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

2015 MDS LATE-BREAKING ABSTRACTS

LBA 1

Occurrence of impulsive compulsive behaviours in patients with Parkinson's disease treated with apomorphine

Pedro Barbosa, Atbin Djamshidian, Cathy Magee, Andrew J Lees; Thomas T Warner

Queen Square Brain Bank for Neurological Disorders, UCL Institute of Neurology, London, United Kingdom

Objectives: To study the role of apomorphine in the development of Parkinson's disease de novo Impulse compulsive behaviours (ICBs) or recurrence of pre-existing ICBs in a retrospective audit.

Background: Impulsive compulsive behaviours (ICBs) such as pathological gambling, compulsive sexual behaviour, compulsive eating and shopping and the overuse of dopaminergic medication can have devastating consequences on the lives of patients with Parkinson's disease (PD) and their family members. Initially it was reported that ICBs occur in 14% of all patients treated with dopamine agonists (DAs) and approximately one quarter of them have more than one addiction. However, more recent studies have shown that ICBs may be far more common, and can affect up to 39% of all PD patients treated with DAs.

Oral DAs ropinirole and pramipexole have high affinity for the D2 and D3 receptors and these drugs do not stimulate D1 receptors, while apomorphine binds to D1 and D2 receptors. Considering that D3 receptors are mainly found on the limbic system some authors have postulated that these differences might be responsible for the increased prevalence of ICBs in patients using DAs.

Apomorphine has a different receptor profile with higher affinity for D1 and D2 receptors, resembling the dopamine's action. Whether this difference translates in decreased risk of developing ICBs is not yet clear but initial reports are conflicting. A two-year follow up study showed no ICBs in patients receiving apomorphine during daytime in combination with night time rotigotine and another audit showing improvement in ICBs after treatment with apomorphine. However, one study reported six de novo ICB cases (excessive eating, compulsive shopping and internet use, and hypersexuality) in patients using apomorphine pump. In one of them the ICBs were severe and apomorphine pump had to be stopped.

Methods: We conducted a retrospective audit of PD patients treated with apomorphine at the National Hospital for Neurology and Neurosurgery, Queen Square London, UK. We included all patients who were registered as active users of apomorphine on the year 2014. We excluded patients whose files were incomplete. All files were reviewed by a Movement Disorders Specialist. Data was analysed using the software Minitab© 15.

Results: In total, we included 36 PD patients (22 male) with mean disease duration of 16.52 years. Mean disease duration when starting apomorphine was 14 years. On average patients were using apomorphine for 33.4 months with a mean maximum daily dosage of 54.87 mg in the pump group and 14.07 mg in the pen group. Eighteen patients had ICBs at some point, 17 prior to the start of apomorphine pump. Eleven of these improved prior to starting apomorphine as a result of reducing/discontinuing their oral DA, and ICBs did not reoccur on apomorphine therapy. Six patients had active ICBs when apomorphine was started. Four of these patients improved and two did not experience any change after apomorphine pump treatment.

Conclusions: The data collected in this audit suggests that apomorphine has a low risk in triggering or worsening addictive behaviour in PD. Furthermore, our results suggest that apomorphine can be considered in patients with active ICBs or who had a history of addictions. Larger, double-blind trials are needed.

LBA 2

A panel of 16 biomarkers from multiple modalities separates Parkinson's disease patients with and without dementia

Yosef Berlyand, Ian Mellis, Daniel Weintraub, Jimit Doshi, Jacqueline Rick, Christos Davatzikos, Leslie M. Shaw, Howard Hurtig, John Q. Trojanowski, Alice S. Chen-Plotkin

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA

Objectives: (1) To determine whether a multimodal biomarker panel can separate cognitively normal Parkinson's disease patients (PD-CN) from PD patients with dementia (PDD) and (2) To define a pathophysiological subtype of cognitive impairment (CI) in PD with a biomar.

Background: Several biomarkers have previously been shown to correlate with PDD or AD at baseline or to predict cognitive decline in PD or AD. However, relationships among these biomarkers, and particularly among biomarkers from different modalities (e.g. biochemical, genetic, imaging markers) have not been explored.

Methods: A panel of 16 biomarkers previously reported to correlate with cognition in Parkinson's disease was evaluated in a cohort of 75 PD (47 CN, 20 PD with mild cognitive impairment, 8 PDD) patients recruited at the Penn Udall Center. These biomarkers represented multiple modalities – including clinical, neuropsychological, biochemical, genetic, and imaging data. Five of these biomarkers (CSF Aβ1-42, CSF total tau, CSF phosphorylated tau, APOE genotype, and the SPARE-AD score, which is a global measure of atrophy trained on AD brain imaging) were designated as "AD-biomarkers" based on existing literature. The utility of these "AD-biomarkers" in classifying AD vs. normal controls was validated on a set of 210 patients (101 AD, 109 CN) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort; this five-marker panel was then used to evaluate the Udall PD cohort.

Results: A bivariate cross-sectional analysis of the biomarker panel comparing PD-CN vs. PDD in the current set of patients (n=55 for PD-CN and PDD patients) confirmed previously-reported associations between cognition in PD and three candidate biomarkers: SPARE-AD score (p=0.003), levels of CSF A β 1-42 (p=0.008), and UPDRS-III score (p<0.001). A principal component analysis (PCA) using all 16 markers separated PD-CN from PDD patients along the first PC with a true positive rate of 0.875, true negative rate of 0.936, and an accuracy of 0.927. Using data from only the five AD-biomarker subset, however, PD-CN and PDD patients overlapped substantially. The poor utility of these five biomarkers in PD classification stands in contrast to their utility in AD subjects, where the same five biomarkers largely separated AD from control subjects in the ADNI cohort.

Conclusions: Analysis of a single-site cohort reveals that with a panel of 16 biomarkers from multiple modalities, it is possible to separate PD-CN patients from those with PDD. Moreover, PD patients, even those with PDD, exhibit a biomarker profile that is distinct from AD subjects, suggesting other underlying pathophysiological mechanisms for cognitive impairment in PD.

LBA 3 Deep brain stimulation of the globus pallidus pars interna or subthalamic nucleus for Parkinson's disease: 3-year follow-up of a randomized controlled trial.

Judith A. Boel, Vincent J.J. Odekerken, Gert J. Geurtsen, Ben A. Schmand, M. Figee, Rob J. de Haan, P. Richard Schuurman, Rob M.A. de Bie, and the NSTAPS study group

Department of Neurology, Department of Medical Psychology, Department of Psychiatry, Clinical Research Unit, Department of Neurosurgery, Academic Medical Center, Amsterdam, The Netherlands. Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands

Objectives: To investigate motor function, cognition, mood, and behavior 3 years after bilateral deep brain stimulation (DBS) of the globus pallidus pars interna (GPi) and subthalamic nucleus (STN) for advanced Parkinson's disease.

Background: GPi DBS and STN DBS are both treatment options for levodopa responsive symptoms in advanced Parkinson's disease. Based on the 12 months results of our study (Odekerken et al., 2013), we hypothesized that after 3 years, STN DBS gives more improvement in motor symptoms in off-drug phase than GPi DBS.

Methods: Patients who were aged 18 years or older with idiopathic Parkinson's disease that were eligible for DBS were recruited from five centers in the Netherlands and randomized between bilateral GPi DBS and bilateral STN DBS (1:1). All patients had at least one of the following symptoms despite optimal pharmacologic treatment: severe response fluctuations, dyskinesias, painful dystonias, or bradykinesia. We report the 3 years follow-up, for which the primary outcome measures were: (1) improvement in motor symptoms in off-drug phase on the Unified Parkinson Disease rating Scale (UPDRS) and (2) a composite score for cognition, mood, behavioral effects, and inability to complete follow-up at 3 years after surgery.

Results: Of the 128 patients enrolled in the trial, 90 were able to complete the 3 years follow-up. On primary outcome measures, we found a significantly better improvement of the motor symptoms after STN DBS (median [IQR] at 3 years, GPi 33 [23-41], STN 28 [20-36], p=0.04). No between-group differences were observed on the composite score (GPi n=39 [83%], STN n=37[86%]). Secondary outcomes showed larger improvement of off-drug functioning on the AMC Linear Disability Score after STN DBS (mean±SD, GPi 65.2 ±20.1, STN 72.6±18.0, p<0.05). Medication (levodopa equivalent dose) was reduced more after STN DBS (median [IQR] at 3 years, GPi 1060 [657-1860], STN 605 [411-875], p<0.001). No differences in adverse effects were recorded. There were more re-operations to a different target after GPi DBS (GPI n=8, STN n=1).

Conclusions: Our findings on 3-year outcome suggest that STN DBS could be the preferred target in patients with advanced Parkinson's disease.

LBA 4

Clinical outcomes in Parkinson's disease for asleep deep brain stimulation with electrodes placed using intraoperative imaging versus awake deep brain stimulation with microelectrode recording

Matthew Brodsky, Joanna O'Leary, Mara Seier, Shannon Donovan, Jennifer Wilhelm, Kitty Leelaamornivichet, Kim Burchiel

Oregon Health & Science University, Portland, OR, USA

Objectives: To compare the difference in clinical outcomes for deep brain stimulation (DBS) surgery for Parkinson's disease (PD) when target localization is performed via intraoperative computed tomography imaging (ICT) versus microelectrode recording (MER).

