, can maintain constant plasma LD concentrations.

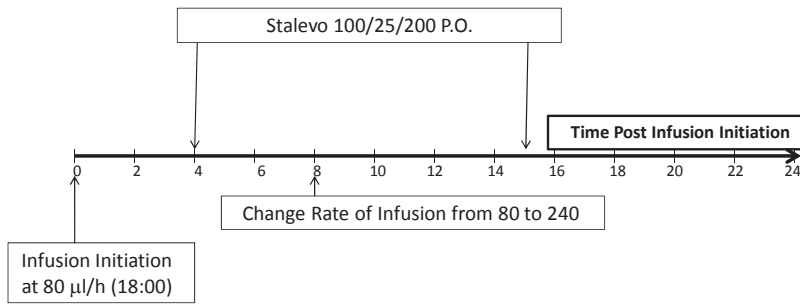
Methods: In a randomized, double blind cross-over study, using a small subcutaneous delivery pump, 8 patients with advanced PD received ND0612 (LD/CD 6%/1.5%) or its placebo during 24 hrs. Rates of administration were 80 µl/h during 8 hrs (night) and 240 µl/h during 16 hrs (day), amounting to a total of 4.5ml/24h (270/67 mg of LD/CD). Stalevo 100 was administered at bed time and again in the morning. Plasma LD, CD and 3-OMD concentrations were quantified at multiple time points. Systemic and local safety and tolerability were assessed.

Results: ND0612 showed good tolerability and safety. In some subjects, small, transient papules could be noticed at deep palpation of infusion sites (as previously noted in healthy volunteers). Plasma steady-state LD concentration following continuous subcutaneous administration of ND0612 was 700-900 ng/ml (50-100% higher than in healthy volunteers). ND0612 significantly reduced (10 to 20-fold) fluctuation in LD plasma concentration.

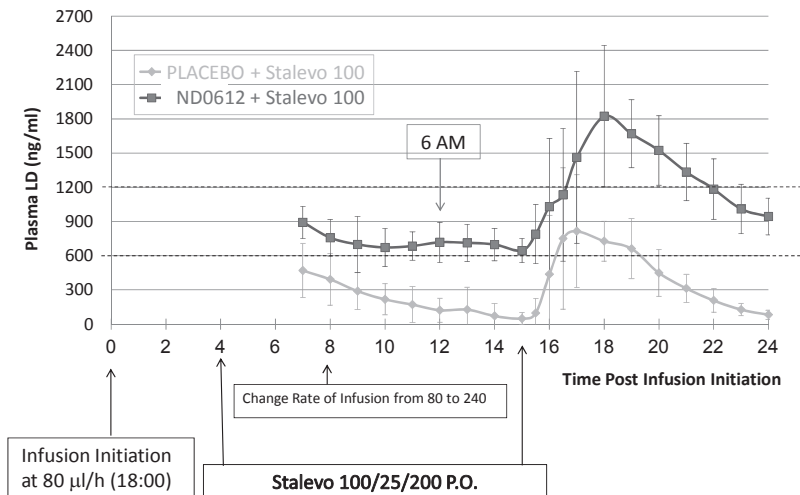
Conclusions: We describe a novel practical way for achieving steady-state therapeutic LD plasma concentration. With ND0612, LD concentration can be adjusted by controlling its infusion rate, by adding an oral COMT inhibitor, or by extra CD/LD. LD plasma concentrations for both day and night can be

programmed. These preliminary findings suggest that continuous SC administration of ND0612 may constitute a promising strategy for ameliorating motor fluctuations in PD.

Study Design Chart



The Effect of Continuous Two-rate SC Administration ND0612 with Oral Stalevo on the PK of LD of



LBA-27

Slowing of brain activity and cognitive deficits jointly predict progression to Parkinson's disease dementia

Kim T.E. Olde Dubbelink MD¹, Arjan Hillebrand PhD², Jos W.R. Twisk PhD³, Jan Berend Deijen PhD⁴, Diederick Stoffers PhD¹, Ben A. Schmand PhD⁵, Cornelis J. Stam MD PhD², Henk W. Berendse MD PhD¹.

Departments of ¹Neurology, Neuroscience Campus Amsterdam, VU University Medical Center, ²Clinical Neurophysiology and Magnetoencephalography Center, VU University Medical Center, ³Clinical

Epidemiology and Biostatistics, VU University Medical Center, ⁴Clinical Neuropsychology, VU University and ⁵Psychology, University of Amsterdam, Amsterdam, The Netherlands

Objective: To assess the ability of neurophysiological markers, in conjunction with cognitive assessment, to predict progression to dementia in Parkinson's disease (PD) patients.

Background: Cognitive testing is often used to assess cognitive decline in PD, but neurophysiological markers derived from either electroencephalography (EEG) or magnetoencephalography (MEG) are generally not included in the clinical work-up. A combination of these measures might, however, substantially improve PD-related dementia (PDD) risk profiling compared to the assessment of individual predictors.

Methods: Baseline cognitive assessments and MEG recordings from 63 prospectively included non-demented PD patients were analyzed in relation to PDD conversion over a period of 7 years. We computed Cox proportional hazard models to assess the risk of converting to dementia conveyed by cognitive and neurophysiological markers in individual as well as combined risk factor analyses.

Results: Nineteen patients (30.2%) developed dementia over the 7-year time period. Baseline cognitive impairments and neurophysiological markers each individually predicted conversion to PDD. Of the cognitive test battery, posterior (pattern recognition memory score < median; Hazard Ratio (HR) 6.80; $p = .001$) and fronto-executive (spatial span score < median; HR 4.41; $p = .006$) task performance most strongly predicted dementia conversion. Of the neurophysiological predictors, beta power < median was the strongest PDD predictor (HR 5.21; $p = .004$), followed by peak frequency < median (HR 3.97; $p = .016$) and theta power > median (HR 2.82; $p = .037$). In combination, baseline cognitive performance and neurophysiological measures had even stronger predictive value, the combination of impaired fronto-executive task performance and low beta power being associated with the highest dementia risk (2 vs 0 positive risk factors: HR 27.3; $p < .001$).

Conclusion: Combining cognitive assessment with neurophysiological biomarkers substantially improves dementia risk profiling in PD over cognitive assessment alone, providing potential benefits for clinical care as well as the future development of therapeutic strategies.

Previously presented: No.

LBA-28

Antidepressant action of the adenosine A_{2A} antagonist istradefylline (KW-6002) in rodent models of depression

K. Yamada, M. Kobayashi, A. Mori, P. Jenner and T. Kanda
(Development Research Laboratories, Kyowa Hakko Kirin Co., Ltd.)

Non-motor symptoms such as depression are common problems in Parkinson's disease (PD) patients. Almost half of PD patients are also considered to have depressive disorders, which can be less treated by pharmacotherapies. Previous findings have indicated that antidepressant-like effects are induced by pharmacological inhibition or genetic manipulation of adenosine A_{2A} receptor function in animal models of depression. Therefore, we investigated the effect of the adenosine A_{2A} antagonist istradefylline (KW-6002) on depression-like behaviors in rodent models, such as forced swimming (FS) test, tail suspension (TS) test and the learned helplessness (LH) test.

Single oral administration of istradefylline significantly decreased the FS-induced immobility time in mice (>0.16 mg/kg) with comparable efficacy to the repeated dose of the tricyclic antidepressant, desipramine. Both single (>0.63 mg/kg) and repeated (>0.16 mg/kg) administration of istradefylline also significantly decreased the FS-induced immobility time in rats and the effects of istradefylline was canceled by co-administration of corticosterone. Thus, the antidepressant-like effects of A_{2A} antagonists may be rapid

onset and, at least in part, attributed to the modulation of hypothalamic-pituitary-adrenal axis. In addition, istradefylline significantly decreased the immobility time in the mouse TS test (> 0.08 mg/kg) and co-administration of istradefylline with a SSRI, fluoxetine, was more potent than either compound alone. In the LH model of depression in rats, escape response was improved by istradefylline (1.25 mg/kg p.o.) without increased inter trial response. The anti-depressant-like effects of istradefylline were reversed by local micro-injection of A_{2A} specific agonist CGS21680 to nucleus accumbens in the brain. These results suggest that istradefylline exerts antidepressant action via the inhibition of adenosine A_{2A} receptor activity in the brain of rodents with depression-like behaviors. In conclusion, adenosine A_{2A} receptor antagonists are useful therapeutic treatment on non-motor symptom as well as motor symptom in PD.

LBA-29

Inverse correlation between radial α -Synuclein inclusion-astrocyte distance and mean astrocyte process length and thickness in multiple system atrophy

Rowan Radford¹, Mathew Wong¹, Marion Quilty², Wei Ping Gai³, Tracey Dickson², Roger Chung⁴ and Dean L Pountney¹

¹Griffith Health Institute, Griffith University, Gold Coast, Australia. ²Menzies Institute, University of Tasmania, Hobart, Australia. ³Centre for Neuroscience, Flinders University of South Australia, Adelaide, Australia. ⁴School of Advanced Medicine, Macquarie University, Sydney, Australia.

Background and Objective: Multiple system atrophy (MSA) closely resembles Parkinson's disease clinically, but with a range of autonomic signs, resulting in its designation as a Parkinson's-plus disease. However, unlike Parkinson's disease that displays primarily neuronal pathology, MSA exhibits widespread astrogliosis and the occurrence of (α -syn) glial cytoplasmic inclusions (GCIs) in mature oligodendrocytes. To investigate the relationship between α -syn inclusions and astrogliosis in MSA, we conducted quantitative morphometric analysis on MSA cases, and cell culture and animal model studies.

Methods: Using Imaris software, we obtained "skinned" three-dimensional models of GFAP-positive astrocytes in MSA tissue (n = 35) from confocal z-stacks and measured the astrocyte process length and thickness and radial distance to GCI.

Results: Astrocyte activation results in highly ramified astrocyte morphology with extended and thickened processes. Astrocytes proximal to GCI-containing oligodendrocytes ($r < 7 \mu\text{M}$) had significantly ($p, 0.05$) longer and thicker processes than distal astrocytes ($r > 20 \mu\text{M}$), with an inverse linear correlation ($m, 92 \mu\text{M}^2$) between mean process length and radial distance to the nearest GCI ($R^2, 0.71$). In primary cell culture studies, α -syn addition caused ERK-dependent activation of rat astrocytes and perinuclear α -syn inclusions in mature (MOSP-positive) rat oligodendrocytes. Moreover, unilateral injection of MSA tissue-derived α -syn into the mouse medial forebrain bundle resulted in widespread astrogliosis in the α -syn-injected, but not sham-injected hemisphere.

Conclusions: Taken together, our data suggests that localized extracellular concentration gradients of α -syn may underlie both astrocyte and oligodendrocyte MSA pathological features.

LBA-30

Bilateral subthalamic stimulation improves aspects of non-motor symptoms in Parkinson's disease

Haidar Salimi Dafsari¹, K. Ray Chaudhuri², Mark William Kellert³, Pablo Martinez-Martin⁴, Christiane Herchenbach¹, Alexandra Rizos², Prashant Reddy², Monty Silverdale⁵, Keyoumars Ashkan², Mike Samuel², Angelo Antonini⁶, Lars Timmermann¹

¹ Department of Neurology, University Hospital Cologne, Cologne, Germany.

² National Parkinson Foundation International Centre of Excellence, Kings College Hospital, London, United Kingdom.

³ Department of Neurology, Spire Manchester Hospital, Manchester, United

⁴ Alzheimer Disease Research Unit and CIBERNED, CIEN Foundation-Reina Sofia Foundation, Alzheimer Center Reina Sofia Foundation, Carlos III Institute of Health, Madrid, Spain.

⁵ Department of Salford Royal Hospital, Salford, Greater Manchester, United Kingdom

⁶ Department of Neurology, IRCCS, San Camillo, Venice, Italy.

Correspondence to:

Dr. Haidar Salimi Dafsari, Department of Neurology, University Hospital, Kerpener Str. 62, D-50937 Cologne, Germany, Tel: +49 221 478 97487; Fax: +49 221 97819,

e-mail: haidar.dafsari@uk-koeln.de

or

Prof. Lars Timmermann, Department of Neurology, University Hospital, Kerpener Str. 62, D-50937 Cologne, Germany, Tel: +49 221 47886416; Fax: +49 221 97819,

e-mail: lars.timmermann@uk-koeln.de

Objective: Our objective was to investigate the effects of continuous bilateral subthalamic deep brain stimulation (DBS) on motor and non-motor symptoms (NMS) and Quality of Life (QoL) in patients with Parkinson's disease (PD) using validated composite measures.

Background: DBS of the basal ganglia (BG) is well established for the symptomatic treatment of motor symptoms and QoL in patients with PD (Deuschl et al., 2006, Follett et al., 2010). However, effects of DBS on NMS (apart from neuropsychiatric) have not been systematically studied. Available studies have methodological limitations due to a lack of objective clinician-based assessment (Nazzaro et al., 2011) and small cohort sizes of 10 subjects (Hwynn et al., 2011, Reich et al., 2011). We hypothesised that bilateral DBS is associated with a reduction of a range of NMS in patients with PD.

Methods: Using postmarketing surveillance methodology we have analysed multicentre European data of the non-motor effects of bilateral subthalamic DBS in real life use in patients with PD as part of an ongoing 5 year natural history study of NMS (NILS). The primary outcome was the Non-motor Symptoms Scale (NMSS), collected preoperatively and 6 months follow-up. Secondary measures included Unified PD Rating Scale (UPDRS) III, PD Quality of Life Questionnaire (PDQ8), and Non-motor Symptoms Questionnaire (NMSQ).

Results: Thus far 27 consecutive patients with advanced PD (14 male, mean age: 63.00±7.21 yrs, mean duration of disease: 9.74±4.04 yrs, median Hoehn &Yahr stage: 3.) have been studied. NMSS-T (NMSS total score; p=0.038), UPDRS-III (p=0.001), PDQ8 (p=0.019) and NMSQ-T (NMSQ total score; p=0.006) improved significantly (student's paired t-test). DBS had small effect sizes on NMSS and PDQ8, a medium effect size on NMSQ and a large effect size on UPDRS-III (Sprangers et al., 2002).

	DBS		
	Relative change	Effect size	% who improved $\geq 1/2$ SD
NMSS	0,27	0,42	33,33
UPDRS-III	0,34	0,91	63,32
PDQ8	0,27	0,48	40,74
NMSQ	0,24	0,69	50,00

(Table)

Conclusions: This multicentre European study provides evidence that bilateral subthalamic DBS improves NMS in patients with PD. Our data is in accordance to previously reported effects of DBS in improving motor symptoms and QoL in PD patients. Effects of DBS on specific NMS domains such as sleep, mood and pain are now being studied.

1. Deuschl G, Schade-Brittinger C, Krack P, Volkmann J, Schafer H, Botzel K, Daniels C, Deutschlandler A, Dillmann U, Eisner W, Gruber D, Hamel W, Herzog J, Hilker R, Klebe S, Kloss M, Koy J, Krause M, Kupsch A, Lorenz D, Lorenzl S, Mehdorn HM, Moringlane JR, Oertel W, Pinsker MO, Reichmann H, Reuss A, Schneider GH, Schnitzler A, Steude U, Sturm V, Timmermann L, Tronnier V, Trottenberg T, Wojtecki L, Wolf E, Poewe W, Voges J (2006) A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med* 355:896-908.
2. Follett KA, Weaver FM, Stern M, Hur K, Harris CL, Luo P, Marks WJ, Jr., Rothlind J, Sagher O, Moy C, Pahwa R, Burchiel K, Hogarth P, Lai EC, Duda JE, Holloway K, Samii A, Horn S, Bronstein JM, Stoner G, Starr PA, Simpson R, Baltuch G, De Salles A, Huang GD, Reda DJ (2010) Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med* 362:2077-2091.
3. Hwynn N, Ul-Haq I, Malaty IA, Resnick AS, Dai Y, Foote KD, Fernandez HH, Wu SS, Oyama G, Jacobson CE, Kim SK, Okun MS (2011) Effect of Deep Brain Stimulation on Parkinson's Nonmotor Symptoms following Unilateral DBS: A Pilot Study. *Parkinsons Dis* 507416:19.
4. Nazzaro JM, Pahwa R, Lyons KE (2011) The impact of bilateral subthalamic stimulation on non-motor symptoms of Parkinson's disease. *Parkinsonism & related disorders* 17:606-609.
5. Reich MM, Ray Chaudhuri K, Ashkan K, Hulse N, Costello A, Moriarty J, Samuel M (2011) Changes in the non-motor symptom scale in Parkinson's disease after deep brain stimulation. *Basal ganglia* 1:131-133.
6. Sprangers MA, Moinpour CM, Moynihan TJ, Patrick DL, Revicki DA (2002) Assessing meaningful change in quality of life over time: a users' guide for clinicians. *Mayo Clinic proceedings Mayo Clinic* 77:561-571.