Background: MER has been the gold standard for lead targeting in DBS, however patients must be awake during this surgery, it requires more instrumentation passes into the brain, and operative time is longer. Targeting can also be performed using intraoperative imaging to place electrodes with equal accuracy. This method is appealing to patients since it is performed under general anesthesia, and further may result in lower morbidity and greater cost effectiveness, however clinical outcomes for PD patients using this technique have yet to be reported.

Methods: Patients with PD and motor complications referred for DBS were prospectively enrolled and underwent implantation in either the STN or GPi using ICT. A historical control PD cohort underwent DBS implantation of the STN or GPi by the same surgeon at the same medical center using MER and test stimulation for target guidance. Baseline UPDRS, motor diaries, and the PD Questionnaire (PDQ-39) was performed at baseline and 6 months. DBS optimization was performed at 1,2,3 and 6 months post-implant.

Results: 30 subjects underwent GPi or STN DBS using imaging guidance (9 STN and 21 GPi, mean age 61.1) and 34 subjects underwent DBS using MER guidance (15 STN and 19 GPi, mean age=62.7). Mean improvement in the off medication/on DBS motor Unified PD Rating Scale (mUPDRS) at 6 months in the ICT group was 14.3 (10.88), and in the MER group was 17.6 (12.26). There was no observable difference in the change of mUPDRS from baseline to 6 months in the off medication/on DBS state between the MER and imaging-guided groups (t=1.15, p=0.25). Secondary outcomes in the ICT group included a 16 point improvement in the mean PDQ-39 from 88.9 to 72.9 (p= 0.005), 5.6 point improvement in mean UPDRS II (ADLs) from 15.0 to 10.6 (p=0.01), an increase in ON time without dyskinesia by 4 hours per day from a mean of 7.4 to 11.4 (p=0.04), and a decrease in ON time with dyskinesia by 3.5 hours per day from a mean of 4.6 to 1.1 (p=0.004). There were no serious adverse events in the subjects who underwent DBS using ICT.

Conclusions: Motor outcomes for asleep DBS using ICT targeting were equivalent to awake DBS using MER targeting. Secondary outcomes of asleep DBS looking at quality of life, activities of daily living, and improvement in motor complications were on par with those previously reported with awake DBS. Asleep DBS was well tolerated with no complications, and should be an option that is offered to PD patients who are candidates for this therapy.

LBA 5

Genome-wide expression profiling identifies potential molecular pathways involved in X-linked dystonia-parkinsonism (XDP, DYT3)

Aloysius Domingo, Ana Westenberger, David Amar, Lillian Lee, Raymond Rosales, Roland Dominic Jamora, Eva Cutiongco-dela Paz, Ron Shamir, Katja Lohmann, Christine Klein

Institute of Neurogenetics, Luebeck, Germany; Edmond Safra Center for Bioinformatics, Tel Aviv, Israel; XDP Study Group, Manila, Philippines; National Institutes of Health, University of the Philippines, Manila; Graduate School for Computing in Medicine and Life Sciences, Luebeck, Germany

Objectives: To discover dysregulated genes and affected molecular pathways in X-linked dystoniaparkinsonism (XDP, DYT3). **Background:** Although the exact molecular mechanisms surrounding XDP pathogenesis are not yet elucidated, genetic studies suggest the involvement of TAF1 (TATA-binding protein associated factor 1), a critical component of RNA polymerase II-based transcription in cells.

Methods: We first compared TAF1 expression in patients and controls using RNA extracted from blood and fibroblasts. To then determine whether the expression difference in TAF1 would have a significant effect on the expression levels of target genes, we performed microarray-based genome-wide expression profiling and subsequent follow-up via qPCR.

Results: TAF1 was underexpressed in patients in blood and in fibroblasts, although with a small foldchange (FC<1.3, p<0.05). In the microarray, at least 110 genes were differentially expressed in fibroblasts, whereas only the succinic semialdehyde dehydrogenase gene (ALDH5A1), which participates in GABA metabolism, was discovered to be downregulated in blood (FC>2.3, p<0.05), exemplifying a profound tissue-specific effect. In XDP mutant fibroblasts, we found significant underexpression of synaptotagmin-like 2 (SYTL2), a gene involved in vesicle docking and exocytosis (FC>2.2, p<0.01), and overexpression of KCND2 (FC>3.2, p<0.1), which codes for a voltage-gated potassium channel involved in neuronal excitability.

Conclusions: Our study is the first to show the transcriptional effect of putative XDP-causing mutations in TAF1 in endogenous models, while also implicating dysregulated genes and potentially diseased pathways (GABA metabolism, neurotransmitter release, neuronal excitability) in the molecular pathogenesis of XDP.

LBA 6

Neuronal Plasmalemmal Disruptions Induce Alterations in Dopaminergic Neurons and Alpha-Synuclein Expression Following Traumatic Brain Injury in Swine

John E. Duda, Carolyn Keating, Marissa Kamarck, James P. Harris, Kevin D. Browne, D. Kacy Cullen

Center for Neurotrauma, Neurodegeneration, and Restoration, Philadelphia Veterans Affairs Medical Center, and the Departments of Neurology and Neurosurgery, University of Pennsylvania, Philadelphia, PA, USA

Objectives: To determine if neurons in the substantia nigra and surrounding nuclei are vulnerable to trauma-induced plasmalemmal damage following single or repetitive closed-head traumatic brain injury (TBI) in swine and to assess the pathophysiological consequences.

Background: TBI may be a risk factor for the development of Parkinson's, Alzheimer's, and chronic traumatic encephalopathy (CTE). However, the mechanisms linking trauma-induced cellular responses to chronic neurodegenerative sequelae are unknown, but are believed to involve the emergence and propagation of pathological isoforms of proteins such as tau, β -amyloid, and α -synuclein.

Methods: Swine were subjected to sham conditions or rotational head velocity/acceleration (80-299 radians/second) using a HYGE pneumatic actuator, either a single injury or two injuries separated by 15 minutes or 7 days. To assess plasmalemmal compromise, Lucifer Yellow (LY), a small (457 Da) cell impermeant dye, was administered into the lateral ventricles in a subset of animals prior to injury. Animals were sacrificed within 15 minutes (those receiving LY), 8 hours, or 7 days post-injury (n=29 total) for immunohistochemical analysis.

Results: Closed-head inertial TBI induced acute plasmalemmal permeability – as shown by intracellular accumulation of LY – in primarily neurons, the extent of which increased as a function of head rotational

velocity. Specifically, LY+ cells were observed in the cerebral cortex, sub-cortical white matter and thalamus/midbrain, concentrated around blood vessels in many cases, following both single or repetitive TBI (each p<0.05 vs. sham). In particular, clusters of permeabilized neurons were observed in the substantia nigra, demonstrating acute vulnerability in inertial TBI. Moreover, increases in α -synuclein expression was observed in some permeabilized neurons, suggesting an acute stress response or other mechanism of over-expression.

Conclusions: This is the first report demonstrating that substantia nigra neurons are vulnerable to acute plasmalemmal damage following closed head rotational TBI in swine, a model with biomechanical fidelity to inertial TBI in humans. These results increase our understanding of the links between the physical and pathophysiological consequences of TBI, and suggest a co-occurrence of plasmalemmal damage with the emergence of α -synuclein over-expression. Further studies will help to understand the relationship between these acute alterations and later developing neurodegenerative pathologies.

LBA 7 Marked parasympathetic denervation in the gut of de novo Parkinson's disease - A [11C]donepezil PET study

Tatyana Fedorova, Erik Danielsen, Nicola Pavese, David Brooks, Per Borghammer

Departments of Nuclear Medicine and Neurology, Aarhus University Hospital, Aarhus, Denmark

Objectives: To investigate [11C]donepezil, an acetylcholinesterase ligand, for PET imaging of peripheral parasympathetic innervation in de novo Parkinson's disease (PD).

Background: Using [11C]donepezil PET, we recently demonstrated that nearly all PD patients at a moderate disease stage display decreased signal in the small intestine, and 2/3 of patients showed a decrease in the pancreas (Gjerløff et al, Brain 2015). Constipation is a highly prevalent premotor symptom, and the dorsal motor nucleus of the vagus exhibit consistent degeneration in early PD. Parasympathetic imaging of internal organs could therefore be a potential diagnostic marker at pre-motor stages of the disease.

Methods: By June 2015, we aim to include 18 PD patients at an early disease-stage (mean 1 year disease duration) and 15 matched control subjects. All study participants receive a PET/CT scan using [11C]donepezil. The PET signal in the myocardium, gastrointestinal tract, and pancreas will be compared between the groups.

Results: Here we present initial results from 14 PD patients and 8 controls. The de novo PD patients displayed significantly decreased [11C]donepezil SUV values in the small intestine (-25%, p=0.0003), and myocardium (-13%, p=0.029), but not in the pancreas (p=0.75) (Figure 1).



Conclusions: Our data suggests that marked parasympathetic denervation in the gut of PD patients is already established at the time of diagnosis, whereas denervation of the pancreas may be a secondary phenomenon. [11C]donepezil PET could therefore have utility as a diagnostic marker in PD – perhaps already at the pre-motor stage. We are currently initiating a longitudinal [11C]donepezil PET study of RBD patients to test this hypothesis.

LBA 8

Stable levodopa plasma levels with ND0612 (levodopa/carbidopa for subcutaneous infusion) in Parkinson's disease (PD) patients with motor fluctuations

Nir Giladi, Yoseph Caraco, Tanya Gurevich, Ruth Djaldetti, Yael Cohen, Oron Yacobi-Zeevi, Shelia Oren, Karl Kieburtz, C. Warren Olanow

Tel Aviv Medical Center, Tel Aviv University, Tel Aviv, Israel; Hadassah Medical Center, Jerusalem, Israel; Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; Tel Aviv University, Tel Aviv, Israel, NeuroDerm Ltd., Rehovot, Israel. Clintrex, USA, Tel Aviv, Israel

Objectives: To assess the safety, tolerability and pharmacokinetics of six dose regimens of ND0612, a novel liquid formulation of levodopa/carbidopa administered subcutaneously through a belt-pump delivery system.

Background: Continuous levodopa/carbidopa administration is considered to be the optimal delivery route for treating PD patients with motor fluctuations, but poor levodopa solubility has prevented the development of a subcutaneously-deliverable formulation. Current infusion systems require gastrointestinal surgery to deliver continuous levodopa directly into the duodenum and are associated with potentially serious complications. ND0612 is a proprietary liquid formulation of levodopa/carbidopa that enables for the first time subcutaneous administration of levodopa/carbidopa to achieve steady levodopa plasma levels.

Methods: Sixteen PD patients currently receiving long-term treatment with oral levodopa/carbidopa and experiencing motor fluctuations were treated with standard oral levodopa on day 1. They were then treated with low-dose ND0612 (ND0612L; n=9) or high-dose ND0612 (ND0612H; n=7) administered with high or low dose carbidopa on days 2 and 3. NDO612H with high dose carbidopa and adjunct oral entacapone was administered on day 4. The levodopa pharmacokinetics of ND0612 were compared to pharmacokinetics of oral levodopa/carbidopa. All patients completed the study.

Results: Fluctuations in levodopa plasma levels were markedly reduced for all ND0612 regimens in comparison to oral levodopa/carbidopa. Levodopa plasma levels were dose proportionate. The levodopa Cmax was: 528 ng/ml for ND0612L/low dose carbidopa; 477ng/ml for ND0612L/high dose carbidopa; 596ng/ml for ND0612L/high dose carbidopa plus adjunct entacapone; 1333ng/ml for ND0612H/low dose carbidopa; and 1807ng/ml for ND0612L/high dose carbidopa carbidopa; and 1807ng/ml for ND0612L/high dose carbidopa plus adjunct entacapone. Treatment with ND0612 was well tolerated; occasional mild, transient local reactions at the infusion site were noted.

Conclusions: The results from this study demonstrate that ND0612H given subcutaneously with carbidopa (both high and low doses) can reach high levodopa plasma levels that are stably maintained. ND0612H may offer a simple and effective treatment option that will minimize the need for surgical intervention in patients with advanced PD.

LBA 9 Alpha-synuclein genetic variability : A biomarker for dementia in Parkinson's disease

Ilaria Guella, Matt Farrer, Silke Cresswell, Joseph Tsui, Martin McKeown, Jon Stoessl, Jan Aasly, Ruey-Mei Wu, Jennifer G. Goldman, John Dalrymple-Alford, Gert J. Geurtsen , Irene Litvan, Lefkos T. Middleton, Laura Parkkinen, their respective Sites and Consortia.

Centre for Applied Neurogenetics, University of British Columbia, Vancouver, BC, Canada

Objectives: To develop a prognostic biomarker of Parkinson's disease (PD), cognitive decline and dementia, to inform physicians, their patients and the design of clinical trials aimed at disease modification.

Background: The relationship between PD, PD with dementia (PDD) and dementia with Lewy bodies (DLB) is long debated. Although PD is primarily considered a motor disorder cognitive impairment is often present at diagnosis, and only ~15% of patients remain cognitively intact in the long term. Alpha-synuclein (SNCA) was first implicated in the pathogenesis of the disease when point mutations and locus multiplications were identified in familial parkinsonism with dementia. In world-wide populations SNCA genetic variability remains the most reproducible risk factor for idiopathic PD. The SNCA gene has been also associated with DLB. However, few investigators have looked at SNCA variability in terms of disease progression or cognitive outcomes.

Methods: We have used targeted next-generation sequencing to comprehensively characterize the 135kb SNCA locus in i) the Progressive Parkinson's Markers Initiative de-novo cohort; ii) the Movement Disorders Society PD-Mild Cognitive Impairment cohort; iii) in clinical and brain bank series of PD and DLB.

Results: Early results from an analysis of 44 tagging single nucleotide polymorphisms (SNPs, with MAF>5%) across the entire SNCA locus show two distinct association profiles for parkinsonism and dementia, respectively towards the 3' or the 5' of the SNCA gene. We define a specific haplotype in SNCA intron 4, more intermediate, that is directly associated with PDD. In a validation study, we extend results to patients with PD and mild cognitive impairment, employing longitudinal neuropsychological data detailing cognitive subtypes and rates of impairment. Uniquely, we have been able to interrogate these SNCA disease-associated haplotypes at single nucleotide resolution, and we have been able to assess the molecular correlates.

Conclusions: A genetic biomarker of dementia in PD has been identified; PD, PDD and DLB, rather than a disease continuum, have distinct genetic aetiologies albeit within one gene.

LBA 10

The ReSPonD trial: Rivastigmine to stabilise gait in Parkinson's Disease. A phase II, randomised, double blind, placebo-controlled trial to evaluate the effect of rivastigmine on gait in patients with Parkinson's disease who have fallen

Emily Henderson (1), Stephen Lord (2), Matthew Brodie (2), Jacqueline Close (2,3), Andrew Lawrence (4), Alan Whone (5,6), Yoav Ben-Shlomo (1)

1.School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, BS8 2PS Bristol, UK. Emily.Henderson@bristol.ac.uk. 2. Neuroscience Research Australia, University of New South Wales, Sydney, Australia. 3. Prince of Wales Clinical School, Department of Geriatric Medicine, Sydney, NSW, Australia. 4. School of Psychology, Cardiff University, Cardiff, UK. 5. Department of

Neurology, Institute of Clinical Neurosciences, University of Bristol, Bristol, UK. 6. North Bristol NHS Trust, Bristol, United Kingdom

Objectives: To investigate the effect of the cholinesterase inhibitor Rivastigmine versus placebo on gait variability in patients with Parkinson's Disease (PD) who have fallen in the past year.

Background: Falls are a common and devastating complication of Parkinson's disease (PD) and are cited as one of the worst aspects of the condition(1). An underlying cholinergic deficit contributes to gait dysfunction and cognitive impairment both of which are significant contributors to fall risk. The cholinesterase inhibitor rivastigmine is licensed for the treatment of PD dementia. Use of rivastigmine in falls prevention could represent a novel and acceptable intervention where few effective therapies currently exist.

Methods: This was a phase II, placebo-controlled, double blind, randomised control trial (RCT) (2). Participants were randomised to receive rivastigmine or placebo. The drug was up-titrated over 4 months to a maximum of 6mg twice a day and then maintained at the highest tolerated dose for the following 4 months. Assessments were completed at baseline and after an 8-month treatment period. The primary outcome measure was step time variability (a proxy marker for falls risk) measured in three conditions; a) normal walking b) simple dual task and c) complex dual task. Analysis was performed on an intention-to-treat basis (ITT) using multivariable linear regression, adjusting for 'a priori' specified determinants of falls risk (cognition, age and previous falls) as well as baseline variability.

	Treatment effect	Standard Error	95% CI	p value
Normal walk	-0.339	0.125	-0.588 to -0.091	0.008*
Simple cognitive task	-0.306	0.127	-0.558 to -0.054	0.018*
Complex cognitive task	-0.285	0.136	-0.554 to -0.016	0.038*

Table 1 Adjusted treatment effects

*significant at p<=0.05

Results: The trial recruited to time and target enrolling 130 participants. Baseline characteristics were comparable between the two groups in respect to PD severity, gait and cognitive features. The multivariable regression model showed that treatment with rivastigmine led to an improvement in step time variability in all three walking conditions. The greatest treatment effect was seen during normal walking (p=0.008), table 1. The trial had a high (94%) retention of participants and at follow-up, more people were still taking the drug in the placebo arm (n=49/65) compared to the active arm (n=37/65). Reported adverse events were consistent with the literature, predominantly mild and not related to trial medication. There were 44 Serious Adverse Events (SAE's) two of which were assessed as 'probably' or 'definitely' related to active treatment.

Conclusions: Whilst rivastigmine improved gait variability it remains to be seen whether this translates into a more clinically meaningful reduction in falls risk as has been suggested by a previous small study of donepezil (3).