LBA-31

Glutathione S-transferase omega 2 modifies the age at onset of Spinocerebellar Ataxia type 2

Almaguer-Mederos LE, PhD¹; Aguilera-Rodríguez R, MD, MSc¹; Almaguer-Gotay D, MSc¹; González Zaldívar Y¹, BSc; Cuello-Almarales D, MSc¹; Laffita-Mesa J, BSc¹; Vázquez-Mojena Y, MSc¹; Zayas-Feria P, BSc¹; Velázquez-Pérez L, MD, PhD¹; MacLeod P, MD²

¹ Center for the Investigation of Hereditary Ataxias (CIRAH), Holguín, Cuba.

² Division of Medical Genetics, Department of Pathology, Laboratory Medicine and Medical Genetics, Victoria General Hospital, Canada.

Objective: To assess potential modifier effects of rs4925 GSTO1 and rs2297235 GSTO2 polymorphisms on age at onset and severity of disease in Spinocerebellar Ataxia type 2 affected individuals.

Background: Spinocerebellar Ataxia type 2 is an autosomal dominantly inherited neurodegenerative disorder caused by abnormal expansions of a CAG repeat sequence in the first exon of ATXN2 gene. The CAG repeat number is the major genetic factor influencing disease onset and severity, but there is still wide phenotypic variation even for individuals carrying ATXN2 alleles with the same CAG repeat number. Clinical variability can be due to GSTO2 had been associated with age at onset in both Alzheimer's (AD) and Parkinson's disease (PD).

Methods: Polymorphisms rs4925 GSTO1 and rs2297235 GSTO2 were genotyped in 124 patients with SCA2 and 100 controls by PCR/RFLP. Multiple linear regression was applied to adjust for factors and covariates.

Results: There were highly significant differences between affected and control individuals for rs2297235 GSTO2 genotypes under additive and dominant models ($p < 0.01$); there were not significant differences for rs4925 GSTO1 genotypes. Allelic frequencies were significantly different only for rs2297235 GSTO2 polymorphism ($\chi^2 = 3.98$; $p = 0.046$). In affected individuals, expanded CAG repeat number explained 37.1% of log transformed age at onset variability. rs2297235 GSTO2 genotypes, under additive and dominant models, significantly influenced on the residual age at onset after adjusting for the expanded CAG repeat number and explained a 3.0% of total variation and about 4.8% of the unexplained variation

in age at onset. Nor rs4925 GSTO1 genotypes neither GSTO1-GSTO2 haplotype combinations significantly influenced on the age at onset under additive, dominant or recessive models ($p>0.05$). SARA scores were significantly influenced by CAG repeat number and disease duration. After adjusting for these two factors by multiple linear regression, nor rs4925 GSTO1 or rs2297235 GSTO2 genotypes neither GSTO1-GSTO2 haplotype combinations significantly influenced on SARA scores ($p>0.05$).

Conclusion: rs2297235 GSTO2 polymorphism is a genetic modifier for the age at onset in Spinocerebellar Ataxia type 2 affected individuals.

LBA-32

An open label, single arm study on the effects of *H. Pylori* eradication in Parkinson's disease

Hasriza H¹, Hamizah R¹, Wan Nur Nafisah WY¹, Tan HJ,¹ Rizal AM², Lim SY,³ Norlinah MI¹

¹Neurology Unit, Department of Medicine, UKM Medical Center, Kuala Lumpur

²Department of Community Health, UKM Medical Center, Kuala Lumpur

³Neurology Division, Department of Medicine, Universiti Malaya Medical Center, Kuala Lumpur

Background: Previous studies have demonstrated a higher prevalence of *H. pylori* infection in patients with Parkinson's disease (PD) compared to controls. *H.pylori* infection affects levodopa absorption and its eradication significantly improves clinical response to levodopa. Here, we studied the prevalence of *H pylori* infection, and its eradication effects among our PD patients.

Methods: A prospective study involving idiopathic PD patients on levodopa therapy. ¹³C-urea breath test (UBT) was used to detect *H.pylori*. UBT positive patients were given standard eradication therapy, and followed up at 6 and 12 weeks. Repeat UBT was performed at 12 weeks. The UPDRS, PD NMSQ and PDQ39 were administered at baseline and post-eradication (6 and 12 weeks). Levodopa 'onset' time and ON duration were recorded.

Results: Of 82 patients recruited, 27 (32.9%) had positive UBT. *H.pylori* positive patients had significantly poorer total UPDRS ($p=0.005$) and PDQ39 ($p<0.0001$) scores compared to *H.pylori* negative patients. At 12 weeks post-eradication, there was a significant reduction in levodopa 'onset' time ($p=0.023$), and improvement in 'ON' duration ($p=0.023$). The total UPDRS scores ($p<0.0001$), scores for parts II ($p<0.0001$), III ($p=0.001$) and IV ($p<0.009$) were significantly better. The total PDQ39 scores ($p<0.0001$) and subdomains mobility ($p=0.001$), ADL ($p<0.0001$), stigma ($p=0.047$) and cognition ($p=0.01$) significantly improved. The PD NMSQ did not show significant improvement.

Conclusions: *H.pylori* eradication in PD patients significantly improves levodopa onset time, ON duration, motor and quality of life parameters. Screening and eradication of *H.pylori* should be recommended in all PD patients, particular those with erratic response to levodopa.

Keywords: Parkinson's disease (PD), *Helicobacter pylori* (*H. Pylori*), ¹³C-Urea Breath Test, Unified Parkinson's Disease Rating Scale (UPDRS), 39-Item Parkinson's Disease Questionnaire (PDQ-39).

LBA-33

Clinical spectral analysis of postmortem validated PSP

Gesine Respondek, MD^{1,2,3}, Maria Stamelou, MD¹, Sigrun Roeber, MD⁴, Hans Kretzschmar, MD⁴, Claire Troakes, PhD⁵, Safa al Sarraj, FRCPath⁵, Ellen Gelpi, MD⁶, Carles Gaig, MD⁶, Wan Zheng Chiu, MD⁷, John C. van Swieten, MD⁷, Wolfgang H. Oertel, MD¹, Leslie W. Ferguson, MD⁸, Alexander Rajput, MD⁸, Günter U. Höglinger MD^{1,2,3}

¹Department of Neurology, Philipps Universität, Marburg, Germany; ²Department of Neurology, Technische Universität München, Munich, Germany; ³German Center for Neurodegenerative Diseases (DZNE), Munich, Germany; ⁴Center for Neuropathology and Prion Research, Ludwig Maximilians University, Munich, Germany; ⁵MRC London Neurodegenerative Diseases Brain Bank, King's College, London, UK; ⁶Neurological Tissue Bank and Neurology Department, Hospital Clinic-IDIBAPS, Barcelona, Spain; ⁷Department of Neurology, Erasmus Medical Centre, Rotterdam, The Netherlands; ⁸Division of Neurology, Royal University Hospital, University of Saskatchewan, Canada.

Background: PSP typically presents with early postural instability, vertical supranuclear gaze palsy, frontal and subcortical dementia, bradykinesia and axial rigidity. Recent work has described several atypical clinical manifestations of pathologically confirmed PSP with differences in the natural disease history and in prognosis (e.g. Mahapatra et al., 2004; Neary et al., 2005; Tsuboi et al., 2005; Williams et al., 2005; Donker Kaat et al., 2007; Josephs and Duffy, 2008; Williams et al., 2007).

Objective: We aimed to quantify the distribution of and to analyse the validity of the NINDS-SPSP criteria for the different PSP-phenotypes.

Methods: Record-based analysis of clinical features of pathologically confirmed PSP cases from five brain banks with expertise in neurodegenerative disorders in Germany, the Netherlands, Spain and Canada. The presence or absence of clinical features was recorded and patients were classified into the PSP-phenotypes according to published criteria.

Results: Clinical characteristics of 100 analyzed PSP cases showed a striking heterogeneity. As many as 37% of the patients' natural history did not fit any pre-described PSP-phenotype. Additional 17% showed features fitting more than one PSP-phenotype. Significantly fewer patients with atypical PSP phenotypes were diagnosed as PSP during life and fulfilled the NINDS diagnostic criteria, when applied retrospectively.

Conclusion: Due to the striking diversity in the natural history, a systematic classification of PSP patients into pre-described phenotypes appears not to capture the entire clinical disease spectrum, mainly due to overlapping features or to absent cardinal symptoms.

LBA-34

Comparison of the effect of volitional relaxation of F wave in patients with restless legs syndrome and healthy controls

Azize Esra GÜRSOY*, Gülsen BABACAN YILDIZ*, Gülşen KOCAMAN*, Mehmet KOLUKISA*, Talip ASİL*

*Bezmialem Vakıf University, Medical Faculty, Department of Neurology, Istanbul, Turkey

Background and Objective: Reversible suppression of F waves has been reported after volitional relaxation for 1–12 hours and it has been suggested that the absence of F waves, usually taken as a sign of conduction block along the motor axons, may also result from spinal loss of excitability after volitional inactivity. Our aim in this study is to evaluate F wave persistency and amplitude changes after volitional immobilization in patients clinically diagnosed with restless legs syndrome (RLS) and to compare with healthy controls.

Materials and Methods: In all, 12 patients (10 females and 2 males) clinically diagnosed with primary RLS according to the International Restless Legs Syndrome Study Group diagnostic criteria and 5 healthy controls were evaluated. None of the patients and controls were on dopaminergic medication. The median age of the patients was 44 ± 9.8 years and of the controls was 34.75 ± 6.6 years. Nerve conduction studies (NCS) were performed with standard surface stimulation and recording techniques using an electromyograph type Keypoint- Medtronic with standard filter settings. Routine NCS included motor conduction studies for the median, ulnar, posterior tibial and common peroneal nerves and

sensory conduction studies for median, ulnar, superficial peroneal and sural nerves. F-waves were recorded from the median (abductor pollicis brevis muscle), ulnar (adductor digiti minimi muscle), peroneal (extensor digitorum brevis muscle) and posterior tibial (abductor hallucis longus muscle) nerves. The participants were asked to relax and facilitation techniques were not used. Fifty stimulations were performed in each case at stimulation frequency of 1 Hz. F-persistence was then expressed as percentage of elicited F-waves, with a minimal amplitude of 20 μ V, during this series of consecutive 50 stimuli. The peak-to-peak amplitude of F waves were calculated. F wave studies were repeated after right hand and right foot immobilization by wrapping elastic bandages for 3 hours.

Results: Motor and sensorial nerve conduction studies were in normal limits in all participants. F-wave persistence decreased from baseline value after volitional relaxation for 3 hours in healthy controls in median nerve from 94% to 77%, in ulnar nerve from 99% to 84%, and in peroneal nerve from 83% to 71%, whereas F-wave persistence remained unchanged in RLS patients (median nerve from 94% to 97%, ulnar nerve from 97% to 96%, peroneal nerve 59% to 58%). Both in healthy controls and in RLS patients the persistency of F waves in tibial nerve remained stable. We found no significant alteration in F wave amplitudes in RLS patients and in healthy controls.

Conclusions: Unchanged F wave persistency after immobilization in RLS patients may be attributed to the dysfunction of different spinal interneurons.

Corresponding Author: Azize Esra Gürsoy, MD,
Bezmialem Vakıf University, Medical Faculty, Department of Neurology, İstanbul
aesragursoy@gmail.com

LBA-35

Individuals with 22q11.2 deletion syndrome are at increased risk of early-onset Parkinson's disease: Identification of a novel genetic form of Parkinson's disease and its clinical implications

NJ Butcher, T-R Kiehl, L-N Hazrati, EWC Chow, E Rogaeva, AE Lang*, AS Bassett,
University of Toronto

* corresponding author: lang@uhnres.utoronto.ca

Objective: To evaluate a possible association between 22q11.2 deletions and Parkinson disease (PD).

Background: Clinical case reports of parkinsonism co-occurring with hemizygous 22q11.2 deletions and the associated multisystem syndrome, 22q11.2 deletion syndrome (22q11.2DS) suggest that 22q11.2 deletions may lead to increased risk of early-onset PD. The prevalence of PD and its neuropathological presentation in this common genetic condition remain unknown.

Methods: We conducted an observational study of the prevalence of PD in the world's largest cohort of well-characterized adults with 22q11.2DS. A total of 159 adults (ages 18.1 to 68.6 years; n=6 with post-mortem tissue) with a molecularly confirmed diagnosis of 22q11.2DS were included. The main outcome measure was a clinical diagnosis of PD made by a neurologist. We investigated neurodegenerative changes in post-mortem brain tissue from 3 individuals with a clinical history of PD and compared findings to those from individuals with no history of a movement disorder.

Results: We found that individuals with 22q11.2DS between the ages of 35 and 64 years had a significantly elevated prevalence of PD compared with standard population estimates (OR=69.7; 95% CI, 25.3-192.3). All cases showed early-onset and typical PD symptom pattern, treatment response, and course. All were negative for a family history of PD and known pathogenic PD-related mutations. The common use of antipsychotics to manage associated schizophrenia in 22q11.2DS delayed diagnosis of PD by up to 10 years. Post-mortem brain tissue revealed classic loss of midbrain dopaminergic neurons in all 3 cases with PD. Typical α -synuclein positive Lewy bodies were present in the expected distribution in two of these cases but absent in the third.

Conclusions: These findings suggest that 22q11.2 deletions represent a novel genetic risk factor for early-onset PD with variable neuropathological presentation reminiscent of LRRK2 associated PD neuropathology. Individuals with early-onset PD and classic features of 22q11.2DS should be considered for genetic testing, and those with a known 22q11.2 deletion monitored for the development of parkinsonian symptoms. Molecular studies of the deleted genes, including DGCR8, may help shed light on the underlying pathophysiology of PD in 22q11.2DS and idiopathic PD.

LBA-36

Assessment of mean platelet volume (MPV) in patients with neurodegenerative diseases: MPV increased in patients with Parkinson's disease

A. Koçer¹, A. Yaman³, E. Liftaniyev³, H. Duruyen³, M. Eryilmaz², E. Kocer³
1Medeniyet University; 2Duzce University; 3Bezmalem University, Istanbul, Turkey

Objective and aim: Platelets induce chronic inflammation which is a key step in atherosclerosis and may be involved in progression of neurodegenerative diseases (NDD). We aimed to measure mean platelet volume (MPV) and platelet number in NDD patients.

Method: The present study was designed to investigate platelet function by measuring MPV, and platelet count (PLC) in NDD. A total of 182 outpatients with Alzheimer's (AD) or Parkinson's diseases (PD) were included. Data were obtained by clinical interview, physical and neurological examinations in outpatient clinics specialized on neurodegenerative disorders, laboratory exams, and CT or MRI. Additionally, we also evaluated the effects of vascular risk factors on platelet functions by measuring MPV and PLC in a blood sample collected. Control group consisted of 104 subjects, who matched for age and sex without dementia, movement disorder, any other neurodegenerative diseases, stroke, and hematologic disease.

Results: Platelet count was similar between groups. But, MPV differed between groups ($p < 0.001$). MPV values of PD patients were higher than AD patients and controls ($p < 0.001$). As it was seen, the other blood parameters recorded were similar between groups. MPV correlated negatively with Heohn and Yahr scale (HYS) score ($p = 0.000$).

Conclusion: The increased MPV in patients with PD may point to a platelet dysfunction. High-grade inflammation presents with low levels of MPV as seen in PD patients with high HYS scores. The assessment of MPV in patients with PD may help identify the patients that could benefit from additional anti-inflammatory therapy.

LBA-37

A Randomized, crossover study of DM-1992, a gastroretentive formulation of Carbidopa/Levodopa in PD patients with motor fluctuations

L Verhagen Metman (Rush University Medical Center), N Stover (University of Alabama at Birmingham), C Chen, V Cowles, R Sathyanarayana and M Sweeney (Depomed Inc)

Background: DM-1992 is a carbidopa/levodopa (CD/LD) bi-layer tablet formulation containing both immediate- and extended-release layers in a polymer-based gastroretentive drug delivery system

Objective: To compare the efficacy and tolerability of DM-1992 to standard immediate-release (IR) CD/LD in advanced Parkinson's patients

Methods: This open label randomized cross-over study consisted of a single 3-day baseline period and two 10-day treatment periods separated by a one-week washout period. Inclusion criteria included daily OFF time of ≥ 2.5 hrs, H&Y stage 2-3 when ON, a LD dose of 400-1600 mg/day with frequency of ≥ 4 /day. Patients were titrated to optimal doses of DM-1992 b.i.d. or IR 3-8 times daily during Days 2-6 after which the regimens remained stable during Days 6-10. Patients recorded "OFF" time, "ON" time with no or non-troublesome dyskinesia or "ON" time with troublesome dyskinesia in diaries during baseline and during the treatments on Days 7-9. The primary outcome was the daily %"OFF" time while awake. Secondary outcomes included hrs of daily "OFF" time, "ON" time with no or non-troublesome dyskinesia or "ON" time with troublesome dyskinesia.

Results: 34 patients were enrolled and completed the study. Their mean (range) body weight was 85 (42-127) kg; age: 61 (38-82) yrs; 8.2 yrs duration of PD and LD dose of 968 mg

Efficacy: Primary outcome: the daily %"OFF" time (mean \pm SD) was 32.5 ± 10 at baseline, 27.2 ± 18.2 with DM-1992 vs 33.5 ± 12.5 with CD/LD IR ($p=0.047$)

Secondary endpoints: Daily OFF time (hrs) was 5.38 ± 1.7 at baseline, 4.53 ± 3.10 with DM-1992 and 5.53 ± 2.07 with IR ($p=0.0498$). These numbers were achieved with two doses/day of DM-1992 and on average 4.8 doses/day of IR.

Patients taking < 1000 mg/day of LD experienced the greatest benefit from DM-1992: 23.6% OFF vs 33% with CD/LD IR ($p=0.015$), with a reduction in total OFF time of 1.62 hrs ($p=0.02$). Patients were permitted to take rescue medication (CD/LD IR) on days 6-10 if they were in the "OFF" state for ≥ 2 hrs. DM-1992 patients took rescue medication 1.3 doses/day vs 0.2 for IR

Safety: Of the 34 patients, 35% experienced adverse events (AEs) while on DM-1992 and 14.7% when on CD/LD IR. One moderate AE in each treatment group, and the rest were mild. No increased dyskinesias were reported

Conclusion: Patients receiving DM-1992 twice a day experienced significantly less off time than those receiving CD/LD IR administered 3-8 times daily. DM-1992 was well tolerated

LBA-38

Long-term outcomes of unilateral MR-guided focused ultrasound (MRgFUS) thalamotomy in essential tremor (ET): 1 and 2 year follow-up

Binit B. Shah¹, Diane S. Huss², Tiffini Voss¹, Johanna Loomba², Mohamed Khaled², Eyal Zadicaro³, Robert C. Fryinger², Madaline Harrison¹, W. Jeffrey Elias²
The University of Virginia Departments of Neurology¹ and Neurosurgery²; Insightec Inc³.

Objective: To evaluate safety, feasibility, and durability of focused ultrasound thalamotomy on ET at 1 and 2 years.

Background: Surgical treatment of ET currently involves deep brain stimulation or radiofrequency lesioning of the ventralis intermedius nucleus (VIM) of the thalamus. Benefit with these has been well established, though many patients do not pursue these despite disabling tremor and tolerance can develop in those treated with DBS.

MRgFUS is a novel technology involving focusing acoustic energy to create thermal lesions. It has FDA approval for uterine fibroids but is investigational for intracranial use. It allows for staged heating of a target with frequent intra-procedural MR imaging and thermometry to titrate treatment, adjust targeting, and assess tremor response and adverse effects in real-time.

Methods: Between February and December of 2011, MRgFUS thalamotomy was performed in the dominant VIM in a pilot study of 15 subjects with ET. For all subjects, dominant hand tremor remained disabling despite medical treatment with at least two anti-tremor medications, one of which was a first line agent (primidone or propranolol).

Primary outcome measures were safety and change from baseline of the clinical rating scale for tremor (CRST) at 1 year (n=15) and 2 years (n=1; **subjects 2 and 3 data will be available by June and will be included in poster**). Secondary outcome measure were change from baseline in CRST subscores for treated upper limbs, quality of life in essential tremor (QUEST) score, and Physical Performance Test simulated eating task score at 1 and 2 years.

Results: For one year subjects, adverse effects included transient sensory, cerebellar, and speech abnormalities and persistent paresthesia in 4. The two year subject had transient paresthesia periorally and in right hand intra-procedurally that resolved by one month.

For 1 year subjects, mean CRST was reduced from 54.9 at baseline to 24.3 at 1 year, treated upper limb subscores reduced from 20.4 to 5.2, QUEST scores improved from 37% to 11%, and eating task score time reduced from 29.4s to 11.6s. The two year subject baseline CRST of 55 reduced to 15 at 1 year and 17 at 2 years. Treated upper extremity subscore was 20 and 10, QUEST was 32% and 5.3%, and simulated eating task times were 45s and 13.37s at baseline and 2 years, respectively.

Conclusion: MRgFUS is a novel modality for the delivery of thermal lesions to deep structures of the brain. It is incisionless and does not involve burr hole placement, common deterrents for patients considering DBS and RF lesioning. Additionally, real-time assessment of adverse effects and benefit prior to delivering a full lesion allows for targeting superior in precision to gamma-knife. Here we show tremor reduction at 1 and 2 years and describe adverse effects with MRG-FUS.

LBA-39

PREQUEL: A multi-center Phase II Study of Coenzyme Q₁₀ in pre-manifest Huntington's disease

Christopher A. Ross (1), Kevin M. Biglan (2), Annie Killoran (3), M. Flint Beal (4), Wayne Matson (5), Elaine Julian-Baros (2), Nadine Yoritomo (1), Shan Gao (2), and Michael P. McDermott (2), and the Huntington Study Group PREQUEL Investigators

1 Johns Hopkins University; 2 Rochester University; 3 West Virginia University; 4 Weil Cornell Medical School;
5 Bedford VA Medical Center

Background: PREQUEL is the first multi-center interventional trial in pre-manifest Huntington disease (HD).

Objective: To assess the safety and tolerability of three different dosages of coenzyme Q₁₀ (CoQ) in subjects with pre-manifest HD, and the feasibility of conducting therapeutic trials in this population.

Methods: PREQUEL is a phase II randomized, double blind, multi-center trial of 600 mg, 1200 mg and 2400 mg per day of CoQ. The 90 study participants were adults who had previously tested positive for the HD CAGn expansion (> 36 repeats) and who were deemed pre-manifest by having a diagnostic confidence score of ≤ 3 on the Unified Huntington's Disease Rating Scale (UHDRS). Tolerability was defined as the ability to complete the 20-week study on the originally randomized treatment assignment. A CoQ dosage was deemed tolerable if the observed tolerability was higher than a pre-specified threshold of 75%.

Results: The mean subject age was 39.5, with 47% male, and 85% employed. The mean total UHDRS motor score was 3.5 and the mean estimated time to HD onset (Langbehn formula) was 11.5 +/- 11.1 years. PREQUEL had 93% retention with 90%, 93% and 84% completing the trial on the originally assigned daily dosages of 600 mg, 1200 mg and 2400 mg of CoQ, respectively, all of which exceeded the pre-defined 75% tolerability threshold. Compliance rates, based on pill counts, were 97%, 95% and 96%, respectively. There were 6 premature withdrawals, all felt to be unrelated to the study drug (4 occurring in subjects on the 2400 mg/day dosage). The incidence of adverse events (45%, 50% and 63%, respectively) was not significantly different among the CoQ dosages; most were mild to moderate.

CoQ levels increased in all dosage groups, and there was no significant difference among the three groups: Mean +/- standard deviation of baseline levels were (in order of CoQ dosage) 0.77 +/- 0.30, 0.74 +/- 0.34, and 0.98 +/- 1.22 micrograms per milliliter, respectively, and 20-week levels were 2.55 +/- 1.82, 2.72 +/- 1.76, and 3.22 +/- 1.72. Recruitment at the 10 initial sites started rapidly but plateaued, and in order to fully enroll, the number of in-person visits was reduced, and three sites were added.

Conclusion: CoQ was well tolerated at dosages up to 2400 mg/day for 20 weeks in subjects with pre-manifest HD, with rates of study completion on the assigned dosage surpassing the pre-defined tolerability threshold in all treatment groups. The study shows the feasibility of conducting clinical trials in this population, but as most pre-manifest subjects are actively employed, future studies should be designed to take this into account.

LBA-40

8OHdG levels in response to Coenzyme Q₁₀ in the PREQUEL study of pre-manifest Huntington's disease

Kevin M. Biglan (1), Christopher A. Ross (2), Annie Killoran (3), M. Flint Beal (4), Wayne Matson (5), Elaine Julian-Baros (1), Nadine Yoritomo (2), Shan Gao (1), and Michael P. McDermott (1), and the Huntington Study Group PREQUEL Investigators

1 University of Rochester; 2 Johns Hopkins University; 3 West Virginia University; 4 Weil Cornell Medical School; 5 Bedford VA Medical Center

Background: PREQUEL is the first multi-center interventional trial in pre-manifest Huntington disease (HD). It is a safety and tolerability study evaluating the anti-oxidant coenzyme Q₁₀ (CoQ). Serum 8-OHdG, a potential biomarker of oxidative stress that is reportedly increased in pre-manifest HD was also measured in study participants.

Objective: To compare mean serum levels of 8-OHdG in response to treatment with three different dosages of CoQ and to examine the association between 8-OHdG level and projected age of disease onset in subjects with pre-manifest HD.

Methods: PREQUEL is a phase II, 20-week, randomized, double blind, multi-center trial of 600 mg, 1200 mg and 2400 mg per day of CoQ. The 90 study participants were adults who had previously tested positive for the HD CAGn expansion (> 36 repeats) and who were deemed pre-manifest by having a diagnostic confidence score of ≤ 3 on the Unified Huntington's Disease Rating Scale (UHDRS). Subjects' serum levels of CoQ and 8-OHdG were measured at baseline and 20 weeks. An analysis was performed on these measurements in relation to CoQ dosage and predicted age of onset from CAGn repeat length (Langbehn formula).

Results: There was a significant increase in serum CoQ levels in all three treatment groups at 20 weeks. Levels (mean +/- standard deviation in mcg/ml) of 8OHdG were (in order of CoQ dosage) 11.75 +/- 3.99, 12.61 +/- 5.35, and 13.62 +/- 5.35 at baseline; and 11.94 +/- 5.51, 11.49 +/- 4.63, and 13.73 +/- 7.14 at 20 weeks. There was no significant change in 8OHdG levels at 20 weeks for any dosage. There was no relationship between 8OHdG level at baseline and the predicted age of onset.

Conclusion: Treatment with 600 mg/day, 1200 mg/day, and 2400 mg/day of CoQ was associated with increases in serum levels of CoQ, but with no change in 8OHdG levels. There was no relationship between 8OHdG level and predicted age of disease onset. These data call into question the utility of serum 8OHdG level as a biomarker of HD in the pre-manifest period and as a biomarker of response to the putative antioxidant CoQ.

LBA-41

The psychological comorbidities and adverse events in pre-manifest Huntington's disease participants of the PREQUEL study

Annie Killoran, Kevin M. Biglan, Michael McDermott, Elaine Julian-Baros, Nadine Yoritomo, and Christopher A. Ross for the Huntington Study Group PREQUEL Investigators

Background: PREQUEL is a study evaluating the safety and tolerability of the anti-oxidant coenzyme Q₁₀ (CoQ). It is the first multi-center interventional trial in subjects with pre-manifest Huntington disease (HD). The psychological aspects of pre-manifest individuals participating in such a clinical trial have not been investigated.

Objective: To assess the psychological status of pre-manifest individuals during their participation in the PREQUEL study.

Methods: PREQUEL is a phase II randomized, double blind, 20-week trial of three dosages (600mg, 1200mg or 2400mg per day) of CoQ. The 90 study participants were adults who had previously tested positive for the HD CAGn expansion (> 36 repeats) and had a diagnostic confidence score of ≤ 3 on the Unified Huntington's Disease Rating Scale (UHDRS). Those with an unstable medical or psychiatric condition or recent drug or alcohol abuse were excluded. We examined UHDRS behavioral questionnaire responses and participants' self-reported medical history at baseline, and the development of psychological adverse events during the trial.

Results: PREQUEL participants had a mean age of 39.5 +/- 10.8 years; 47% were male and 23% were smokers. At baseline, psychiatric disturbances were common, including depression (36.7%), anxiety (35.6%), mood disturbances (26.7%), obsessional thinking (15.6%) and sleep disturbances (13.3%). During the course of the trial, the following psychological adverse events occurred: depression (n=3), sleep dysfunction (n=3), and anxiety (n=2). All were felt to be unrelated to the study drug.

Conclusion: The PREQUEL cohort had prominent baseline psychiatric features and psychological adverse events. Future trials in this population may need to be cautious regarding potential psychological aspects.

LBA-42

Qualitative and quantitative assessment of motor signs in Parkinson's disease by automated gait analysis

Jochen Klucken¹, Jens Barth^{1,2,3}, Björn Eskofier², Juergen Winkler¹

¹: Department of Molecular Neurology, University Hospital Erlangen

²: Pattern Recognition Lab, Friedrich-Alexander-University Erlangen-Nuremberg

³: ASTRUM IT GmbH

Objective: To develop a rater independent mobile gait analysis system using integrated inertial sensors and pattern recognition approaches that allow an objective and individualized rating of motor symptoms correlating to the UDPRS-III motor score in Parkinson's disease (PD).

Background: Objective and rater independent analysis of motor symptoms in PD is one of the most challenging tasks in medical engineering. Especially, assessment of motor symptoms defines the clinical diagnosis in PD. Main symptoms (bradykinesia, rigor, tremor, and postural instability) are clinically rated by the Unified Parkinson Disease Rating Scale (UPDRS – Part III). Objective and non-invasive strategies

are an urgent need in order to achieve a time and rater independent assessment. A sensor-based system to measure motor impairment would convincingly complement the clinical evaluation of PD.

Methods: We developed an automated biosensor based Embedded Gait Analysis using Intelligent Technology (eGalT). eGalT consist of accelerometers and gyroscopes attached to shoes recording motion signals during standardized gait examination. We evaluated objectively measured sensor signals during standardized gait tasks in a study with 92 PD patients and 81 age- and gender-matched controls. Pattern recognition approaches were developed to classify H&Y stages. Multiparametric regression analysis correlated eGalT based rating of motor symptoms to the UPDRS-III motor score.

Results: Automated classification of H&Y stages revealed a validated correct classification rate of up to 91% with increasing H&Y stages (H&YIII: 100% sensitivity,82% specificity). Furthermore, multiparametric regression analysis was able to predict UPDRS-III values by eGalT with a Paerson's correlation coefficient 0.61 and a mean absolute error of 6.8 points.

Conclusion: The present mobile and objective biosensor based gait analysis system recognizes PD associated gait symptoms and allows both an objective and individualized prediction of the present UPDRS (Part III) score. Thus, it allows a rater independent and objective rating of motor deficits and efficacy of therapeutic interventions, thereby offering a valuable tool for therapeutic decisions. Finally, this approach reduces inter-rater variability in assessing motor deficits in clinical studies.

LBA-43

Movement disorders and development of the Dopamine Neuron

Masaya Segawa, M.D.
Segawa Neurological Clinic for Children
Tokyo, Japan

Objective: In Movement Disorders a certain lesion in the nigrostriatal (NS) dopamine (DA) neuron or the basal ganglia develop particular symptoms through the adjacent nervous structures functioning normally. In developmental brain particular symptoms appear after maturation of these structures. Thus we evaluate the dopamine deficiency disorders based on the developmental of the NS-DA neuron Basal ganglia.

As for the NS-DA neuron, tyrosine hydroxylase (TH) of the terminal in the striatum shows high activities in early childhood which decreases exponentially with age and attains basement levels in late teens. While TH in the substantia nigra (SN) begins to increase the activities linearly from late childhood and exceed the levels of the terminal TH in late twenties.

Methods: Clinical features and neuropathological findings of Segawa disease (SD) and juvenile parkinsonism (JP) (PARK II) were evaluated. Those of two cases with Rett syndrome (RT) were evaluated as a disorder with DA deficiency in the substantia nigra (SN) occurring in early childhood.

Results: Clinical course of SD is well explained by reduction of the terminal TH and an autopsied case confirmed reduction of the terminal TH with preservation of TH in the SN. Parkinsonism observed in a late onset case showed ipsilateral involvement of the dominantly involved side of the extremities and the sternocleidomastoideus suggested involvement of the NS-DA neuron innervating to the subthalamic nucleus.

Cases with Park II developed dystonic feature in teens and parkinsonism in twenties.

One case of RTT with failure of the antigravity activity throughout the cause showed impairment of locomotion and the autopsied brain at the age of 13 years showed marked decrease of TH in the SN. While another case, trained locomotion from early childhood showed improvement of antigravity activity. This case did not show parkinsonism after 30 years. She died of accident in 33years. The autopsied brain showed normal DA activities in the SN.

Conclusion: These clinical evidences show these are at least two NS-DA neuron, one involves DA transmission with high TH in the terminal and the other with high TH in the SN. Besides there is NS-DA neuron projecting to the STN. Each neuron is considered to have different output of the basal ganglia and projects to particular nervous system. Also, each has particular roles in development of the nervous system in particular month or years of age.

LBA-44

Antidyskinetic effect of cerebellar modulation in Parkinson's disease is related to regaining motor cortical LTP-like plasticity

Asha Kishore, MD, DM¹, Traian Popa, MD, PhD², Ammu Balachandran, B.Tech¹, Febina Backer, B.Tech¹, Syambabu Chandran, MD, DM¹ and Sabine Meunier, MD, PhD². ¹Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India and ²U975, INSERM, Paris, France.