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LBA 11

A non-human primate model of Parkinson's disease based on viral vector mediated overexpression of alpha-synuclein

James Koprich, Tom Johnston, John Seibyl, Ken Marek, Yilong Ma, David Eidelberg, Chuantao Zuo, Yi Hui Guan, Jeffrey Kordower, Susan Fox, Jonathan Brotchie

Atuka Inc., Toronto, Canada; Molecular Neuroimaging, New Haven, USA; Feinstein Institute for Medical Research, Manhasset, USA; PET Center, Huashan Hospital, Fudan University, Shanghai, China; Rush University Medical Center, Chicago, USA; Movement Disorders Clinic, University Health Network, Toronto, Canada, Toronto, ON, Canada

Objectives: To develop a new non-human primate model of Parkinson's disease (PD) based on viral vector mediated overexpression of A53T alpha-synuclein (aSyn) to serve as a preclinical testing platform for evaluating potential therapeutics.

Background: Parkinson's disease is an alpha-synucleinopathy. While rodent models of synucleinopathy have proven useful in better understanding normal aSyn function, pathology and biochemistry, currently lacking in the field is a robust, well-characterized non-human primate model based on aSyn overexpression to optimally transition therapeutic development between rodent and human.

Methods: 12 cynomolgus macaques were enrolled in the study (female, 9yrs old). Each received baseline behavioural assessments on motor activity, non-human primate parkinsonian disability rating scale (MPPrs) and were trained to conduct a fine motor task (mMAP test). Behaviour was assessed once monthly. Baseline PET scans were obtained using 18F-labelled AV133 (VMAT-2) and FDG (fluorodeoxyglucose) and were both conducted every 2 months. Animals were bilaterally injected with either AAV1/2 A53T aSyn or empty vector (EV) (both, 1.7 x 10exp12 gp/ml) into each hemisphere of the substantia nigra (SN). Animals were sacrificed 8 months post surgery.

Results: Postmortem results showed a 42% and a 39% reduction in putaminal DA and DAT, respectively, compared to controls (all, P<0.05), along with a reduction in TH positive neurons in the SN. Immunolabeling of the SN showed Lewy pathology revealed by accumulations of aSyn using LB509 and pS129 antibodies and furthermore accumulations were positive for thioflavin-S. Neurites also showed transgene expression throughout the striatum and had a dystrophic Lewy morphology. Behaviourally, by 5 months post surgery, A53T aSyn macaques showed 45% less motor activity in the 2-4 hr period of a 4 hr observation, compared to EV controls (P<0.05). This deficit persisted through to the final month (53%, 56% and 60%, respectively, to month 8, [all, P<0.05]). No significant effect was observed on mMAP performance at any time point. PET imaging showed no significant change in striatal VMAT-2 to assess dopaminergic activity or change in FDG uptake evaluated to derive the Parkinson related pattern (PrP).

Conclusions: The macaque model of PD alpha-synucleinopathy produced here is in a position to assess therapeutics aimed at reducing or preventing aSyn accumulation in the nigrostriatal system, endpoints include: striatal neurochemistry and DAT, aSyn load per DA neuron, striatal aSyn levels, number of TH neurons remaining and locomotor activity. Furthermore, this primate model, with its robust aSyn

expression, can be used to screen potential aSyn PET ligands with the goal of identifying an agent to use for assessment of disease modification.

LBA 12 Functional NIRS-mediated neurofeedback for cerebellar ataxia: potential therapy for augmenting rehabilitative intervention.

Masahito Mihara, Hiroaki Fujimoto, Noriaki Hattori, Teiji Kawano, Megumi Hatakenaka, Hajime Yagura, Ichiro Miyai, Yoshiyuki Watanabe, Shigeru Kitazawa, Hideki Mochizuki

Dept. of Neurology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

Objectives: According to the notion that the functional recovery after brain damage is associated with reorganization of functional brain network, we hypothesized that the neurofeedback technique, which can modulate the impaired brain network, may augment the effect.

Background: Degenerative cerebellar ataxia is the progressive and intractable disorder involving the cerebellum and its related brain network. Despite the extensive researches, there are few pharmacological treatment options for the patients with degenerative ataxia. Previous findings that the intensive rehabilitation is effective even for patients with ataxia, suggesting that the physical practice could adjust the impaired brain network. In addition to the conventional rehabilitative approach, novel techniques that modulate the functional brain network directly could facilitate the functional reorganization and functional recovery.

Neurofeedback is the technique in which subjects try to modulate their own neural activity voluntarily with real-time feedback using functional neuroimaging. As a functional neuroimaging technique for convenient and useful neurofeedback system to augment functional recovery, we suppose that fNIRS-mediated neurofeedback could be useful since it is safe and less onerous for patients without any stimulation and constraint.

Methods: We recruited the 20 patients with degenerative cerebellar ataxia (mean \pm SD age: 58.7 \pm 11.8 years, Male: Female = 11:9, Mean disease duration is 7.5 \pm 4.9 years) admitted to the Morinomiya hospital, Osaka Japan for inpatient intensive rehabilitation. Patients were provided 4 weeks of intensive rehabilitation up to 180min per day for 7 days for a week. In first 2 weeks, patients also participated 6 sessions of neurofeedback training. In neurofeedback training, patients were asked to increase their supplementary motor area (SMA) activity during motor imagery of postural and gait-related task according to the real-time feedback signal, which is representing the task-related cortical activity without extra-brain artifact.

Clinical measures including Scale for the assessment and rating for ataxia (SARA), gait speed, Timed-up and go test (TUG), and Berg balance scale (BBS) were assessed before, immediately after, and 2 weeks after feedback. Patients were randomly assigned to two groups (Real- and Sham-FB groups). In Real-FB, patients were provided their own cortical activity, whereas other subjects' data were provided in Sham-FB. Group information was blinded for subjects and assessors (double blinded).

Unpaired t-test was used for group comparison of baseline clinical characteristics, and repeated measures ANOVA were used for investigate group × time interaction. Statistical significance was set at P<0.05.

Results: As an interim analysis, group assignment was unveiled and it revealed that Real- and Sham-FB group includes 9 and 11 patients, respectively. There was no complication or adverse effect related to the

neurofeedback intervention in both groups, and baseline clinical status was not different between both groups.

After 4weeks of intensive rehabilitation, patients with both groups improved their clinical status significantly. Repeated ANOVA revealed significant interaction between group × time in TUG and the Real-FB group showed more improvement (Real-FB: $28.7 \pm 11.5 \text{ s}$ to $21.1 \pm 12.1 \text{ s}$, Sham-FB $21.7 \pm 12.9 \text{ s}$ to $18.5 \pm 14.2 \text{ s}$, F2,36 = 3.4, p<0.05). Although repeated measures ANOVA only showed non-significant trend for SARA, 8 out of 9 patients in Real-FB group, whereas 5 out of 11 patients in Sham-FB group were improved more than 1.5 point from baseline.

Conclusions: Mental practice using motor imagery combined with fNIRS-mediated neurofeedback is safe and feasible rehabilitation technique, and our preliminary data revealed the potential augmenting effect of the neurofeedback for rehabilitative intervention to patients with degenerative ataxia.

LBA 13 Loss of phosphodiesterase 10A signalling is associated with progression and severity in patients with Parkinson's disease

Flavia Niccolini, Thomas Foltynie, Tiago Reis Marques, Nils Muhlert, Andri C Tzortzi, Graham E Searle, Sridhar Natesan, Shitij Kapur, Eugenii A Rabiner, Roger N Gunn, Paola Piccini, Marios Politis

Neurodegeneration Imaging Group, Department of Basic and Clinical Neuroscience, King's College London, Division of Brain Sciences, Imperial College London, Sobell Department of Motor Neuroscience, UCL Institute of Neurology, Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, School of Psychology, Cardiff University, Imanova Ltd., Centre for Imaging Sciences, Hammersmith Hospital, Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

Objectives: To assess the availability of phosphodiesterase 10A (PDE-10A) in vivo in Parkinson's disease (PD) patients, using [11C]IMA107 PET.

Background: PDE-10A is a dual substrate enzyme highly expressed in the striatal medium spiny neurons, where it regulates cAMP/cGMP signaling cascades, thus having a key role in the regulation of the striatal output pathways, and in promoting neuronal survival.

Methods: We have quantified the availability of PDE-10A in 24 patients with levodopa-treated PD (13 males, mean-age: 67 years, mean-PD-duration: 9.7 years, H&Y range: 1-4, UPDRS-III: 36.2) and compared to a group of 12 healthy controls. Parametric images of [11C]IMA107 binding potential relative to non-displaceable binding (BPND) were generated from the dynamic [11C]IMA107 scans using implementation of the simplified reference tissue model with the cerebellum as the reference tissue. To facilitate anatomical delineation of regions of interest (ROIs), PET images were co-registered and resliced to the corresponding volumetric MRI using the Mutual Information Registration algorithm in SPM8. Striatum (caudate and putamen) and globus pallidus ROIs were manually delineated on the co-registered MRIs using ANALYZE11.

Results: PD patients had significantly lower mean [11C]IMA107 BPND in the caudate (28.4%; P<0.001), putamen (25.5%; P<0.001) and globus pallidus (14.2%; P<0.05) compared to healthy controls. Longer PD duration correlated with lower [11C]IMA107 BPND in caudate (r=-0.65; P<0.01;), putamen (r=-0.51; P<0.01), and globus pallidus (r=-0.47; P<0.05;). Higher UPDRS-III scores correlated with lower [11C]IMA107 BPND in caudate (r=-0.48; P<0.05), and globus pallidus (r=-0.70; P<0.001;). Higher UDysRS scores in those Parkinson's patients with levodopa-induced dyskinesias

(n=12), correlated with lower [11C]IMA107 BPND in caudate (r=-0.73; P<0.05) and putamen (r=-0.74; P<0.05).

Conclusions: Our findings suggest loss of PDE-10A signalling in PD, which is associated with the progression and severity of the disease. [11C]IMA107 PET may provide a valuable tool to understand the pathophysiology of PD. PDE-10A is an enzyme that could be targeted with novel pharmacotherapy, which may help to alleviate PD symptoms and complications.

LBA 14 PREDICT-PD: Identifying Risk of Parkinson's disease in the Community

Alastair Noyce, Jonathan Bestwick, Niccolo Mencacci, Christopher Hawkes, John Hardy, Gavin Giovannoni, Andrew Lees, Anette Schrag

1) UCL Institute of Neurology, University College London. 2) Wolfson Institute of Preventative Medicine, Barts and the London SMD, Queen Mary University. 3) Blizard Institute, Barts and the London SMD, Queen Mary University, London, United Kingdom

Objectives: To determine longitudinal performance of the internet-based PREDICT-PD algorithm to identify subjects at increased risk of Parkinson's disease (PD).

Background: The prodromes of Parkinson's disease (PD) can begin many years before eventual clinical diagnosis and may offer a window of opportunity to identify individuals in earlier stages of the disease. In the PREDICT-PD pilot study (www.predictpd.com), early features and risk factors are assessed online and compared with the frequency of "intermediate" markers for PD. Here we present follow-up data to examine whether the algorithm provides consistent results over two years and whether the algorithm predicts increased rate of intermediate markers of PD and diagnosis PD during this time.

Methods: Participants aged 60-80 years without PD completed an online survey on risk factors and early features of PD, and a keyboard-tapping task at baseline, one and two years of follow-up. Smell testing was performed at baseline only. Risk scores were calculated based on survey answers and the results of a systematic review of published literature. Risk scores were ranked to enable comparative analyses between subjects with the highest 15% and lowest 15% risk scores for "intermediate markers" of PD (smell loss, REM-sleep behaviour disorder and tapping speed) and by correlating PD risk scores across the whole cohort with markers each year. DNA was obtained from a sample of higher and lower risk subjects, to compare the frequency of GBA variants and LRRK2 mutations as markers of genetic risk, and new cases of PD were established during the follow-up period.

Results: 1323 subjects were recruited at baseline, with 1036 completing the survey in year one and 934 in year two. Intermediate markers were significantly different between the higher and lower-risk groups in all years (all p<0.001), and risk scores correlated significantly with intermediate markers each year (all p<0.015). Higher and lower-risk groups defined at baseline differed significantly for all intermediate markers during follow-up (p<0.001), and the majority remained in the same risk group each year.

6/75 higher-risk subjects and 1/110 lower-risk subjects were found to have a GBA variant (OR 9.48, 95% CI 1.12-80.47, p=0.018), whilst none of those sampled were carriers of LRRK2 mutations. Four individuals have been diagnosed with PD during follow-up so far, of whom three were in the highest-risk and one in the middle-risk group at baseline (p=0.01).

Conclusions: The PREDICT-PD web-based risk stratification appears to perform consistently over time. Prospective data on intermediate and genetic markers, and new diagnosis of PD provide preliminary evidence that the algorithm enriches populations for risk of PD.

LBA 15

Initiating regular exercise behaviors is associated with slower decline in quality of life in Parkinson's disease (National Parkinson Foundation Quality Improvement Initiative data)

Miriam Rafferty (1), Peter Schmidt (2), Fernando Cubillos (2), Connie Marras (3), Mark Guttman (4), Eugene Nelson (5), Tanya Simuni (6)

 University of Illinois at Chicago, Chicago, IL, USA; 2. National Parkinson Foundation, Miami, FL, USA;
 Movement Disorders Centre, Toronto Western Hospital, University of Toronto, and the Edmond J Safra Program in Parkinson's disease Toronto, Canada; 4. Centre for Movement Disorders, Toronto, Canada;
 The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, NH, USA; 6. Northwestern University, Chicago, IL, USA

Objectives: To determine whether increasing exercise behavior to meet physical activity guidelines is associated with slower decline in quality of life in people with Parkinson's disease (PD).

Background: Exercise has been associated with improved quality of life (QOL). It is currently unknown whether patients who change their regular exercise behavior, outside of structured exercise interventions, can prevent long-term decline in PD-related QOL as measured by the Parkinson's Disease uestionnaire-39 (PDQ-39) summary index.

Methods: Data included 2940 patients from 20 sites affiliated with the National Parkinson Foundation Quality Improvement Initiative. The PDQ-39 summary index was measured across 3 visits: baseline, 1 year, and 2 year follow ups. At each time point, patients were classified as exercisers (E) if they exercised greater or equal to 2.5 hours per week as recommended by the Center for Disease Control and Prevention Physical Activity Guidelines (2008). They were classified as non-exercisers (N) if they exercised less than 2.5 hours per week. A subset of patients with moderately impaired QOL (PDQ-39 = 15% to 30%), who all began the study as non-exercisers, were compared to determine the effect of starting to exercise on QOL.

Results: All patients who exercised regularly at baseline and the following 2 years (EEE) demonstrated a 2.3% (95% CI \pm 0.7) increase (worsening) in PDQ-39 summary index from a baseline average of 18%. Patients who did not exercise regularly (NNN) worsened by 4.1% (95% CI \pm 0.8) from a baseline of 27%. Patients who started to exercise after the first visit (NEE) had significantly less decline in QOL over 2 years (1.4%) than those who started to exercise the following year (NNE) (3.2%; p < 0.05). In contrast, when patients transitioned from E to N, the transition was accompanied by a greater worsening of QOL. The subset analysis revealed that the group who began to exercise after their initial visit (NEE) had significantly less worsening of PDQ-39 than non-exercisers (1.4% \pm 1.2% vs 4.1% \pm 0.8; p=0.00005).

Conclusions: Increasing physical activity to greater than 2.5 hours of exercise per week is associated with a slower decline in total PDQ-39. Clinicians should encourage patients to meet at least 2.5 hours of exercise per week.

LBA 16 Veering in Hemi-Parkinson's Disease: Primacy of Visual over Motor Contributions

Xiaolin Ren, Robert Salazar, Sandy Neargarder, Serge Roy, Terry D. Ellis, Elliot Saltzman, Alice Cronin-Golomb

Boston University, Boston, MA, USA

Objectives: We examined the competing visual and motor hypotheses underlying veering in individuals with Parkinson's disease.

Background: The inability to maintain a straight trajectory while walking is often reported in individuals with Parkinson's disease (PD). It is as yet unclear as to whether the mechanism underlying veering, or lateral drift, is predominantly vision-based (asymmetrical perception of the visual environment) or motoric (asymmetry between relatively affected body side and relatively non-affected body side).

Methods: We assessed veering in 21 non-demented individuals with PD and 13 matched normal control participants (NC). The PD group included 9 with initial/current predominant left-side onset of motor symptoms (LPD) and 12 with right-side onset (RPD). Participants walked in a corridor under three conditions: eyes-open, eyes-closed, and Egocentric Reference Point (ECRP; walk toward a subjectively perceived center of a target at the end of the corridor). Kinematic data were collected. The visual hypothesis predicted that LPD, with a known tendency toward mild left spatial hemineglect, would veer rightward, in line with their perception of the visual target as right of center, whereas RPD would show leftward veering. The motor hypothesis predicted the opposite pattern of results: LPD would veer leftward because their left (more affected) body side had shorter step length than the right (less affected) body side, with RPD, for the same reason, veering rightward.

Results: Results supported the visual hypothesis. On both the eyes-open and ECRP conditions, RPD lateral drift significantly differed from NC, with RPD veering leftward despite a shorter stride length on the right body side and LPD veering rightward despite a shorter stride length on the left body side, though the LPD-NC difference was not significant. The results also revealed significantly reduced lateral drift and stride length asymmetry in LPD when they walked in ECRP condition than in eyes-open condition.

Conclusions: The findings suggest that interventions to correct walking abnormalities such as veering in PD should incorporate vision-based strategies rather than solely addressing motor asymmetries, and should be tailored to the distinctive navigational profiles of LPD and RPD.