Objective: To test (1) if inhibitory cerebellar stimulation enhances the deficient plasticity of M1 associated with levodopa-induced dyskinesias (LIDs) in Parkinson's disease (PD) and, if so, (2) whether it explains the antidyskinetic effect of repeated sessions of inhibitory cerebellar stimulation.

Background: The plasticity of primary motor cortex (M1) in patients with PD and LIDs is severely impaired and L-DOPA unresponsive (Morgante et al. 2006; Kishore et al. 2012). We reported that inhibitory cerebellar stimulation with continuous theta burst stimulation (cTBS) enhances sensori-motor plasticity of M1 induced by paired associative stimulation (PAS) in healthy subjects (Popa et al. 2012). The mechanism of the antidyskinetic effect of cerebellar stimulation (Koch et al. 2009) is not fully understood.

Methods: Study 1: Sixteen PD patients with LIDs were evaluated thrice: (1) patient in OFF and PAS delivered to M1 opposite the hemibody with the worse dyskinesias (2) patient in ON and cTBS to the ipsilateral cerebellum followed by PAS to the opposite M1 (3) patient in ON and sham stimulation to the ipsilateral cerebellum and PAS to opposite M1. Responsiveness of M1 to PAS was tested before and after the stimulations. **Study 2:** Twenty PD patients with LIDs received 10 days of bilateral inhibitory stimulation of the cerebellum. Dyskinesias were scored blindly on videos before start of sessions and at the end of the 2nd, 4th and 8th week after the end of repeated sessions. Responsiveness of M1 to PAS was tested at each visit.

Results: Study 1. PAS-induced response of M1 was weak in PD patients both in OFF and ON (rANOVA $P = 0.5, 0.7$ respectively). M1 gained responsiveness to PAS ($P < 0.001$) after real but not sham cerebellar stimulation. A control study replacing PAS with iTBS of M1 did not yield a significant effect. **Study 2.** Repeated real but not sham cerebellar stimulation, led to a decrease of the total ($P < 0.04$) and worst ($P < 0.007$) dyskinesia scores at the 2nd week follow-up. This effect was over at the 4th week. The clinical improvement was paralleled by a sustained good responsiveness of M1 to PAS. The larger the additional plasticity in a single session, the greater was the decrease in the worst dyskinesia score after 10 days of stimulation ($P < 0.007, R^2 = 0.6$).

Conclusions: Cerebellar cortical inhibition permits better sensori-motor integration, most probably by increasing the gain of the sensory afferent volley to M1, thereby reducing LIDs. We propose that cerebellar sensory processing is affected in advanced PD and it might lead to inappropriate filtering of the relevant sensory volley and a maladaptive state of cortical plasticity. This could predispose to the selection of incorrect motor programs and LIDs.

Previously Presented: To be presented at the 5th International Conference on Non-Invasive Brain Stimulation, March 19 - 21, 2013 in Leipzig, Germany

MDS Study Group Abstracts

SG-1

Molecular genetics of multiple system atrophy: results from the Japan Multiple System Atrophy Research Consortium

JAMSAC (Japan Multiple System Atrophy Research Consortium), Jun Mitsui, Yaeko Ichikawa, Jun Goto, Shoji Tsuji
Department of Neurology, The University of Tokyo Hospital

Objective: To elucidate the natural history and the molecular mechanisms of multiple system atrophy (MSA).

Background: The Japan Multiple System Atrophy Research Consortium (JAMSAC) was established in 2005 to elucidate the natural history and the molecular mechanisms of MSA. Although MSA has widely been considered as a nongenetic disorder, identification of multiplex MSA families suggests involvement of genetic components.

Methods: MSA patients fulfilling the criteria of Gilman were enrolled in the study. Additional criteria based on MRI findings are adjunctively employed. We employed UMSARS, parts of ICARS, parts of UPDRS and Barthel index for evaluation of clinical features and the severity of MSA. For molecular genetic studies, two approaches were employed: 1. Enrollment of six multiplex MSA families for linkage analysis and whole-genome sequencing to identify causative genes, and 2. Exome sequencing and subsequent association studies in 437 MSA cases and 342 control subjects to investigate the association of rare coding variants with MSA.

Results: We evaluated the rating scales from 171 patients (93 men, and 78 women) whose mean age at onset was 58.5 years (range 40-79). About 70% of MSA patients were MSA-C in the Japanese population, whereas MSA-P shares only 30% of the patients. There is a significant correlation between the duration from onset and variable rating scales ($P < 0.0001$). Parametric linkage analysis revealed that there was no single locus showing linkage compatible with autosomal recessive inheritance, indicating genetic heterogeneities in multiplex MSA families. Whole-genome sequencing of the proband in one of the multiplex families generated 187.5 Gb of short reads and 3,492,429 variants. In the exome-association studies, we identified 139,224 functional SNVs (nonsense, missense, or splice-site variants) with allele frequencies less than 5% in the controls. These variants are used for genome-wide association studies to identify disease-relevant functional SNVs.

Conclusions: MSA-C is more frequent in the Japanese population compared with those in European or North American populations. Identifications of causative genes involved in multiplex families and of susceptibility genes based on exome-association studies are expected to provide new insights into the molecular basis of MSA. To boost genetic research in MSA, further global collaborations with other MSA study groups are needed.

SG-2

The *Movement Disorder Society* Study Group on Multiple System Atrophy: Mission and goals

Gregor K. Wenning¹, Florian Krismer¹, Werner Poewe¹, on behalf of EMSA-SG; Phillip A. Low², on behalf of NAMSA-SG/ARDC; Shoji Tsuji³, on behalf of JAMSA-C

¹ ... Department of Neurology, Innsbruck Medical University, Austria

² ... Department of Neurology, Mayo Clinic, Rochester, MN, USA

³ ... Department of Neurology, Graduate School of Medicine, University of Tokyo

Objective: The overall aim of the Movement Disorder Society (MDS) Study Group on Multiple System Atrophy (MoDiMSA-SG) is to provide a framework for global collaborative research on multiple system atrophy (MSA).

Background: In the last decades, clinical and preclinical MSA research has frequently been limited to single sites reflecting a lack of collaboration at an international level.

Methods: We will provide an administrative framework for global collaborative MSA research assigning short-term goals to focused working groups. The coordination of the study group will involve regular telephone conferences as well as study group meetings during the annual MDS congress. In addition, we will actively recruit leading academic centres into the network.

Results: We plan to develop a minimal data set, including disease-specific validated rating scales for harmonized data acquisition. Second, we intend to launch a global MSA patient registry. Third, we will provide standard operating procedures for the storage of biomaterial enabling us to subsequently launch studies with a focus on the discovery of diagnostic and surrogate (bio)markers, as well as determination of environmental and genetic underpinnings. Finally, we will develop consensus (best-practice) guidelines for diagnosis and management in MSA (based on the principles of evidence-based medicine). To this end, working groups have been initiated.

Conclusions: MoDiMSA-SG brings the leading MSA research centres together and, for the first time, provides a global platform for collaborative MSA research.

SG-3

Dynamics of red flags in multiple system atrophy: An analysis of the EMSA-SG natural history study cohort

Florian Krismer¹, Susanne Duerr¹, Klaus Seppi¹, Sylvia Boesch¹, Werner Poewe¹, Gregor K Wenning¹ and on behalf of EMSA-SG. ¹Department of Neurology, Innsbruck Medical University, Innsbruck, Austria, 6020.

Objective: To prospectively study the presence and dynamics of clinical red flags in patients with MSA.

Background: MSA is an adult-onset atypical parkinsonian disorder characterized by early autonomic failure associated with either levodopa-refractory parkinsonism (MSA-P) or cerebellar ataxia (MSA-C). Certain clinical features such as early instability, rapid progression, Pisa syndrome, disproportionate antecollis, contractures of hands or feet, diurnal or nocturnal inspiratory stridor, inspiratory sighs, severe dysphonia or dysarthria, severe dysphagia, and emotional incontinence have been proposed as clinical pointers or red flags suggesting a diagnosis of MSA in subjects with parkinsonism. Finally, MSA red flags may be assigned to six categories (early instability, rapid progression, abnormal postures, bulbar dysfunction, respiratory dysfunction, emotional incontinence).

Methods: 141 patients with a clinical diagnosis of MSA were recruited in a natural history study conducted by EMSA-SG. Patients were followed up for two years with a complete neurological examination every six months. During follow-up, an extensive MSA red flags checklist was completed by the treating investigator.

Results: At baseline, all patients had bulbar symptoms. Early instability was present in 70.2%, a rapid progression was observed in 60.7%, abnormal postures occurred in 42.4%, respiratory dysfunction was noted in 45.0% and 26.9% experienced emotional incontinence. All of these red flags categories became more common during follow-up. The presence of abnormal postures (including the Pisa syndrome, disproportionate antecollis and contractures of hand or feet) separated MSA-P from MSA-C patients with a positive predictive value of 81.1%. Conversely, severe dysarthria was more common in MSA-C ($p = 0.006$). Out of 14 patients who converted from possible to probable MSA during follow-up, 71.4% could

have been diagnosed at baseline already utilizing possible Gilman criteria plus the presence of at least two categories of red flags.

Conclusions: MSA red flags were frequently present at baseline visit and steadily increased during follow-up. The utilization of MSA red flags may be useful to support an early diagnosis of probable MSA.

SG-4

Progression of autonomic failure in multiple system atrophy: An analysis of the EMSA-SG Natural history study cohort

Florian Krismer¹, Susanne Duerr¹, Klaus Seppi¹, Sylvia Boesch¹, Werner Poewe¹, Gregor K Wenning¹ and on behalf of EMSA-SG. ¹Department of Neurology, Innsbruck Medical University, Innsbruck, Austria.

Objective: To prospectively study the progression of autonomic failure in patients with multiple system atrophy (MSA).

Background: MSA is a fatal neurodegenerative disorder that is characterised clinically by marked autonomic failure, parkinsonism and cerebellar ataxia in various combinations. Previous studies indicated rapid progressive autonomic failure affecting primarily orthostatic and urogenital domains.

Methods: 141 consecutive patients with a clinical diagnosis of MSA were recruited in a natural history study conducted by the European MSA study group (EMSA-SG). The consensus diagnostic criteria were applied retrospectively. The follow-up period was two years with a comprehensive neurological examination every six months. Autonomic failure was assessed by the Composite Autonomic Symptom Scale (COMPASS), the COMPASS Change Scale (COMPASS-CSS) and the autonomic subscore of the Unified MSA Rating Scale (UMSARS).

Results: At baseline - on average 5.5 years after symptom-onset – measurement of self-perceived impairment using COMPASS indicated the presence of severe autonomic failure. During follow-up autonomic failure steadily progressed, particularly in the urogenital domain as reflected by increasing COMPASS-CSS and UMSARS autonomic subscores. In addition, COMPASS-CSS OH subscore indicated that MSA patients also perceived a deterioration of OH symptoms during their disease course.

Conclusions: Severe autonomic failure was evident at baseline already and steadily worsened during follow-up, particularly in OH and urogenital domains. These observations are in line with previous studies showing a marked autonomic involvement in MSA patients. Rigorous symptomatic treatment of autonomic symptoms is required to alleviate MSA-associated disease burden.

SG-5

Randomized treatment trial of Rifampicin in MSA patients

P Low¹, D Robertson², S Gilman³, H Kaufmann⁴, W Singer¹, I Biaggioni², R Freeman⁵, S Perlman⁶, R Hauser⁷, W Cheshire⁸, S Lessig⁹, S Vernino¹⁰, J Mandrekar¹, W Dupont², T Chelimsky¹¹ and W Galpern¹². ¹Mayo Clinic, Rochester, MN, United States; ²Vanderbilt, Nashville, TN, United States; ³U of M, Ann Arbor, MI, United States; ⁴NYU, New York, NY, United States; ⁵Beth Israel, Boston, MA, United States; ⁶UCLA, Los Angeles, CA, United States; ⁷USF, Tampa, FL, United States; ⁸Mayo Clinic, Jacksonville, FL, United States; ⁹UCSD, La Jolla, CA, United States; ¹⁰UTSW, Dallas, TX, United States; ¹¹MCW, Milwaukee, WI, United States and ¹²NIH, Bethesda, MD, United States.

Objective: To determine the efficacy of Rifampicin on multiple system atrophy (MSA) in a Phase III study.

Background: MSA is a rapidly progressive disorder characterized by autonomic failure with parkinsonism and/or cerebellar ataxia. Its hallmark is glial cytoplasmic inclusions consisting of aggregated α -synuclein. In a transgenic mouse model of MSA, Rifampicin inhibits formation and disaggregates α -synuclein fibrils and improves both behavioral and neuropathological changes.

Methods: We undertook a randomized, double-blind, placebo-controlled 12-month clinical safety/efficacy study of 100 patients with possible or probable MSA, 50% consigned to active drug (Rifampicin 300 mg BID), 50% to placebo (Riboflavin capsules BID). Subjects recruited from 10 US sites. Inclusion criteria include subjects of either gender; ages 30 to 80 years; <4 years from diagnosis; expected survival \geq 3 years; MMSE $>$ 24. Primary outcome measure was rate of change from baseline to 12 months in total UMSARS I score (minus Q11). Interim analysis was planned after 30 subjects had completed 12 months of study.

Results: 100 subjects were randomized: 43% women and 57% men, mean age 61.7 ± 9.2 (mean \pm std dev), age range 41.7 to 79.9 years, 48% possible MSA, 52% probable MSA. There were 3 serious adverse events, 2 on placebo and one on Rifampicin, none considered likely due to treatment. 9 subjects withdrew from study. Interim analysis of primary endpoint, the rate of change (slope) of UMSARS I, was 0.47 ± 0.48 in placebo (N=15) and 0.62 ± 0.85 in Rifampicin (N=15), $P=0.76$. This analysis was performed in all patients who had completed the protocol. The analysis of all evaluable subjects found a slope of 0.54 ± 0.59 in placebo (N=50) vs. 0.53 ± 0.72 (N=48) in Rifampicin, $P=0.69$. The DSMB recommended the study stop as futility criteria were met.

Conclusions: Rifampicin was well-tolerated. The study fulfilled statistical criteria for futility and is undergoing closure.

SG-6

Multiple system atrophy: Prognostic indicators of survival

Juan J Figueroa, Wolfgang Singer, Ajay K Parsaik, Eduardo E Benarroch, J Eric Ahlskog, Paola Sandroni, Jay Mandrekar, Phillip A Low and James H Bower. ¹Neurology, Mayo Clinic, Rochester, MN, United States.

Objective: To determine the early clinical features that predict survival in multiple system atrophy (MSA) based on autopsy cases.

Background: Although autonomic failure is a frequent early clinical feature of MSA its prognostic role is not fully established.

Methods: Retrospective survival analysis in 49 MSA cases (median age at onset, 56.1 years; 16 women) confirmed by autopsy at Mayo Clinic. Clinical records were reviewed for age at onset, sex, clinical phenotype, and early development of motor disability, autonomic symptoms and severe dysautonomia. When available, the 10-point composite autonomic severity score (CASS) derived from the autonomic reflex screen provided laboratory quantification of generalized autonomic failure and the thermoregulatory sweat test (TST) quantitated body surface anhidrosis.

Results: Phenotype was MSA-P in 65% and MSA-C in 35%. Onset was autonomic in 50%, parkinsonian in 30% and cerebellar in 20% with a median survival time of 8.6 (95% CI, 6.7-10.2) years. On Kaplan-Meier analysis, survival time was shorter in patients with early laboratory evidence of generalized (CASS \geq 6) autonomic failure (7.0 [95% CI, 3.9-9.8] vs. 9.8 [95% CI, 4.6-13.8] years; $P=0.036$) and early requirement of bladder catheterization (7.3 [95% CI, 3.1-10.2] vs. 13.7 [95% CI, 8.5-14.9] years; $P=0.003$) compared to those without these clinical features. On Cox proportional analysis, prognostic indicators of shorter survival were older age at onset (HR, 1.04, 95% CI, 1.01-1.08; $P=0.03$), age-adjusted early requirement of bladder catheterization (HR, 7.9; 95% CI, 1.88-38.63, $P=0.004$) and age-adjusted early generalized (CASS \geq 6) autonomic failure (HR, 2.8; 95% CI, 1.01-9.26; $P=0.047$). Gender, phenotype, and

early development of gait instability, aid-requiring ambulation, orthostatism, neurogenic bladder or significant anhidrosis (TST \geq 40%) were not indicators of shorter survival.

Conclusions: Our data suggests that early development of severe autonomic failure more than triples the risk of shorter survival in patients with MSA after adjusting for age.

Previously Presented: 23rd International Symposium on the Autonomic Nervous System, Oct-Nov 2012, Paradise Island-Bahamas

SG-7

The setting up of a multi-specialty international Parkinson's Non-Motor Research Group: The MDS Non Motor Study Group

K Ray Chaudhuri¹, P Martinez-Martin²

1. *National Parkinson Foundation Centre of Excellence, Dept of Neurology, King's College Hospital, and Kings Health Partners, Kings College, London, UK*
2. *Research Unit and CIBERNED, Alzheimer Center Reina Sofia Foundation , ISCIII, Madrid, Spain*

Background: Till 2004 there were:

1. no specific validated instruments either self- or health care professionals (HCP) completed for Parkinson's disease (PD)
2. no validated global measure for non motor symptoms (NMS) burden in clinical trials. These issues have become increasingly relevant because it is now established that:
 - a. PD is as much a non motor disorder as a motor disorder
 - b. Non-dopaminergic systems are involved probably before motor symptoms emerge
 - c. NMS are the key determinant of quality of life¹

Objectives: The PDNMG was formed from a multi-speciality group of international experts:

1. To develop and validate specific comprehensive (not piecemeal) tools for non motor assessment in clinic/ clinical trials
2. To use these instruments and address impact on quality of life in PD
3. Setting up and performing clinical studies of characterization of non motor endophenotypes
4. Develop research towards animal models of NMS of Parkinson's

Methods: PDNMG was set up by KRC in 2004 with an international multispecialty group led by KRC and Pablo Martinez-Martin, supported and endorsed by Parkinson's UK and adopted by MDS as a formal study group in 2013.

Results: Publication of NMSQuestionnaire (NMSQuest, 2006) and NMS scale (NMSS, 2007), the first validated tools for NMS self declaration and HCP completed tool. Now in worldwide use and recommended via MDS, NINDS, Parkinson's UK.

1. Use of NMSS in international clinical trials as non motor outcomes (e.g. RECOVER, CONFIDENT, PANDA)
2. Global validation of NMSS (Europe, USA, Asia, South Africa, Japan)
3. Key NMS prevalence studies (Martinez-Martin et al, 2007)
4. Recent publication of NMSB staging addressing endophenotypes²
5. Over 20 peer reviewed publications to date

Conclusion: The PDNMG has been highly successful in signposting the importance of NMS in PD at a time where focus was entirely on motor symptoms and NMS only existed in isolated symptoms category such as cognitive problems and depression. The adoption of PDNMG by MDS will lead to formalization of the role of PDNMG and cutting edge clinically relevant, real life research in the area of NMS of Parkinson's.

References: Martinez-Martin P, Rodriguez-Blazquez C, Kurtis MM, Chaudhuri KR on behalf of the NMSS Validation Group. The Impact of Non Motor Symptoms on Health-Related Quality of Life of patients with Parkinson's disease. *Mov Disord* 2011;26(3):399-406.

1. Chaudhuri KR, Rojo JM, Schapira AHV, Brooks DJ, Stocchi F, Odin P, Antonini A, Brown RG, Martinez-Martin P: A proposal for a comprehensive gradation of Parkinson's disease severity combining motor and non motor assessments: meeting the unmet need. *PLOS One*. 2013; 8 (2). e57221

SG-8

A prospective observational study of dopamine agonist withdrawal syndrome in Parkinson's clinic: The EuroDaws study

A Todorova¹, M Parry¹, A Martin¹, P Odin¹, P Martinez-Martin¹, A Antonini¹, A Rizos¹, W Jost¹, R Koch¹, G Ebersbach¹, L Gallagher¹, G Macphee¹, H Reichmann¹, A Storch¹, C Schneider¹, M Wolz¹ and K Ray Chaudhuri¹. ¹Movement Disorders Society Non Motor Study Group and EUROPAR, King's College Hospital, London, United Kingdom, SE59RS.

Objective: We have started a European multicentre prospective study (EuroDaws) addressing frequency of Dopamine Agonist Withdrawal Syndrome (DAWS) in people with Parkinson's disease (PwP) as retrospective case note surveys indicate a high prevalence of 14-18%.

Background: Recently, DAWS has been reported (symptoms similar to addictive drug withdrawal) in PwP who decrease or stop their dopamine agonist (DA) treatment.

Methods: In the preliminary phase of this study, 16 patients (12 m/4 f, mean age 71.2 ± 10.8 yrs; PD duration 11.0 ± 5.3 yrs) were noted to have decreased/ stopped their dopamine agonists and the Non Motor Symptoms Questionnaire (which addresses core features of DAWS) was administered at clinical follow up at 1 month.

Results: Five out of 16 patients (31%) reported DAWS with symptoms of anxiety, sweating and depression after the withdrawal of Ropinirole, Pramipexole, and Cabergoline which were stopped owing to impulse control disorders or hallucinations.

Conclusions: In this first prospective evaluation of DAWS in the clinic, preliminary data indicates a high rate after discontinuation of a range of DAs. Continuation of EuroDaws would hopefully address the issue in a larger cohort of PwP across Europe.

SG-9

The EuroInf Study: A multi-centre European comparative study of apomorphine versus intrajejunal levodopa infusion in a real life cohort of Parkinson's patients

P Reddy¹, P Martinez-Martin¹, A Todorova¹, A Antonini¹, P Odin¹, A Martin¹, A Rizos¹, D Calandrella¹, T Henricksen¹, N Bryndum¹, A Glad¹, S Dafsari¹, L Timmermann¹, G Ebersbach¹, M Kramberger¹, A Ceballos-Baumann¹, K Wenzel¹, V Tomantschger¹, A Storch¹, H Reichmann¹, Z Pirtosek¹, M Trost¹, R Katzenschlager¹, P Svenningsson¹, S Palhagen¹, J Volkmann¹, K Ray Chaudhuri¹ and Movement Disorders Society Non Motor Study Group. ¹Movement Disorders Society Non Motor Study Group and EUROPAR, King's College Hospital, London, United Kingdom, SE5 9RS.

Objective: Intrajejunal levodopa infusion (IJL) and sub-cutaneous apomorphine infusion (Apo) are established treatments for advanced Parkinson's disease (PD).

Background: We initiated a novel case control study to compare motor and non motor effects of these therapies (EuroInf study) and to report multi-centre European data from a real life setting of intrajejunal levodopa (44 patients) and apomorphine infusion (43 patients) in matched cases with advanced PD

Methods: IJL: 44 advanced PD cases,(age: 62.66±9.09 yrs, mean duration of disease: 16.06±6.7yrs, median Hoehn &Yahr (H&Y) stage: 3), Apo: 43 cases,(age 62.25±10.60 yrs, disease duration 14.04±4.4 yrs, median HY: 3), were assessed with Unified PD Rating Scale (UPDRS) III and IV, Non Motor Symptoms Scale (NMSS) and Parkinson's disease questionnaire (PDQ-8) scores before initiation of therapy and after 6 months of therapy.

Results: Both groups were matched in terms of age, duration of PD, median HY stage, levodopa equivalence dose. Effect size of both interventions on UPDRS III&IV, and PDQ-8 scores were big (>0.8). Concerning the NMSS, differential effects were observed with sleep/fatigue and gastroenterological/urinary symptoms showing greater response to IJLI, while mood was better improved with apomorphine with no worsening of hallucinations.

	Change Baseline-Follow up				
	Difference in Score		Relative Change (%)		
	Duodopa	Apomorphine	Duodopa	Apomorphine	p
UPDRS- Part 3	-12.23±11.45	-13.33±11.24	-44.79	-43.26	NS
UPDRS- Part 4	-5.57±3.53	-4.09±4.30	-56.06	-40.84	NS
NMSS					
Cardiovascular	-1.5±3.14	-1.12±4.42	-44.64	-35.11	NS
Sleep/Fatigue	-8.05±10.87	-4.00±11.43	-48.23	-23.56	0.017
Mood/Apathy	-3.91±12.10	-8.84±15.78	-24.75	-47.00	0.030
Perceptual/Hallucinations	-1.59±4.27	-1.63±4.71	-44.79	-53.97	NS
Attention/Memory	-2.61±6.86	-2.98±7.19	-25.60	-33.98	NS
Gastrointestinal	-5.23±6.02	-1.56±5.13	-55.17	-25.12	0.004
Urinary	-6.02±8.98	-1.14±7.92	-52.36	-12.57	0.0001
Sexual functioning	-3.41±7.59	-0.63±3.48	-59.51	-24.61	0.001
Miscellaneous	-4.98±8.66	-4.28±9.44	-33.97	-31.08	NS
Total score	-37.30±36.13	-26.16±44.72	-41.01	-31.76	NS
PDQ-8 Summary index	-16.62±20.29	-14.83±18.61	-34.21	-29.75	NS

Conclusions: To our knowledge this is the first case control comparative multicentre study comparing IJLI and Apo in advanced PD. We report a robust improvement in motor and quality of life scores with a large effect size with both therapies while a differential effect on NMSS is noted. Specifically of note is that apomorphine infusion improved mood dysfunction and did not worsen hallucinations.

Previously Presented: This is a follow up dataset analysis to the first EuroInf data presented at the MDS congress in Dublin, 2012. The NMSS analysis is novel.

SG-10**European Multicentre Study of tolerability and impulse control disorders with short and extended release dopamine agonists in real life PD**

Alexandra Rizos, MSc¹, Pablo Martinez-Martin, MD PhD², Anne Martin, RGN¹, Tove Henriksen, MD³, Belinda Kessel, MD⁴, Ines Koch¹, Gregor Durner¹, Sandeep Bassi, MSc¹, Louise Gallagher, RGN¹, Miriam Parry, RGN¹, Angelo Antonini, MD PhD⁵, Per Odin, MD PhD⁶, Cristian Falup-Pecurariu, MD⁷, Monty Silverdale, MD⁸, Graeme MacPhee, MD⁹, K Ray-Chaudhuri, MD DSc¹, on behalf of EUROPAR and the MDS Non Motor Study Group. ¹Kings College Hospital, London, United Kingdom; ²Alzheimer Centre Reina Sofia Foundation, Madrid, Spain; ³Bispebjerg Hospital, Copenhagen, Denmark; ⁴Elderly Medicine Department, Princess Royal University Hospital, Orpington, United Kingdom; ⁵University of Padua, Venice, Italy; ⁶University of Lund, Lund, Sweden; ⁷Transilvania University, Brasov, Romania; ⁸Hope Hospital, Salford, United Kingdom and ⁹Southern General Hospital, Glasgow, United Kingdom.

Objective: A multicentre real life observational study of tolerability (at least 6 months use) and impulse control disorders (ICD) if dopamine agonists (DA) with a focus on extended release formulations: rotigotine skin patch (RTG), ropinirole (ROP IR/XL) and pramipexole (PPX IR/PR) across several European centres.

Background: Tolerability/retention rate and occurrence of impulse control disorder on prolonged release DA therapy are unknown in real life clinical populations of people with Parkinson's (PwP).

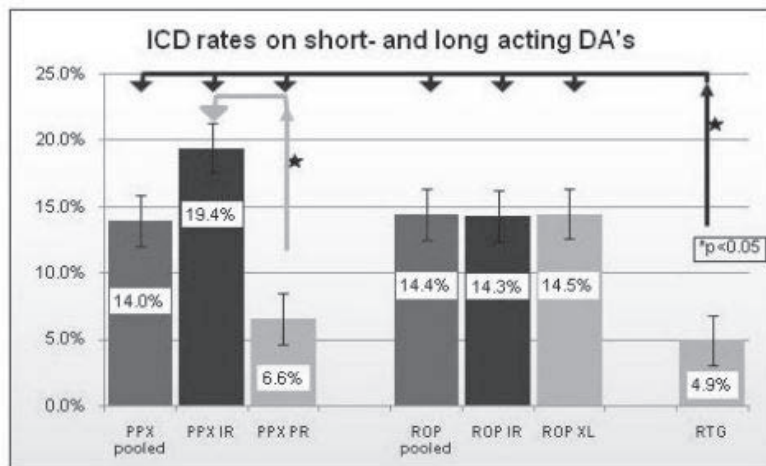
Methods: Prospective case note/interview based survey of patients across all stages and age groups initiated on above DA.

Results: 425 cases were included for analysis (median age 69 yrs, range: 37-90; median duration of disease 6 yrs, range: 0-37), 31.5% of which were ≥ 75 yrs (old PD).

1. Tolerability rates were high with no significant differences between the groups in young or old PD.

Tolerability rates for extended release DA's			
	PPX PR	ROP XL	RTG
% on DA	17.9	39.1	8.4
Mean dose (mg)	2.8	12.4	8.4
Tolerability (<75 yrs)	93.5%	93.1%	86.8%
Tolerability (≥75 yrs)	95.2%	90.7%	79.2%

2. ICD rates were judged by questionnaires and interviews. Rate of ICD with RTG was significantly lower than with any other extended or immediate release DA except for PPX PR. Rate of ICD for PPX PR was significantly lower than for PPX IR.



59.6% of the reported ICD cases have been exposed to shorter acting agonists previously and discontinuation rates with ICD were low.

Conclusions: Tolerability rate of all prolonged release DAs are high including older (≥ 75 yrs) PwP who are often excluded from DA use. For the first time a relatively low rate of ICD with use of prolonged release DA is reported, especially for RTG.

Previously Presented: Preliminary data presented to EFNS 2011, WFN 2011, MDS 2012.

SG-11

Criteria for mild cognitive impairment in Parkinson's disease: Applicability and validity

Gert J Geurtsen, PhD¹, Ben A Schmand, PhD¹, Irene Litvan, PhD², Jennifer G Goldman, PhD³ and Alexander I Tröster, PhD⁴. ¹Department of Neurology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; ²Department of Neurosciences, University of California, San Diego, CA, United States; ³Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, United States and ⁴Muhammad Ali Parkinson Center, Barrow Neurological Institute, Phoenix, AZ, United States.

Objective: on behalf of the MDS Study group "Validation of Mild Cognitive Impairment in Parkinson Disease".

Background: Dementia in Parkinson's disease (PD) is a serious health issue and a major concern for many patients. Mild cognitive impairment (MCI) is considered a transitional stage between normal cognitive functioning and dementia. In 2012 diagnostic criteria for MCI in PD (PD-MCI) were proposed by the Movement Disorder Society (MDS). The next step is to validate these criteria and to investigate whether they can be applied to obtain a uniform and valid definition of PD-MCI. The definition of this clinical entity is important both for the early identification and management of those at risk for the development of dementia and for future research on etiology, disease course, and disease modifying or causative treatment.

Methods: The MDS Study group "Validation of Mild Cognitive Impairment in Parkinson Disease" is an international consortium that will pool existing cross-sectional and longitudinal data of more than 3000 PD patients and more than 1000 controls. These data will be analyzed to determine the applicability of the PD-MCI criteria.

Results: Therefore, the presence of PD-MCI will be scored using the levels I and II of the MDS PD-MCI criteria. For validity we will determine whether PD-MCI predicts further cognitive decline as well. Moreover, since currently there is no consensus on the details (e.g. precise tests and cut off scores) that would

determine PD-MCI, we will study which method (e.g. cut off scores, cognitive profile) best predicts conversion to dementia.

Conclusions: The criteria will be discussed and preliminary results of the study concerning the applicability and validity will be presented.

Previously Presented: Presented at 9th international congress on mental dysfunction and other non-motor features in Parkinson's disease and related disorders, Seoul, April 18-21 2013.

SG-12

The Movement Disorders Society-Endorsed PSP Study Group

Authors: Günter U. Höglinger*, Kailash Bhatia, Adam L. Boxer, Dennis Dickson, Lawrence Golbe, Keith A. Josephs, Irene Litvan, Brit Mollenhauer, Huw R. Morris, Ulrich Müller, Wolfgang Oertel, Maria Stamelou, Gerard Schellenberg, John C van Swieten, Jennifer Whitwell, David Williams, for the MDS PSP Study Group
*German Center for Neurodegenerative Diseases e.V. (DZNE) & Technical University Munich (TUM), Dept. for Translational Neurodegeneration, Max Lebsche Platz 30, D-81377 Munich, Germany, Guenter.Hoeglinger@DZNE.de

Objectives:

1st To provide an evidence-based revision of the diagnostic criteria for PSP.

2nd To promote cooperative clinical research into PSP.

3rd To promote clinical trials aiming to cure PSP.

Background: PSP is an adult-onset neurodegenerative disorder with cerebral tau pathology leading to an akinetic-rigid syndrome with oculomotor dysfunction, postural instability, frontal lobe and bulbar dysfunction. The diagnostic gold standard is pathological diagnosis (Hauw et al., *Neurology*. 1994;44:2015-9). The clinical diagnosis remains a challenge. The National Institute of Neurological Disorders and Stroke and the Society for PSP (NINDS-SPSP) criteria have been proposed for the clinical diagnosis (Litvan et al., *Neurology* 1996; 46:922-930). Validation of these criteria in independent sets of patients demonstrated a high positive predictive value, albeit low sensitivity particularly during the early course of the disease (Osaki et al., *Mov Disord*. 2004;19:181–189; Respondek et al., *Mov Disord*. 2013 doi: 10.1002/mds.25327). Particularly, the NINDS-SPSP criteria do not allow the recognition of the recently described variable phenotypic PSP presentations. No curative treatment options are available at present. Clinical research into this rare disorder is limited in power due to its fragmentation.