LBA 17 Motor speech impairment indicates prodromal neurodegeneration in REM sleep behaviour disorder

Jan Rusz, Evžen Růžička, Karel Šonka, Jan Hlavnička, Tereza Tykalová, Jitka Bušková, Olga Ulmanová

Charles University in Prague, First Faculty of Medicine, Department of Neurology and Centre of Clinical Neuroscience; Czech Technical University in Prague, Faculty of Electrical Engineering, Department of Circuit Theory, Prague, Czech Republic

Objectives: (i) To assess prodromal neurodegeneration using acoustic analysis of speech in subjects with idiopathic rapid eye movement sleep behaviour disorder (RBD).

(ii) To quantitatively characterize speech disorders in RBD.

(iii) To estimate their specificity and sensitivity in differentiating between RBD and healthy control subjects.

Background: Subjects with RBD are at substantial risk of developing Parkinson's disease (PD) or related neurodegenerative disorders. Speech is an important indicator of motor function and movement coordination and therefore can be an extremely sensitive early marker to changes due to prodromal neurodegeneration. However, a systematic assessment of speech disorder in RBD has never been performed.

Methods: Speech data were acquired from 16 RBD subjects and 16 age- and sex-matched healthy control individuals. Objective acoustic assessment of 15 speech dimensions representing various phonatory, articulatory, and prosodic deviations was performed. Statistical models were applied to characterize speech disorders in RBD and estimate sensitivity/specificity for differentiation between RBD and control subjects.

Results: 14/16 RBD subjects manifested at least two affected speech dimensions. Articulatory deficits were the most prominent findings. In comparison to controls, RBD subjects presented significant alterations in speech dimensions of irregular alternating motion rates (p = 0.009) and articulatory decay (p = 0.01). The combination of speech features including aperiodicity, irregular alternating motion rates, articulatory decay, and dysfluency led to 96% sensitivity and 79% specificity in discrimination between RBD and healthy control subjects. Speech impairment was significantly more pronounced (p = 0.02) in 7 RBD subjects with slight motor impairment according (UPDRS III equal or higher than 5), compared to the other RBD individuals.

Conclusions: Simple quantitative speech motor measures may be suitable to reliably detect prodromal neurodegeneration in subjects with RBD and therefore might provide important outcomes for future therapy trials.

LBA 18

Evaluation of dual-phase 123I-FP-CIT SPECT imaging in parkinsonism

Kazuya Sako, Akiko Hamauchi, Hirokazu Kikuchi, Takenori Abe, Atsuko Nihira, Masahiro Mizobuchi, Hidetoshi Ono

Department of Neurology, Radiology, Nakamura Memorial Hospital, Sapporo, Hokkaido, Japan

Objectives: We investigated the usefulness of early phase images of 123I-FP-CIT SPECT in addition to the usual late phase dopamine transporter (DAT) images after each injection of 123I-FP-CIT. Patients of parkinsonism caused by several etiologies were employed for this study.

Background: 123I-FP-CIT is a useful SPECT tracer for assessing DAT in the straitum and thus indicates the functionality of presynaptic dopamine neuron terminals. The DAT image is acquired after it reaches to the steady state. 123I-FP-CIT is, however, rapidly distributed to the whole brain including the cerebral and cerebellar cortices as well as the striatum immediately after the administration. The early phase images presumably reflect relative regional cerebral blood flow (rCBF) coupled with cerebral metabolism. The patterns of the cortical uptake changes can potentially provide another information for the differential diagnosis of parkinsonism.

Methods: Eighty subjects who had the following clinical diagnoses were underwent dual-phase 123I-FP-CIT SPECT: 31 males, mean age 68.5 years (37-89 years); 40 idiopathic Parkinson's disease (PD), 7 Parkinson's disease with dementia (PDD), 7 dementia with Lewy bodies (DLB), 10 progressive supranuclear palsy (PSP), 4 corticobasal syndrome (CBS), 4 multiple system atrophy-parkinson type (MSA-P), 5 multiple system atrophy-cerebellar type (MSA-C) and 3 essential tremor (ET). SPECT images were started to obtain immediately for the early phase and 3 hours for the late phase (DAT) after an intravenous administration of 167 MBq of 123I-FP-CIT. SPECT data were collected using a triple-head γ-camera (GCA9300A/PI,Toshiba) equipped with high-resolution fanbeam collimators. In addition to the conventional axial images, we created the three-dimensional stereotactic surface projections (3D-SSP) images of the Z-scores with reference to the normal subject database of 123I-IMP SPECT. Some subjects were also analyzed with 123I-IMP SPECT aiming for the comparisons of rCBF patterns. The striatal DAT binding patterns and specific binding ratio (SBR) counted in the fixed regions of interest (ROIs) by the standardized semiquantitative analysis, were assessed.

Results: DAT images revealed the decreased striatal patterns in groups of PD, PDD, DLB, PSP, CBS and MSA-P, while they remained normal in ET and MSA-C. Average SBR in the respective disease showed 3.5 (PD), 1.7 (PDD), 2.5 (DLB), 2.3 (PSP), 3.3 (CBS), 2.2 (MSA-P), 6.4 (ET) and 5.8 (MSA-C). It appeared to be difficult to differentiate etiologies by judging from DAT images alone. In the early phase, all ET and most of PD patients showed no characteristic patters, although reduced uptake areas were demonstrated in the parieto-occipital and/or frontal cortices in some PD patients. Most of PDD and DLB patients showed more pronounced uptake reduction in the parieto-occipital and/or frontal cortices than the decreased subjects of PD. PSP patients showed decreased regional uptakes most pronounced in the frontal cortex. Asymmetric uptakes in the frontal including motor areas were observed in typical CBS patients. All MSA-C and some MSA-P patients showed decreased regional uptake in the cerebellar cortex. 3D-SSP images of the early phase in 123I-FP-CIT SPECT closely resembled those of 123I-IMP SPECT in most of the applied subjects.

Conclusions: Dual phase 123I-FP-CIT SPECT imaging can simultaneously demonstrate striatal DAT and cortical uptake changes correlating with rCBF in one challenge of the injection. This imaging method may save cost, time and radiation exposure while maintaining the diagnostic accuracy compared with respective inspections of SPECT for DAT and rCBF.

LBA 19

Results from a randomized, double-blind, placebo-controlled, single ascending-dose study in healthy subjects with PRX002, an anti-alpha-synuclein monoclonal antibody

Dale Schenk,1, Martin Koller,1, Daniel Ness,1, Sue Griffith,1 Michael Grundman,1 Jay Soto,1 George Atiee,2 Susanne Ostrowitzki,3 Gene Kinney,1

1Prothena Biosciences Inc; 2Worldwide Clinical Trials, Inc.; 3Roche Pharmaceutical Research and Early Development, Roche Innovation Center, 1South San Francisco, California, United States; 2Beverly Hills, California, United States; 3Basel, Switzerland

Objectives: The primary objective of this clinical study was to evaluate the safety, tolerability, and pharmacokinetics of PRX002 in healthy subjects. Secondary and exploratory objectives were to evaluate the immunogenicity and pharmacodynamic effects of PRX002.

Background: Alpha-synuclein is found in neurons and is a major component of pathologic inclusions that characterize neurodegenerative disorders, including Parkinson's disease. Current symptomatic therapies for Parkinson's disease eventually lead to dose-limiting side effects, become less effective at controlling symptoms as the disease progresses, and do not address some symptoms at all. There is a significant unmet medical need to develop disease-modifying therapies that may slow or halt the progression of Parkinson's disease. PRX002 is a monoclonal antibody that targets alpha-synuclein and that has been

tested in cellular and animal models of alpha-synuclein–related disease. PRX002 is hypothesized to slow or reduce the progressive neurodegeneration associated with the actions of pathogenic forms of alpha-synuclein. Here we report the results of the first study of PRX002 in human subjects (NCT02095171).

Methods: The study was a phase 1, randomized, double-blind, placebo-controlled, single ascendingdose study of PRX002 in healthy subjects. Eight subjects were enrolled into each of 5 dose cohorts and were randomly assigned to receive intravenous infusions of PRX002 at doses of 0.3, 1.0, 3.0, 10, or 30 mg/kg (n = 6/cohort; n = 30 across PRX002 doses) or placebo (n = 2/cohort; n = 10 across cohorts).

Results: No serious adverse events (AEs), discontinuations due to AEs, or dose-limiting toxicities were reported. Eighteen subjects reported a total of 37 treatment-emergent AEs (TEAEs). Five subjects receiving placebo reported 10 TEAEs, and 13 subjects receiving PRX002 reported 27 TEAEs. Two of 30 PRX002 subjects each reported venipuncture site pain, headache, viral infection, nausea, neutropenia, and upper respiratory infection. Of these TEAEs, 1 of 10 placebo subjects also reported venipuncture site pain, headache, and viral infection. Serum PRX002 exposure was dose proportional; the average terminal half-life across all doses was 18.2 days (Figure 1). A dose-dependent, statistically significant reduction in free (unbound) serum alpha-synuclein was apparent within 1 hour (P < 0.0001; Figure 2). The pharmacodynamic responses of increased total alpha-synuclein (free and bound) were dose-dependent for both time and concentration maximums.