Aims: We aim to improve the diagnostic criteria for PSP, to create clinical research networks, and to initiate measures facilitating therapeutic clinical trials in PSP.

Methods: We initiated the establishment of international S3-guidelines for the clinical diagnosis of PSP based on published evidence. Secondly, we aim to characterize the earliest clinical signs and symptoms occurring over the disease course of pathologically confirmed PSP. Thirdly, we are undertaking studies to facilitate clinical trials in PSP, including an improvement of early diagnosis for early recruitment and protocol development and refinement for clinical trials.

Results: Working groups have been created for 'clinical course', 'neuropsychology', 'oculomotor dysfunction', 'MR imaging', 'nuclear medicine', 'genetics', 'biomarker'. Key questions and search terms have been defined for a systematic literature research. A retrospective analysis of original clinico-pathological datasets has been initiated. Clinical research networks have been initiated in the US, UK and Germany.

Conclusions: The MDS PSP Study Group has set up studies to improve early diagnosis and treatment of PSP.

SG-13**Deep brain stimulation of the pedunclopontine area in Parkinson's disease and progressive supranuclear palsy (PPN DBS Working Group)**

Elena Moro^{1,2}, Joachim Krauss³, Michael S. Okun⁴, Tipu Aziz⁵, Andres M Lozano⁶, Bastiaan R. Bloem⁷, Bettina Debû², on behalf of the MDS PPN DBS Working Group

¹ Division of Neurology, Grenoble University Hospital, Grenoble, France

² J. Fourier University, Grenoble, France

³ Department of Neurosurgery, Hannover, Germany

⁴ Division of Neurology, Gainesville, FL, USA

⁵ Department of Neurosurgery, Oxford, UK

⁶ Department of Neurosurgery, Toronto Western Hospital, University of Toronto, Toronto, Canada

⁷ Department of Neurology, Radboud University Nijmegen Medical Center, The Netherlands

Background: Postural instability and gait difficulties (PIGD) are severely debilitating symptoms that inevitably affect almost all patients with advanced Parkinson's disease (PD). These symptoms emerge much earlier in the disease for progressive supranuclear palsy (PSP). These PIGD symptoms generally respond suboptimally to medical treatment and can be alleviated temporarily prior to axial disease progression by subthalamic nucleus and globus pallidus internus deep brain stimulation (DBS). Pedunclopontine nucleus area (PPNa) DBS has recently been tested as an alternative DBS target site, however the initial results were mixed. These results have raised a number of issues regarding patient selection, target localization, optimal parameter settings and outcome measures.

Objective: It will be important to clarify the benefits and limitations using the current literature and also the worldwide experience implanting PPNa DBS.

Methods: The MDS PPNa DBS working group consists of neurologists, neurosurgeons, neurophysiologists, gait specialists, bioengineers, and neuropsychologists with experience in PPN DBS. The main objective is to develop an instrument (core assessment protocol, CAP) that will provide movement disorder centers implanting DBS devices with a common set of pre- and post selection criteria and outcome measurements for both PD and PSP patients selected for PPNa DBS. Additionally, the group aims to provide recommendations for intra-operative targeting and post-operative management.

Results and Conclusions: Following a systematic and thorough review of available evidence-based studies, conclusions will be drawn and recommendations made for patient selection (inclusion/exclusion criteria), management and evaluation (short and long term), as well recommendations for surgery procedures and targeting (intra-operative recording and stimulation, appropriate imaging, adequate surgical hardware).

Guided Poster Tours

GUIDED POSTER TOUR 1 –

Basic science

Bayside Level 1, Bayside Gallery A

12:30 – 14:00

Monday, June 17, 2013

Tour Leaders:

Anthony Schapira, *London, United Kingdom*

- 1004 RNAi-mediated silencing of VPS35 exacerbates phenotypic and locomotor abnormalities in α -synuclein transgenic drosophila**
T. Hasegawa, M. Konno, E. Miura, N. Sugeno, Y. Nagai, N. Fujikake, M. Suzuki, A. Kikuchi, M. Aoki, A. Takeda (Sendai, Japan)
- 1005 Nedd4 E3 ubiquitin ligase facilitates the endosomal targeting of alpha-synuclein**
N. Sugeno, T. Hasegawa, M. Konno, E. Miura, A. Kikuchi, M. Aoki, A. Takeda (Sendai, Japan)
- 1008 Impaired redox balance and autophagosome clearance in fibroblasts from Parkinson's disease patients with LRRK2 G2019S mutation**
A. Grünewald, B. Arns, P. Seibler, B. Meier, A. Rakovic, C. Klein (Lübeck, Germany)
- 1017 Role of the ubiquitin proteasome system and the lysosomal system in PINK1-/ parkin-dependent mitophagy in human primary fibroblasts**
K. Shurkewitsch, A. Rakovic, C. Klein (Lübeck, Germany)
- 1018 Cholinergic olfactory centrifugal inputs are reduced in patients with neurodegenerative disorders and MPTP treated monkeys**
I.C. Mundiñano, M. Hernandez, C. Ordoñez, C. Di Cauda, I. Marcilla, T. Tuñon, M.R. Luquin (Pamplona, Spain)
- 1024 Copper pathology in the vulnerable substantia nigra in Parkinson's disease**
K.M. Davies, S. Bohic, R. Ortega, V. Cottam, D.J. Hare, J.P.M. Finberg, G. Halliday, J.F.B. Mercer, K.L. Double (Sydney, Australia)
- 1034 Withdrawn by Author**
- 1039 Overexpression of cannabinoid CB2 receptors attenuated the progressive motor impairment and nigrostriatal dopaminergic neurons loss in MitoPark mouse**
F. Navarrete-Rueda, J.M. Pérez-Ortiz, M.S. Garcia-Gutierrez, J.A. Molina-Arjona, C. Leiva-Santana, J. Manzanares (San Juan de Alicante, Spain)
- 1049 Using the anterior olfactory nucleus to study lewy pathology in olfactory structures**
S. Rajan, R. Bandopadhyay, A. Kingsbury, H. Ayling, W. Sterlacci, W. Poewe, H. Maier, M. Ezquerro, A. Lees, T. Revesz, L. Silveira-Moriyama (London, United Kingdom)
- 1052 Catecholamine substrates of behavioral inflexibility in a rat model of Parkinson's disease**
E.M. Vazey, K.M. Fender, Z.A. Cope, S.B. Floresco, G. Aston-Jones (Charleston, SC, USA)

GUIDED POSTER TOUR 2 –

Parkinson's disease: Behavioral disorders

Bayside Level 1, Bayside Gallery B

12:30 – 14:00

Monday, June 17, 2013

Tour Leaders:

Hubert Fernandez, *Cleveland, OH, USA*

Daniel Weintraub, *Ardmore, PA, USA*

Supported by an unrestricted educational grant from UCB Pharma SA.

- 338 A novel α -synuclein-GFP mouse model displays progressive motor impairment, olfactory dysfunction and accumulation of α -synuclein-GFP**
C. Hansen, T. Björklund, G.H. Petit, M. Lundblad, R.P. Murmu, P. Brundin, J.Y. Li (Lund, Sweden)
- 345 I finally see what you see: A window into Parkinson's disease hallucinations**
G.T. Stebbins, C.G. Goetz, J.G. Goldman, C.L. Vaughan (Chicago, IL, USA)
- 354 Gray matter neuroimaging signatures of Parkinson's disease hallucinations**
J.G. Goldman, V. Dinh, G.T. Stebbins, B. Bernard, L. deToledo-Morrell, C.G. Goetz (Chicago, IL, USA)
- 355 Decisions under risk in Parkinson's disease: Evaluating probability and magnitude for gain and loss**
M.E. Sharp, J. Viswanathan, M.J. McKeown, S. Appel-Cresswell, A.J. Stoessl, J.J.S. Barton (Vancouver, BC, Canada)
- 357 Dopamine agonists rather than deep brain stimulation cause reflection impulsivity in Parkinson's disease**
A. Djamshidian, S.S. O'Sullivan, T. Foltynie, I. Aviles-Olmos, P. Limousin, A. Noyce, L. Zrinzo, A.J. Lees, B.B. Averbeck (London, United Kingdom)
- 359 Modulation of attentional network coherence during manipulation of cognitive load in patients with Parkinson's disease and freezing of gait**
J.M. Shine, E. Matar, M. Gilat, S.J. Bolitho, P.B. Ward, S.L. Naismith, S.J.G. Lewis (Sydney, Australia)
- 360 Sedentary behavior increases over 18 months in early Parkinson's disease**
S. Lord, A. Godfrey, B. Galna, D. Mhiripiri, D. Burn, L. Rochester (Newcastle upon Tyne, United Kingdom)
- 366 Assessment of impulse control disorders in Parkinson's disease patients with infusion therapies: A single center experience**
A. Todorova, A. Martin, D. Okai, M. Samuel, R. Brown, A. David, K. Ray Chaudhuri (London, United Kingdom)
- 375 Psychiatric comorbidities among hospitalized Parkinson's disease patients**
M. Minen, N. Mejia (Boston, MA, USA)
- 382 Long-term cognitive follow-up of impulse control disorders in Parkinson's disease: A prospective longitudinal controlled study**
C. Siri, A. Colombo, B. Pozzi, E. Reali, N. Meucci, M. Canesi, A.L. Zecchinelli, C.B. Mariani, G. Sacilotto, M. Zini, C. Ruffmann, G. Pezzoli, R. Cilia (Milan, Italy)

Guided Poster Tours

GUIDED POSTER TOUR 3 – Parkinson's disease: Neuropharmacology

Bayside Level 2, Bayside 201-203

12:30 – 14:00

Monday, June 17, 2013

Tour Leaders:

Mark Guttman, *Markham, ON, Canada*

Cristina Sampaio, *Princeton, NJ, USA*

- 580 Behavioural, biochemical and cellular correlates in the neuroprotective potential of HMG-CoA reductase inhibitors (atorvastatin and simvastatin) against 6-hydroxydopamine (6-OHDA) induced Parkinson-like symptoms in rats**
J. Mishra, N. Sharma, A. Kumar (Chandigarh, India)
- 587 Inosine inhibited the neurotoxicity of MPTP on the dopaminergic neurons**
T. Tsujii, M. Kubo, H. Iwaki, W.T. Kyaw, N. Nishikawa, M. Nagai, R. Andoh, F. Islam, M. Nomoto (Tohon, Japan)
- 589 Performance of a task learned when “on” deteriorates when subsequently practiced in “off” state**
E.D. Anderson, E. Murdock, H. Fay, J.G. Nutt (Portland, OR, USA)
- 593 Chronic treatment with MPEP, an mGlu5 receptor antagonist, normalizes basal ganglia glutamate neurotransmission in L-DOPA-treated parkinsonian monkeys**
N. Morin, M. Morissette, L. Grégoire, B. Gomez-Mancilla, F. Gasparini, T. Di Paolo (Quebec, QC, Canada)
- 594 Identifying the transcriptomic signature of L-DOPA-induced dyskinesias**
L.M. Smith, E.J. Duncan, L.C. Parr-Brownlie, M.A. Black, P.K. Dearden, J.N.J. Reynolds (Dunedin, New Zealand)
- 596 The EuroInf study: A multi-centre European comparative study of apomorphine versus intrajejunal levodopa infusion in a real life cohort of Parkinson's disease patients**
P. Reddy, P. Martinez-Martin, A. Todorova, A. Antonini, P. Odin, A. Martin, A. Rizos, D. Calandrella, T. Henriksen, N. Bryndum, A. Glad, S. Dafsari, L. Timmermann, G. Ebersbach, M. Kramberger, A. Ceballos-Baumann, K. Wenzel, V. Tomantschger, A. Storch, H. Reichmann, Z. Pirtosek, M. Trost, R. Katzenschlager, P. Svenningsson, S. Pahlagen, J. Volkman, K.R. Chaudhuri, The Movement Disorder Society Non Motor Study Group (London, United Kingdom)
- 600 Investigating the neuroprotective effects of valproate, an epigenetic histone deacetylase inhibitor, in Parkinson's disease using preclinical magnetic resonance imaging**
I.F. Harrison, D.T. Dexter (London, United Kingdom)
- 607 Withdrawn by Author**
- 612 Effects of chronic D2/3 agonist ropinirole medication on rodent models of gambling behaviour**
M. Tremblay, J.G. Hosking, C.A. Winstanley (Vancouver, BC, Canada)
- 619 Time-to-levodopa depending on initial PD medication: A retrospective cohort study**
J.P. Reese, U.O. Mueller, W.H. Oertel, R. Dodel, K. Kostev (Marburg, Germany)

GUIDED POSTER TOUR 4 – Sleep disturbance and RLS

Bayside Level 2, Bayside 204

12:30 – 14:00

Monday, June 17, 2013

Tour Leaders:

K. Ray Chaudhuri, *London, United Kingdom*

Supported by an unrestricted educational grant from UCB Pharma SA.

- 651 Rare variants in restless legs syndrome**
E. Schulte, F. Knauf, B. Schormair, P. Lichtner, C. Trenkwalder, B. Högl, B. Frauscher, K. Berger, I. Fietze, N. Gross, K. Stiasny-Kolster, W. Oertel, C. Bachmann, W. Paulus, A. Zimprich, A. Peters, C. Gieger, B. Müller-Myhsok, J. Winkelmann (München, Germany)
- 623 Withdrawn by Author**
- 624 Plasma urate in REM sleep behavior disorder**
R. Uribe-San Martín, P.F. Venegas, F.I. López, A.G. Jones, J.R. Salazar, J.F. Godoy, J.M. Santín, C. Juri (Santiago, Chile)
- 626 The impact of daytime napping on executive cognitive dysfunction in Parkinson's disease**
S.J. Bolitho, S.L. Naismith, S.J. Lewis (Sydney, Australia)
- 628 REM sleep behavior disorder after bilateral subthalamic stimulation in Parkinson's disease**
G. Ehm, Y.E. Kim, B.S. Jeon, Y.J. Jung, J.Y. Kim (Seoul, Korea)
- 629 REM sleep behavior disorder in Parkinson's disease: Association with abnormal ocular motor findings**
Y.E. Kim, B.S. Jeon, H. Park, Y.J. Jung, H.J. Kim (Seoul, Korea)
- 630 Excessive chin EMG activity during rapid eye movement sleep in Parkinson's disease: Is a marker?**
Y. Shen, K.P. Xiong, Y. Gong, X.Y. Zhang, W.D. Hu, J.M. Xu, J. Cheng, C.F. Liu (Suzhou, China)
- 631 The decrease of sleep apnea in Parkinson's disease associated with excessive electromyography (EMG) activity**
K.P. Xiong, Y. Gong, Y. Shen, Q. Tang, J.M. Xu, J. Cheng, C.F. Liu (Suzhou, China)
- 636 Worldwide record of REM sleep time in a patient with pedunculopontine nucleus area (PPNa) stimulation**
D. Neutel, D. Grabli, C. Karachi, M.L. Welter, C. Ewencyk, E. Bardinet, C. François, I. Arnulf (Paris, France)
- 643 Circadian expression profile of clock genes in early Parkinson's disease patients**
R.R. Vuono, D.P. Breen, K. Fisher, A.B. Reddy, R.A. Barker (Cambridge, United Kingdom)

Guided Poster Tours

GUIDED POSTER TOUR 5 – Dystonia

Bayside Level 1, Bayside Gallery A

12:30 – 14:00

Tuesday, June 18, 2013

Tour Leaders:

Alberto Albanese, *Milan, Italy*

Susanne Schneider, *Kiel, Germany*

- 4 Basal ganglia circuit disturbances and symptomatology in primary focal dystonia (PFD)**
B.D. Berman, M. Hallett (Aurora, CO, USA)
- 7 Generation and characterisation of mice rescuing the DYT1-knockout phenotype**
B.T. Fabry, L. Lotzer, S. Moll, J. Hettich, O. Riess, K. Grundmann, T. Ott (Tübingen, Germany)
- 9 Unraveling cellular phenotypes of novel torsinA mutations**
F. Vulinovic, P. Seibler, J. Graf, A. Ferbert, A. Rolfs, A. Schmidt, C. Klein, K. Lohmann (Lübeck, Germany)
- 27 Genome sequencing reveals a mutation in the TUBB4 gene as the cause of whispering dysphonia (DYT4 dystonia)**
K. Lohmann, R.A. Wilcox, S. Winkler, A. Ramirez, A. Rakovic, J.S. Park, J.L. Groen, M. Kasten, N. Brüggemann, A. Schmidt, F.J. Kaiser, K.R. Kumar, M. Agzarian, L.J. Ozelius, A.P.M. Langeveld, C.M. Sue, M.A.J. Tijssen, C. Klein (Luebeck, Germany)
- 28 Genome-wide association of a locus on chromosome 17 with musician's dystonia**
C. Klein, A. Schmidt, A. Schillert, S. Winkler, F. Baas, N. Brüggemann, G. Deuschl, J. Graf, L.J. Groen, J. Hagenah, H.C. Jabusch, M. Kasten, S. Schreiber, M.A.J. Tijssen, K.E. Zeuner, E. Altenmüller, A. Ziegler, K. Lohmann (Luebeck, Germany)
- 47 The phenotypic spectrum of DYT23 due to ANO3 mutations**
M. Stamelou, G. Charlesworth, C. Cordivari, S. Schneider, G. Kaegi, U. Sheerin, I. Rubio-Agusti, A. Batla, H. Houlden, N. Wood, K.P. Bhatia (London, United Kingdom)
- 49 ANO3 - A novel cause of primary dystonia**
G. Charlesworth, V. Plagnol, K.M. Holmström, J. Bras, U.M. Sheerin, E. Preza, I. Rubio-Agusti, M. Ryten, S.A. Schneider, M. Stamelou, D. Trabzuni, A.A. Abramov, K.P. Bhatia, N.W. Wood (London, United Kingdom)
- 58 Withdrawn by Author**
- 89 Development of a comprehensive cervical dystonia rating scale**
C.L. Comella, G.T. Stebbins, M. Zurovski, H.A. Jinnah, J.S. Perlmutter, T.A. Waliczek, A.R. Rosen, W. Galpern (Chicago, IL, USA)
- 95 Abnormal thalamocortical tractography in cervical dystonia**
J.L. Waugh, J.K. Kuster, S. Woodman, M.L. Makhlof, N. Makris, H.C. Brieter, T.J. Multhaupt-Buell, L.R. Sudarsky, N. Sharma, A.J. Blood (Boston, MA, USA)

GUIDED POSTER TOUR 6 – Parkinsonisms (parkinson plus and secondary)

Bayside Level 1, Bayside Gallery B

12:30 – 14:00

Tuesday, June 18, 2013

Tour Leaders:

Tove Henriksen, *Copenhagen, Denmark*

Günter Höglinger, *Munich, Germany*

- 771 Prevalence and risk factors for parkinsonism among retired Filipino boxers**
L.L. Shiong Shu, R.D.G. Jamora, P.A.D. Canto, C.P.C. Dioquino, L.K. Ledesma (Manila, Philippines)
- 781 Clinical and neuropathological features of synucleinopathy associated with G51D SNCA mutation**
A.P. Kiely, Y.T. Asi, E. Kara, P. Limousin, H. Ling, P. Lewis, C. Proukakis, N. Quinn, A. Lees, J. Hardy, T. Revesz, H. Houlden, J.L. Holton (London, United Kingdom)
- 782 Auditory cues at person-specific asymmetry and cadence improve gait stability only in people with Parkinson's disease (PD)**
M.A.D. Brodie, T.R. Beijer, S.R. Lord, C.G. Canning, J. Menant, S. Smith, R.T. Dean (Randwick, Australia)
- 788 Genetic influences of MAPT and SNCA on age at onset of Parkinson's disease**
Y. Huang, G. Wang, D. Rowe, Y. Wang, J. Kwok, Q. Xiao, F. Masterglia, J. Liu, G. Halliday, S. Chen (Sydney, Australia)
- 794 The "Lazy lid" sign supports the clinical diagnosis of progressive supranuclear palsy**
S. Lorenzl, G. Nübling (Munich, Germany)
- 796 Primary lateral sclerosis with marked supranuclear gaze palsy and postural instability but normal dopamine transporters imaging: A distinct PLS phenotype**
M. Stamelou, A. Pisani, M. Edwards, K.P. Bhatia (London, United Kingdom)
- 810 Young-onset and old-onset multiple system atrophy: Clinical comparison study**
J. Kim, M.J. Kim, Y.J. Kim, S.R. Kim, M.S. Kim, S.J. Chung (Seoul, Korea)
- 813 Why do patients with PSP fall?**
B.M. Schoneburg, M. Mancini, F.B. Horak, J.G. Nutt (Portland, OR, USA)
- 829 The role of statin use on incidence of Parkinson's disease: A meta-analysis of observational studies**
K. Undela, K. Gudala, S. Malla, D. Bansal (Mysore, India)
- 841 Selegiline rescues gait deficits and dopaminergic cells in subacute MPTP mouse model of Parkinson's disease**
Q. Zhao, Y. Bai, D. Fang (Shanghai, China)

Guided Poster Tours

GUIDED POSTER TOUR 7 – Rating scales and assessment tools

Bayside Level 2, Bayside 201-203

12:30 – 14:00

Tuesday, June 18, 2013

Tour Leaders:

Christopher Goetz, *Chicago, IL, USA*
Cristina Sampaio, *Princeton, NJ, USA*

- 325 Fatigue in Parkinson's disease: Prevalence and associated factors**
C.M. Trase Kwok, K.F. Hui, K.Y. Wong (Hong Kong)
- 294 Prevalence of gastroparesis symptoms in patients with early Parkinson's disease**
S.L. Marrinan, A.V. Emmanuel, D.G. Grosset, D.J. Burn (Newcastle upon Tyne, United Kingdom)
- 295 Test-retest reliability of a Parkinson's disease monitoring system**
D.A. Heldman, A.J. Espay, P.A. LeWitt, J.P. Giuffrida (Cleveland, OH, USA)
- 328 Semi-automatic scoring method for torticollis by using kinect**
T. Nakamura, M. Sato, H. Kajimoto (Chofu, Japan)
- 302 A computer vision framework for finger-tapping evaluation in Parkinson's disease**
T. Khan, D. Nyholm, J. Westin, M. Dougherty (Falun, Sweden)
- 303 A web-based system for visualizing upper limb motor performance of Parkinson's disease patients**
M. Memedi, U. Bergqvist, J. Westin, D. Nyholm (Borlänge, Sweden)
- 309 Bradykinesia-akinesia incoordination test: Validating an online keyboard test of upper limb function**
A. Nagy, S. Acharya, S. Hadavi, J.P. Bestwick, J. Fearnley, A.J. Lees, G. Giovannoni, A.J. Noyce (London, United Kingdom)
- 310 The utilization of a one-leg balance task for assessing balance and disease bilaterality in people with Parkinson's disease**
B. Hu, T. Clark, S. Cihal (Calgary, AB, Canada)
- 316 Quantification of speed, amplitude and fatigue in PD**
L. Verhagen, L. van Imhoff, S. van den Munckhof, S. Gardon, B. Ouyang (Chicago, IL, USA)
- 321 BradyAn: A new reliable tool for measuring bradykinesia**
E. Ruzicka, R. Krupicka, K. Zarubova, Z. Szabo, R. Jech (Prague, Czech Republic)

GUIDED POSTER TOUR 8 – Surgical therapy: Parkinson's disease

Bayside Level 2, Bayside 204

12:30 – 14:00

Tuesday, June 18, 2013

Tour Leaders:

Paul Krack, *Grenoble, France*
Jens Volkmann, *Wuerzburg, Germany*

- 1252 Steering deep brain stimulation: An exploratory study with a new 32-contact lead**
M.F. Contarino, L.J. Bour, R.M.A. de Bie, P. van den Munckhof, P.R. Schuurman (Amsterdam, Netherlands)
- 1260 Simultaneous targeting of STN and GPi can be useful for DBS therapy in advanced Parkinson's disease**
P. Hedera, M.K. Cooper, F.T. Phibbs, P.D. Charles, P.E. Konrad, J.S. Neimat, T.L. Davis (Nashville, TN, USA)
- 1263 Successful long-term bilateral subthalamic nucleus deep brain stimulation in VPS35 Parkinson's disease**
V. Fleury, C. Wider, J. Horvath, A. Zacharia, J. Bally, P. Pollak, C. Pollo, F.J.G. Vingerhoets, P.R. Burkhard (Geneva, Switzerland)
- 1264 A new DBS lead: Simultaneous 32-contact local field potential recording in the Parkinsonian STN**
L.J. Bour, R. Verhagen, F. Contarino, R.M.A. De Bie, G. Van Elswijk, H.C.F. Martens, P. Van den Munckhof, R. Schuurman (Amsterdam, Netherlands)
- 1266 Stimulation of electrode contacts within zona incerta directly blocks levodopa-induced dyskinesias in PD patients**
C.P. Souza, M.G.S. Ghilardi, R.G. Cury, R.B.M. Rodrigues, E.R. Barbosa, M.J. Teixeira, E.T. Fonoff (São Paulo, Brazil)
- 1268 Different combinations of subthalamic nucleus (STN) and pedunclopontine nucleus (PPN) deep brain stimulation (DBS) lead to variable effects in saccades and antisaccades in advanced Parkinson's disease (PD)**
M.J. Naushahi, A.N. Khan, Q. Arshad, P.Y. Lee, S. Khalid, N. Yousif, N. Pavese, P.G. Bain, A.M. Bronstein, D. Nandi (Cambridge, United Kingdom)
- 1269 The impact of age at surgery on long term outcome of bilateral STN-DBS**
A. Shalash, A. Alexoudi, K. Knudsen, J. Volkmann, M. Mehdorn, G. Deuschl (Cairo, Egypt)
- 1274 Influence of speech task and utterance length on measurement of pitch variability in the speech of Parkinson's disease patients after deep brain stimulation**
J. van Doorn, F. Karlsson (Umeå, Sweden)
- 1288 Parkinson study group survey of impulsive and compulsive disorders in Parkinson's disease pre and post deep brain stimulation**
N. Hack, A. Thompson-Avila, E. Moro, M. York, K. Nestor, S. Fayad, H. Ward, M. Okun (Gainesville, FL, USA)
- 1318 Practice change in DBS target for Parkinson's disease 2010-2012 Influence of the VA/NIH cooperative study #468**
M. San Luciano, N. Galifianakis, C. Racine, L. Markun, P. Starr, P. Larson, R. Taylor, W. Marks, Jr., M. Katz, K. Mills, M. Volz, J. Ostrem (San Francisco, CA, USA)

Guided Poster Tours

GUIDED POSTER TOUR 9 – Parkinson's disease: Cognition

Bayside Level 1, Bayside Gallery A

12:00 – 13:30

Wednesday, June 19, 2013

Tour Leaders:

Murat Emre, *Istanbul, Turkey*

Jennifer Goldman, *Chicago, IL, USA*

- 505** **Characterising mild cognitive impairment in incident Parkinson's disease: The ICICLE-PD study**
A.J. Yarnall, D.P. Breen, G.W. Duncan, R.A. Barker, D.J. Burn (Newcastle-upon-Tyne, United Kingdom)
- 508** **The relationship between small vessel disease (SVD), vascular risk factors (VRFs) and motor and cognitive impairment in Parkinson's disease (PD): A clinicopathological study**
R.S. Schwartz, G.M. Halliday, D.J. Cordato, J.J. Kril (Sydney, Australia)
- 512** **The neuropsychological domain differences between Parkinson's disease patients with and without mild cognitive impairments; a longitudinal investigation**
P. Hobson, J. Meara (Rhyl, United Kingdom)
- 519** **Evaluation of driving ability in patients with Parkinson's disease using a driving simulator**
R. Andoh, W.T. Kyaw, T. Tsujii, H. Iwaki, N. Nishikawa, M. Nagai, M. Nomoto (Tohon, Japan)
- 526** **Relationships between non-motor symptoms in Parkinson's disease, and their genetic and pathologic basis**
G. Wang, Y. Huang, W. Chen, S. Chen, Y. Wang, Q. Xiao, J. Liu, P. Sachdev, V.S.C. Fung, D. Rowe, G. Halliday, S. Chen (Sydney, Australia)
- 531** **Motor timing in Parkinson's disease patients who freeze**
C.M. Tolleson, S.A. Wylie, O.C. Roman, S. Barton, M. Kubovy, D. Claassen (Nashville, TN, USA)
- 533** **Fronto-striatal atrophy correlates of inhibitory dysfunction in Parkinson's disease**
C. O'Callaghan, S.L. Naismith, J.R. Hodges, S.J.G. Lewis, M. Hornberger (Sydney, Australia)
- 550** **Principal component analysis of PiB distribution in Parkinson's and Alzheimer's diseases**
M.C. Campbell, J. Markham, H. Flores, J.M. Hartlein, A.M. Goate, N.J. Cairns, T.O. Videen, J.S. Perlmutter (Saint Louis, MO, USA)
- 559** **Functional MRI abnormalities on cognitive tasks in newly diagnosed PD patients- ICICLE-PD study**
C. Nombela, J.B. Rowe, A. Hampshire, A.M. Owen, D. Breen, T.K. Khoo, M. Firbank, A. Yarmall, G. Duncan, S. Winder-Rhodes, J.T. O'Brien, D.J. Burn, D.J. Brooks, R.A. Barker (Cambridge, United Kingdom)
- 562** **Mild cognitive impairment in Parkinson's disease: Cut-off and responsiveness values of the Parkinson's disease-cognitive rating scale (PD-CRS)**
J. Pagonabarraga, R. Fernández de Bobadilla, S. Martínez-Horta, B. Pascual-Sedano, A. Campolongo, J. Kulisevsky (Barcelona, Spain)

GUIDED POSTER TOUR 10 – Genetics

Bayside Level 1, Bayside Gallery B

12:00 – 13:30

Wednesday, June 19, 2013

Tour Leaders:

Christine Klein, *Luebeck, Germany*

Daniel Healy, *Dublin, Ireland*

- 1107** **Paroxysmal kinesigenic dyskinesia and PRRT2 mutations: Clinico-genetic correlations**
K. Methawasin, E.W.L. Teng, A.R.J. Ng, S.H. Seah, W.L. Au, J.J. Liu, J.N. Foo, Y. Zhao, E.K. Tan, L.C.S. Tan (Nakorn-Nayok, Thailand)
- 1110** **Phenotypic spectrum of mutations in GNAL: A novel cause of cranio-cervical dystonia**
K.R. Kumar, K. Lohmann, R. Miyamoto, A. Ferbert, T. Lohnau, M. Kasten, J. Hagenah, N. Brueggemann, J. Graf, A. Muenchau, V.S. Kostic, C.M. Sue, A.R. Domingo, R.L. Rosales, L.V. Lee, Y. Mukai, T. Kawarai, R. Kaji, C. Klein, A. Schmidt (Lübeck, Germany)
- 1117** **Clinical features of onset in monogenic Parkinson's disease**
A.E. Elia, J. Azzollini, C. Bagella, M. Carecchio, C. Barzaghi, B. Garavaglia, A. Albanese (Milan, Italy)
- 1123** **SPG11 sequencing in worldwide populations of familial and sporadic spastic paraplegia patients reveals frequent mutations and the common association of parkinsonian features**
E. Kara, L. Schottlaender, A. Berardo, R. Reisin, J. Hehir, D. Hughes, R. Paudel, J. Hersheson, Y.T. Liu, E. Preza, P. Lewis, A. Martin, P. Korlipara, K.P. Bhatia, A. Lees, T. Foltynie, N. Wood, J. Hardy, H. Houlden (London, United Kingdom)
- 1130** **Behavioral characteristics of asymptomatic G2019S mutation carriers of the LRRK2 gene**
A. Thaler, A. Mirelman, K. Yasinovski, M. Zalis, A. Shkedy, A. Hilel, K. Marder, S. Bressman, A. Orr-Urtreger, T. Gurevich, N. Giladi (Tel-Aviv, Israel)
- 1132** **New insights into the genetics of X-linked dystonia-parkinsonism**
A. Domingo, A. Westenberger, R. Rosales, R.D. Jamora, P.M. Pasco, K. Lohmann, L.V. Lee, C. Klein (Lübeck, Germany)
- 1137** **PRRT2 gene mutation analysis in Korean familial and sporadic patients with paroxysmal kinesigenic dyskinesia**
J. Youn, Y. Jeong, J.Y. Ahn, J.W. Cho (Seoul, Korea)
- 1162** **DRD3 receptor polymorphism may confer risk for younger onset Parkinson's disease**
A. Hassan, M.S. Okun, D.J. Serie, M.G. Heckman, J.E. Ahlskog, R.J. Uitti, Z. Wszolek, O.A. Ross (Rochester, MN, USA)
- 1167** **Withdrawn by Author**
- 1168** **A novel heterozygous mutation in ATP synthase (electron transport chain complex V) subunit c gene ATP5G3 causes autosomal dominant dystonia and spastic paraplegia**
D.L. Gilbert, N.D. Leslie, R.B. Hufnagel, D.E. Neilson (Cincinnati, OH, USA)

Guided Poster Tours

GUIDED POSTER TOUR 11 – Lewy body dementia and other dementias in movement disorders