Conclusions: In this first-in-human study, single doses of PRX002 demonstrated favorable safety, tolerability, and pharmacokinetic profiles at all dose levels tested. PRX002 engaged its target in vivo and significantly reduced free serum alpha-synuclein. This pharmacodynamic response was predicted based on preclinical data. Results presented here show for the first time that alpha-synuclein can be modulated in humans in a dose-dependent manner following single intravenous doses of an anti–alpha-synuclein antibody. A phase 1 multiple ascending-doses study with PRX002 in patients with Parkinson's disease is ongoing.

LBA 20

Tau-PET Imaging in Progressive Supranuclear Palsy Using [18F] AV-1451

Daniel Schonhaut, Brad Dickerson, Irene Litvan, Murray Grossman, Sasha Ashall, Abhinay Joshi, Andrew Siderowf, Michael Devous, Erik Roberson, David Russell, Bruce Miller, Keith Johnson, William Jagust, Adam Boxer, Gil Rabinovici

Dept. of Neurology, UCSF; Dept. of Neurology, Massachusetts General Hospital; Dept. of Neurology, UCSD; Dept. of Neurology, University of Pennsylvania; UC Berkeley; Avid Radiopharmaceuticals; University of Alabama Birmingham; Institute for Neurodegenerative Disorders, San Francisco, CA, USA

Objectives: To describe the binding pattern of the tau PET tracer [18F] AV-1451 in patients with progressive supranuclear palsy (PSP) included in a multi-site study.

Background: PSP is an atypical parkinsonian disorder characterized by progressive motor and cognitive dysfunction due to underlying 4-repeat tau pathology. Imaging tau in PSP could help facilitate an early and accurate diagnosis, enhance our understanding of pathophysiology, and aid in drug development. [18F] AV-1451 is a novel tau ligand that selectively binds to tau-positive inclusions in post-mortem samples.

Methods: [18F] AV-1451-PET was performed in 14 patients with PSP (mean age 69.2, 10 male, mean PSP Rating Scale 31.4/100) and 30 cognitively normal controls (NC, mean age 75.7, 13 male) recruited

from four centers (Table 1). 10 mCi of [18F] AV-1451 was injected IV and images were acquired 80-100 min post-injection. PET images were co-registered to MRI, and 80-100min Standardized Uptake Value Ratio (SUVR) images were created, normalizing by cerebellar gray matter (excluding dentate nucleus). We performed voxelwise contrasts of [18F] AV-1451 images between patients and controls using SPM8, adjusting for age. Additionally, we assessed mean SUVR in eight regions of interest (ROIs) defined on probabilistic imaging atlases: caudate, pallidum, putamen, thalamus, subthalamic nucleus (STN), substantia nigra, dentate nucleus of the cerebellum (DN) and pons.

Results: Individual patients showed increased tracer uptake in midbrain and putamen, though these regions also showed binding in most NC. Binding more distinct to PSP was seen in pallidum in all patients, and in DN and frontal gray and white matter in a subset of patients (Figure 1). Voxelwise contrasts showed elevated [18F] AV-1451 retention in bilateral pallidum, putamen, thalamus, STN, midbrain, DN, and frontal white matter in PSP patients compared to NC (Figure 2; p<0.05, uncorrected). A single right pallidum cluster survived Family Wise Error correction for multiple comparisons (p<0.05). Region-of-interest analyses were consistent with voxelwise results (Figure 3), with significantly increased binding in pallidum, putamen, STN, and DN (p<0.05, Bonferroni adjusted), and in thalamus (p<0.05).

Conclusions: [18F] AV-1451 retention was elevated in patients compared to controls in regions that closely match the pathological distribution of tau at autopsy. These findings suggest [18F] AV-1451 PET may be a useful in vivo biomarker of tau burden in PSP. Ongoing studies are underway to verify these findings in a larger sample, correlate them with clinical and other imaging measures, and assess longitudinal change.

LBA 21

Incident impulse control disorder behaviors and serial dopamine transporter imaging in early Parkinson's disease

Kara M. Smith, Sharon X Xie, Daniel Weintraub

University of Philadelphia, Philadelphia, PA, USA

Objectives: a) To describe incidence of impulse control disorder (ICD) behaviors in early Parkinson's disease (PD), and b) to determine clinical and neurobiologic risk factors for incident ICD behaviors in subjects using serial dopamine transporter (DAT) imaging.

Background: ICDs present an important challenge in clinical management of PD. Risk is increased by dopaminergic therapy, and patients may experience worsening symptoms and withdrawal upon weaning offending medications. It is critical to identify predictive factors to avoid this complication. Prior studies have shown associations between clinical characteristics and DAT imaging and ICDs in PD. We examined predictive clinical and neurobiological factors, both baseline and longitudinal, in a large, prospective cohort of de novo PD subjects who were ICD negative at diagnosis.

Methods: The Parkinson's Progression Markers Initiative (PPMI) is an international, multicenter, prospective cohort study of newly diagnosed, de novo PD. Subjects were included if they had at least baseline and year 1 clinical data available, and screened negative for ICD behaviors on the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) short form at baseline. Neuropsychiatric risk factors were screened with State-Trait Anxiety Inventory, Geriatric Depression Scale, and Montreal Cognitive Assessment. 319 PD subjects without ICD behaviors completed the baseline visit (mean age 61.7 (SD 9.5)), and 284, 217 and 96 completed years 1, 2, and 3 visits. Subjects started PD medications as clinically indicated (65.1% at 1 year). Kaplan-Meier curves were created to

examine cumulative frequency of incident ICD behaviors. Incidence rates at each visit were compared between medication groups with Fisher's exact test. Generalized estimating equations models were used to evaluate for predictors of incident ICD behaviors.

Results: 54 PD subjects developed incident ICD behaviors. Estimated incident rates of ICD behaviors in the entire population were 8% at year 1, 18% at year 2, and 25% at year 3. Incident rates increased with each year in those on PD medications and decreased in those not on medications. Younger baseline age was associated with significantly increased risk of ICD development (OR=0.97, p=0.02); gender, education, and baseline motor severity, anxiety symptoms, depressive symptoms, and cognitive performance were not. For DAT imaging, lower right and left putamen DAT binding ratios at a given postbaseline visit were associated with a higher risk of developing ICD at that visit (OR=.17, p=.04; OR=.17, p=.03). In the subgroup on PD medications, a greater decrease in right caudate and mean striatal DAT binding ratios over the first year was associated with higher risk of ICD (OR=3.74, p=0.02; OR=6.23, p=.05).

Conclusions: The rate of incident ICD behaviors increases with time and initiation of PD medications in early PD. While younger age is a significant risk factor for ICD, other neuropsychiatric symptoms may be secondary comorbidities rather than premorbid risk factors. A greater decrease in DAT binding over time increases risk of incident ICD, conferring a larger risk to those taking PD medications. The relationship between DAT binding over time and ICD development warrants further study as it may shed light on the pathogenesis of ICDs and lead to new therapeutic approaches.

LBA 22

Comparison of the effects on cognition and behaviour in patients with Parkinson's disease treated with subthalamic stimulation or with continuous Levopoda Duodenal infusion

Francesc Valldeoriola, Pilar Santacruz, José Ríos, Yaroslau Compta, Jordi Rumià, Ana Cámara, Mariateresa Buongiorno, José Esteban Muñoz, María José Martí, Eduardo Tolosa

Institut de Neurociències, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain

Objectives: We have studied a group of patients with advanced PD that were selected to receive CLDI or STN-DBS in order to investigate the effects of these therapies on cognition and behavior after one year. These data were compared with those of a control group of patients with similar clinical characteristics treated with standard oral medication.

Background: The effects on behavior and cognition of continuous levodopa duodenal infusion (CLDI) and subthalamic stimulation (STN-DBS), both used in the treatment of advanced Parkinson's disease (PD) have been investigated in several studies. However, the practical consequences derived from such studies remain controversial. Moreover, there are not comparative studies showing possible different influences of these two therapies on cognition and behavior.

Methods: We have studied a group of patients with advanced PD that were selected to receive CLDI or STN-DBS in order to investigate the effects of these therapies on cognition and behavior after one year. These data were compared with those of a control group of patients with similar clinical characteristics treated with standard oral medication. This was an open-label, non-randomized study for pre and post intervention analyses. Twenty-four patients were considered good candidates to be treated with CLDI or STN-DBS.

Results: Patients receiving CLDI improved several neuropsychological functions (memory, frontal, and visuospatial) compared both to patients receiving STN-DBS and control patients. CLDI patients improved

the Scopa-cog scores during the study compared with control patients. Patients treated with DBS showed no significant changes in any of the tests administered with respect to controls at one year follow-up.

Conclusions: Patients treated with CLDI may significantly improve some specific neuropsychological functions when compared with patients receiving STN-DBS and with PD patients receiving conventional medical treatment after one year from the intervention; there are not significant cognitive or behavioral changes in patients treated with STN-DBS when compared to PD patients receiving conventional medical treatment after one year from the intervention.