Bayside Level 2, Bayside 201-203

12:00 – 13:30

Wednesday, June 19, 2013

Tour Leaders:

John Dalrymple-Alford, *Christchurch, New Zealand*
Glenda Halliday, *Randwick, Australia*

- 501** **Meta analysis: Donepezil in the treatment of cognitive impairment dementia in patients with Parkinson's disease**
E.A. Barcelon, L. Shiong Shiu, P.M.D. Pasco (Manila, Philippines)
- 1179** **Metabolic impairments of brain in patients with probable dementia of lewy bodies**
Y. Yang, S. Kim (Seoul, Korea)
- 1180** **Omi-mediated detoxification of α -synuclein-induced neurotoxicity in a drosophila model of Parkinson's disease**
M.M. Rahman, S. Akhter, M.S. Islam, H.J. Kim, S.T. Hong (Jeonju-si, Korea)
- 516** **Cognitive impairment after deep brain stimulation: A follow-up study and influence of age**
E. Herrera, S. González, R. Merino, R. Ribacoba, E. Suárez, F. Cuetos (Oviedo, Spain)
- 522** **Cognitive function and postural instability in people with Parkinson's disease**
D. Xu, M. Cole, K. Mengersen, P. Silburn, G. Kerr (Brisbane, Australia)
- 525** **Criteria for mild cognitive impairment in Parkinson's disease: Applicability and validity**
G.J. Geurtsen, B.A. Schmand, I. Litvan, J.G. Goldman, A.I. Tröster (Amsterdam, Netherlands)
- 528** **Could depression confound performance on neuropsychological testing in Parkinson's disease (PD) patients?**
T.P. Lin, J.N. Caviness, J.G. Hentz, S.A. Jacobson, C.M. Belden, M.N. Sabbagh, H.A. Shill, E.D. Driver-Dunckley, T.G. Beach, C.H. Adler, Arizona Parkinson Disease Consortium (Scottsdale, AZ, USA)
- 549** **Pathological organization of resting-state functional brain networks in Parkinson's disease: A longitudinal MEG graph theoretical analysis**
K.T.E. Olde Dubbelink, A. Hillebrand, D. Stoffers, J.B. Deijen, J.W.R.W. Twisk, C.J. Stam, H.W. Berendse (Amsterdam, Netherlands)
- 558** **Object / scene recognition in patients with Parkinson's disease with and without visual hallucination**
P. Maruque, F. Ory, L. Saint-Aubert, F. Remy, N. Bacon-Macé, M. Fabre-Thorpe, E.J. Barbeau, C. Brefel-Courbon (Toulouse, France)
- 568** **The prevalence and nature of mild cognitive impairment in Parkinson's disease (PD-MCI) identified using automated cognitive tests**
K.A. Wesnes, D.J. Burn (Goring on Thames, United Kingdom)

GUIDED POSTER TOUR 12 – Surgical therapy of movement disorders other than Parkinson's disease

Bayside Level 2, Bayside 204

12:00 – 13:30

Wednesday, June 19, 2013

Tour Leaders:

Joachim Krauss, *Hannover, Germany*
Elena Moro, *Grenoble, France*

- 1217** **Withdrawn by Author**
- 1224** **Effect of spinal cord stimulation on gait with patients with PSP**
T. Ichikawa, H. Oshima, Y. Fumimura, Y. Nishida (Ageo City, Japan)
- 1225** **Influence of electrode position and outcome following deep brain stimulation surgery in the management of childhood primary and secondary dystonias**
D.E. Lumsden, J. Ashmore, H. Gimeno, R. O'Gorman, G. Charles-Edwards, K. Ashkan, R. Selway, J.P. Lin (London, United Kingdom)
- 1228** **A new procedure of selective denervation and myotomy for laterocollis cervical dystonia: Results in 66 cases**
J. Liang, S. Ji, A. Ma (Wuhan, China)
- 1229** **Long-term follow-up study for patients with primary generalized dystonia treated by bilateral pallidal stimulation**
M. Sobstyl, M. Zabek, Z. Mossakowski (Warsaw, Poland)
- 1234** **Long-term follow-up of GPi deep brain stimulation in generalized dystonia: Primary dystonia compared to cerebral palsy**
L.M. Romito, G. Zorzi, M.L. Ciceri, C.E. Marras, A. Franzini, N. Nardocci, A. Albanese (Milan, Italy)
- 1235** **Long-term follow up of chronic spinal cord stimulation in medically intractable orthostatic tremor**
T. Sauer, C. Blahak, G. Luetjens, A. Saryyeva, H. Baezner, H.H. Capelle, J.C. Woehrle, M.G. Hennerici, J.K. Krauss (Mannheim, Germany)
- 1242** **Deep brain stimulation of the caudal zona incerta and the posterior subthalamic area in essential tremor, is there an optimal area for stimulation?**
A. Fytgoridis, M. Åström, P. Blomstedt (Stockholm, Sweden)
- 1245** **Causes of therapeutic failure of pallidal deep brain stimulation in primary dystonia**
K.A.M. Pauls, J.K. Krauss, C.E. Kämpfer, C. Schrader, M. Südmeyer, N. Allert, R. Benecke, C. Blahak, J.K. Boller, W. Fogel, F. El Majdoub, J. Kessler, J. Kuhn, J. Voges, M. Wittstock, A.A. Kühn, E. Moro, J. Volkmann, K.P. Bhatia, M. Maarouf, L. Timmermann (Köln, Germany)
- 1247** **Gammaknife thalamotomy for intractable tremors: Clinical outcome and correlations with neuroimaging features**
T. Witjas, R. Carron, J.P. Azulay, J. Regis (Marseille, France)

Guided Poster Tours

GUIDED POSTER TOUR 13 – Huntington's disease

Bayside Level 1, Bayside Gallery A

13:00 – 14:30

Thursday, June 20, 2013

Tour Leaders:

Elizabeth McCusker, *Westmead, Australia*

Ralf Reilmann, *Muenster, Germany*

751 **Mutant huntingtin impair mitochondrial movement and trafficking in hippocampal neurons**

B. Zhang, J. Tian, Y. Yan (Hangzhou, China)

754 **Withdrawn by Author**

756 **Withdrawn by Author**

757 **FTY720 is neuroprotective in Huntington's disease**

V. Maglione, A. Di Pardo, E. Amico, M. Favellato, R. Castrataro, S. Fucile, F. Squitieri (Pozzilli, Italy)

758 **Abnormal implicit prediction in rhythmical saccadic movement of manifest Huntington patients: A 12 months longitudinal study**

E.A. Toh, M. MacAskill, J. Dalrymple-Alford, D. Myall, S. MacLeod, L. Livingston, T. Anderson (Christchurch, New Zealand)

764 **Changes in cerebral vasculature in patients with Huntington's disease**

J. Drouin-Ouellet, I. Saint-Amour, W.L. Kuan, M. Saint-Pierre, R.A. Barker, F. Cicchetti (Cambridge, United Kingdom)

765 **The pharmacokinetics of extended release SD-809, a deuterium-substituted analogue of tetrabenazine**

D.A. Stampler, F. Brown, M. Bradbury (La Jolla, CA, USA)

767 **Quantifying Huntington's disease (HD) burden internationally**

J. Dorey, F. Squitieri, C. Verny, D. Zielonka, J. Cohen, M. Tuomi (Lyon, France)

768 **Potential neuroprotective effects of pridopidine in Huntington's disease**

A. DiPardo, V. Maglione, M.G. Favellato, E. Amico, F. Squitieri (Pozzilli, Italy)

769 **Model-based meta-analysis (MBMA) of UHDRS-Total motor score in Huntington's disease (HD) clinical trials**

Y. Jin, S. Ahadieh, S. Papapetropoulos, J. Liu (Cambridge, MA, USA)

GUIDED POSTER TOUR 14 – Parkinson's disease: Clinical trials

Bayside Level 1, Bayside Gallery B

13:00 – 14:30

Thursday, June 20, 2013

Tour Leaders:

Jeffrey Kordower, *Chicago, IL, USA*

Robert Hauser, *Tampa, FL, USA*

383 **Withdrawn by Author**

389 **Efficacy of rasagiline 1mg/day on key motor symptoms of early Parkinson's disease: Post-hoc analysis from the Attenuation of Disease progression with Azilect® Glven Once-daily (ADAGIO) study**
E. Tolosa (Barcelona, Spain)

395 **Zonisamide improves wearing-off in Parkinson's disease: A nation-wide randomized, double-blind study**

M. Murata, K. Hasegawa, J. Fukasaka, K. Kochi, I. Kanazawa, T. The Japan Zonisamide on PD Study Group (Tokyo, Japan)

404 **Malignant melanoma in early treated Parkinson's disease: The NET-PD trial**

R. Constantinescu, E.F. Augustine, P. Auinger, S. Sharma, L. Khadim, K. Kiebertz (Rochester, NY, USA)

442 **Exercise for falls prevention in Parkinson's disease: A randomised controlled trial**

C.G. Canning, C. Sherrington, S.R. Lord, J.C.T. Close, G. Heller, S. Heritier, K. Howard, N.E. Allen, S.S. Paul, S.M. Murray, S.D. O'Rourke, V.S.C. Fung (Sydney, Australia)

444 **A phase 2, placebo-controlled, randomized, double-blind trial of tozadenant (SYN-115) in patients with Parkinson's disease with wearing-off fluctuations on levodopa**

R.A. Hauser, C.W. Olanow, K. Kiebertz, A. Neale, C. Resburg, U. Maya, S. Bandak (Tampa, FL, USA)

446 **A placebo controlled, randomized, double-blind study to assess the safety and clinical benefit of rasagiline as an add-on to dopamine agonist monotherapy in early Parkinson's disease (PD): The ANDANTE study**

R.A. Hauser, D. Silver, A. Choudhry, S. Isaacson (Tampa, FL, USA)

452 **Constant therapeutic levodopa (LD) plasma concentrations maintained by continuous subcutaneous (SC) administration of ND-0612, a novel formulation of LD/carbidopa (CD)**

Y. Caraco, S. Oren, P. LeWitt (Ness Ziona, Israel)

468 **Impact of droxidopa treatment in patients with Parkinson's disease and symptomatic neurogenic orthostatic hypotension (study 306)**

S.H. Isaacson, R.A. Hauser, C.B.N. Szakacs, C.C. Cioffi (Boca Raton, FL, USA)

499 **Sustained-release carbidopa-levodopa (accordian pill) in patients with advanced Parkinson's disease: Pharmacokinetic and clinical experience**

P. LeWitt, H. Friedman, N. Giladi, T. Gurevich, H. Shabtai, R. Djaldetti, N. Roizen, S. Hassin-Baer, O. Cohen, G. Yahalom, I. Schlessinger, M. Nassar, R. Milo, M. Anka, P. Farkas, N. Navon (West Bloomfield, MI, USA)

Guided Poster Tours

GUIDED POSTER TOUR 15 – Parkinson's disease: Phenomenology

Bayside Level 2, Bayside 201-203

13:00 – 14:30

Thursday, June 20, 2013

Tour Leaders:

Timothy Lynch, *Dublin, Ireland*

David Riley, *South Euclid, OH, USA*

- 860** **Tract-based spatial statistics and voxel based analysis in Parkinson's disease patients with freezing of gait**
J. Youn, Y. Jeong, J.Y. Ahn, J.W. Cho (Seoul, Korea)
- 862** **Ancillary investigations to diagnose Parkinson's disease and atypical Parkinsonism: A prospective clinical study**
M.B. Aerts, R.A.J. Esselink, W.F. Abdo, F.J.A. Meijer, M.M. Verbeek, B.R. Bloem (Nijmegen, Netherlands)
- 866** **Synergic and independent influences of MAPT and SNCA on the motor decline in Parkinson's disease**
G. Wang, S. Chen, Y. Wang, Q. Xiao, J. Liu, S. Chen, Y. Huang (Sydney, Australia)
- 878** **Bedside test facilitates differentiation between PISA and scoliosis in PD patients**
F. Gandor, D. Gruber, G. Ebersbach (Beelitz-Heilstätten, Germany)
- 880** **A cluster analysis on newly diagnosed untreated PD patients**
R. Erro, C. Vitale, M. Picillo, M. Amboni, P. Barone (Naples, Italy)
- 886** **Is carrying the G2019S mutation in the leucine-rich repeat kinase 2 gene associated with a different rate of progression of Parkinson's disease?**
G. Yahalom, Y. Orlev, O.S. Cohen, R. Inzelberg, E. Kozlova, E. Friedman, U. Goldbourt, S. Hassin-Baer (Tel-Hashomer, Israel)
- 889** **FBX07 mutation: Phenotypic variability from chorea to early-onset asymmetric parkinsonism within a family**
A. Gunduz, A. Gündogdu Eken, K. Bilgüvar, M. Günel, A.N. Basak, H. Hanagasi, S. Ertan (Istanbul, Turkey)
- 890** **Motor and cognitive features discriminate new fallers from non-fallers in an incident cohort of Parkinson's disease**
B. Galna, S. Lord, D. Mhiripiri, D. Burn, L. Rochester (Newcastle upon Tyne, United Kingdom)
- 904** **Subthreshold depression and subjective cognitive complaints in Parkinson's disease**
G. Santangelo, C. Vitale, L. Trojano, M.G. Angrisano, M. Picillo, D. Errico, V. Agosti, D. Grossi, P. Barone (Caserta, Italy)
- 909** **Increased activation of the frontal lobe is associated with freezing of gait in patients with Parkinson's disease: An fNIRS study**
I. Maidan, H. Bernad-Elazari, E. Gazit, M. Brozgol, N. Giladi, A. Mirelman, J.M. Hausdorff (Tel-Aviv, Israel)

GUIDED POSTER TOUR 16 – Tremor

Bayside Level 2, Bayside 204

13:00 – 14:30

Thursday, June 20, 2013

Tour Leaders:

Mark Edwards, *London, United Kingdom*

- 939** **Sensitivity to change of the essential tremor rating assessment scale (TETRAS)**
B. Voller, E. Lines, G. McCrossin, A. Artilles, S. Tinaz, C. Lungu, M. Hallett, D. Haubenberger (Bethesda, MD, USA)
- 941** **Continuous home monitoring of essential tremor using motion sensors**
D. Heldman, C. Pulliam, S. Eichenseer, C. Goetz, O. Waln, C. Hunter, J. Jankovic, D. Vaillancourt, J. Giuffrida (Cleveland, OH, USA)
- 947** **Patients with scans without evidence of dopaminergic deficit (SWEDD) do not have Parkinson's disease- A long term follow up study**
A. Batla, M. Stamelou, K.P. Bhatia (London, United Kingdom)
- 948** **Alcohol responsiveness in different tremor disorders**
P. Schwingenschuh, M. Koegl-Wallner, U. Werner, C. Ghadery, T. Pendl, S. Seiler, K. Wenzel, R. Schmidt, P. Katschnig-Winter (Graz, Austria)
- 949** **Lateralization of structural abnormalities in right cerebellum in essential tremor: An observation from voxel based morphometry study**
K. Bhalsing, N. Upadhyay, R. Yadav, J. Saini, A. Gupta, P. Pal (Bangalore, India)
- 954** **Movement disorders associated with chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS)**
A.D. Ha, J.D. Parratt, S. Babu, S.D. Kim, N. Mahant, V.S.C. Fung (Westmead, Australia)
- 957** **Diagnosing postural tremor using intermuscular coherence and cumulant analysis**
A.M.M. van der Stouwe, L. Woudt, J.W. Elting, M.A.J. de Koning-Tijssen, N.M. Maurits (Groningen, Netherlands)
- 958** **Spatiotemporal parameters from three-dimensional tremor analysis may help to differentiate essential tremor from parkinsonian tremor**
C. Blahak, T. Sauer, M.E. Wolf, J.C. Wöhrle, M.G. Hennerici (Mannheim, Germany)
- 976** **Tremor retraining as therapeutic strategy for patients with psychogenic tremor: A proof-of-concept study**
A.J. Espay, G. Oggioni, M.J. Edwards, N. Phielipp, H. Gonzalez-Usigli, C. Pecina, D.A. Heldman, J. Mishra, A.E. Lang (Cincinnati, OH, USA)
- 978** **Ataxia is common in patients with orthostatic tremor**
D. Bhatti, C. Srikanth-Mysore, J. Bertoni, D. Torres-Russotto (Omaha, NE, USA)



STOCKHOLM
sweden
JUNE 8-12, 2014

**18TH INTERNATIONAL CONGRESS OF PARKINSON'S DISEASE
AND MOVEMENT DISORDERS**



The Movement Disorder Society

2014 Important Dates

October 1, 2013

Abstract Submission Opens

December 2, 2013

Registration Opens

January 6, 2014

Abstract Submission Closes

April 11, 2014

Early Registration Deadline

May 9, 2014

Final Pre-registration Deadline

June 8-12, 2014

18th International Congress of Parkinson's
Disease and Movement Disorders



SAVE THE DATE