LBA 23

Cognitive impairment as a feature of prodromal Parkinson's disease: evidence from the PARS study

Daniel Weintraub, MD 1,2,3, Lama Chahine, MD 1, Keith Hawkins, PsyD 4, Andrew Siderowf, MD, MSCE 5; Shirley Eberly, MS 6; David Oakes, PhD 6; John Seibyl, MD 7; Matthew B. Stern, MD 1; Kenneth Marek, MD 7; Danna Jennings, MD 7; and the PARS Investigators

1 Department of Neurology, Perelman School of Medicine at the University of Pennsylvania; 2 Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania; 3 PD Research, Education and Clinical Center, Philadelphia Veterans Affairs Medical Center; 4 Department of Psychiatry, Yale University School of Medicine; 5 Avid Radiopharmaceuticals; 6 Department of Biostatistics, University of Rochester School of Medicine; 7 The Institute for Neurodegenerative Disorders, 1, 2, 3, 5 Philadelphia, Pennsylvania, USA; 4, 7 New Haven, Connecticut, USA; 6 Rochester, New York, USA

Objectives: We describe the cognitive profile of individuals at risk for PD in the Parkinson Associated Risk Study (PARS).

Background: PARS identified a cohort of healthy adults with hyposmia and dopamine transporter (DAT) reduction to characterize prodromal Parkinson's disease (PD).

Methods: Individuals age >50 years without a diagnosis of PD were recruited. 225 completed cognitive testing and were included in the final analysis. A neuropsychological test battery was administered and normative scores created for global cognition, memory, executive function/working memory, processing speed/attention, visuospatial abilities, and language domains. Other non-motor symptoms (cognition, constipation, depression, anxiety, and REM sleep behavior disorder in a subset with a bed partner) were assessed through patient-completed questionnaires.

Results: Individuals with both hyposmia and DAT reduction (n=38) had lower mean scores for global cognition, executive function/working memory, and memory compared with all other participants combined (n=187). In multivariate logistic regression models, lower global cognition (OR=1.97, 95%CI=1.24-3.12), and specifically executive function/working memory (OR=1.84, 95%CI=1.21-2.81), memory (OR=1.64, 95%CI=1.09-2.48), and processing speed/attention (OR=1.53, 95%CI=1.00-2.34) domain scores, predicted membership in the hyposmia with DAT reduction group. Combining hyposmia with impairment on specific cognitive domains improved prediction of DAT reduction compared to hyposmia alone, with the greatest increase in odds for hyposmia plus executive function/working memory impairment (68% increase in OR from 4.14, 95%CI=1.68-10.16 to 6.96, 95%CI=1.97-24.64).

Conclusions: Changes in global cognitive abilities, and specifically executive function/working memory, memory, and processing speed/attention, are present in the prodromal phase of PD. Combining non-motor features, including cognition, improves prediction of DAT reduction.

LBA 24 ApoE genotype mediates recurrent falls risk in early Parkinson's disease

Alison Yarnall, Sue Lord, Rosie Morris, Patrick Chinnery, Gavin Hudson, David Burn, Lynn Rochester

Institute of Neuroscience, Newcastle University, Newcastle, United Kingdom

Objectives: To determine whether apolipoprotein E (ApoE) genotype is associated with prospective falls in a cohort of early Parkinson's disease (PD).

Background: Falls represent a substantial and debilitating problem in PD. The precise pathophysiology is complex, heterogeneous and may vary between subjects, but is likely to involve cholinergic loss and amyloid- β deposition, in addition to Lewy body pathology. Presence of ApoE e4 allele has been shown to influence motoric decline, gait speed and disability in older adults, but to date there have been no studies examining the relationship between ApoE and falls in PD.

Methods: Participants (n=119) were recruited as part of the Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation (ICICLE-GAIT). Falls were collected prospectively for 30 months from diagnosis using monthly falls diaries. Genotyping for ApoE e2-4 was performed on 110 subjects. Descriptive statistics were used to compare ApoE e4 carriers (n=45) vs. non-carriers (n=65) and entered into a logistic regression model to determine adjusted odds ratios (OR) of recurrent falls at 30 months.

Results: At baseline, 26 (21.8%) had fallen, increasing to 55.5% at 30 months. Non-fallers (n=39) vs. recurrent fallers (n=40) at 30 months were well matched with the exception of lower UPDRS II and higher postural instability gait difficult (PIGD) scores in recurrent vs. non-fallers. 60.5% of those with recurrent falls vs. 29.7% who had not fallen were ApoE e4 carriers (p=0.011). Median time (days) to first fall was 281 in carriers vs. 801 in non-carriers. ApoE genotype (OR 5.2, 95% CI 1.5-17.6), age (OR 1.1, 95% CI 1.0-1.2) and PIGD score (OR 6.6, 95% CI 1.4-30.6) were significant independent predictors of recurrent falls in a regression model, whereas cognition was not.

Conclusions: This preliminary study suggests that ApoE e4 mediates falls risk in early PD, potentially via amyloid deposition or vascular disease. This work contributes to the neurobiology of falls and highlights that interventions targeted at ApoE e4 carriers may reduce falls burden in our PD subjects.

LBA 25 Submandibular gland needle biopsy for the diagnosis of early Parkinson's disease

Charles Adler, Brittany Dugger, Joseph Hentz, Michael Hinni, David Lott, Erika Driver-Dunckley, Shyamal Mehta, Geidy Serrano, Lucia Sue, Amy Duffy, Douglas Walker, Thomas Beach

Mayo Clinic Arizona, Banner Sun Health Research Institute, Scottsdale, AZ, USA

Objectives: This study investigates submandibular gland biopsies in living patients with early Parkinson's disease (PD).

Background: We have previously investigated Lewy-type alpha-synucleinopathy (LTS) in submandibular glands from autopsied subjects with PD and using needle biopsies of living patients with advanced PD.

Methods: Patients with PD for <5 years and control subjects underwent outpatient transcutaneous needle core biopsies (16 gauge) of one submandibular gland. Tissue was fixed in formalin and serial 5-7

 μ m paraffin sections were immunohistochemically stained for phosphorylated alpha-synuclein and reviewed for evidence of LTS.

Results: Twenty five PD patients and 10 controls were biopsied. In the PD group (15 males, 9 females) the mean (SD) age was 69.5 (8.3) and disease duration 2.6 (1.1) years. The Control group (3 males, 7 females) mean age was 64.8 (8.0). All the PD subjects had an abnormal DAT scan. Six PD and one control did not have adequate glandular tissue to determine LTS positivity. Of the 19 remaining PD cases 14 (74%, 95%CI 49% to 91%) were LTS positive and five negative while 2/9 (22%, 95%CI 40% to 97%) of the Controls were LTS positive. Adverse events (mainly swelling and bruising) were common (27/35, 77% of cases), but were minor and transient with no serious events.

Conclusions: Submandibular gland needle biopsies identified Lewy-type synucleinopathy in 74% of clinically diagnosed early PD subjects and 22% of Controls. The Controls may represent prodromal PD. As clinical diagnosis of early PD may be only 50-60% accurate, submandibular needle biopsy may be an improvement over this. Follow-up to autopsy will be needed to provide a clear gold standard with which to assess these results. The potential value of submandibular gland biopsies for early PD would be to aid in clinical trial inclusion/exclusion and possibly serve as the gold standard for biomarker studies short of autopsy confirmation of diagnosis.

2015 MDS STUDY GROUP ABSTRACTS

SG 1 The International Parkinson and Movement Disorder Society-Endorsed PSP Study Group

Günter Höglinger, Angelo Antonini, Kailash Bhatia, Yvette Bordelon, Adam L. Boxer, Carlo Colosimo, Jean Christophe Corvol, Lawrence Golbe, Keith A. Josephs, Tony Lang, Irene Litvan, Stefan Lorenzl, Brit Mollenhauer, Huw R. Morris, Ulrich Müller, Christer Nilsson, Wolfgang

German Center for Neurodegenerative Diseases & Technical University Munich, Munich, Germany

Objectives: The International Parkinson and Movement Disorder Society endorsed PSP Study Group has been initiated to improve the diagnostic criteria, to create collaborative clinical research networks, and to initiate measures facilitating therapeutic clinical trials in PSP. Therefore, we aim to 1. Characterize the earliest clinical signs of pathologically confirmed PSP,

2. Improve the diagnostic criteria for PSP to incorporate the extended clinical spectrum of PSP,

3. Improve the quality of future clinical trials, including improvements of early diagnosis, registries to establish trial-readiness, refinement of study protocols by optimizing natural history, neuroimaging and biomaterial data.

4. Disseminate knowledge about PSP.

Background: Progressive Supranuclear Palsy (PSP) is an adult-onset neurodegenerative disorder with distinct cerebral tau pathology. Its classical clinical manifestation, termed Richardson-Syndrome, includes an akinetic-rigid syndrome with oculomotor dysfunction, postural instability, frontal lobe and bulbar dysfunction. Clinico-pathological studies in recent yrs. have demonstrated a striking clinical heterogeneity, positioning the disease into the spectrum spanning from movement disorders to fronto-temporal dementias, which is both challenging and exciting for clinical neurologists. No curative treatment options are available at present. Clinical research into this rare disorder is limited in power due to its fragmentation.

Methods: A retrospective collection of a large multi-centric clinico-pathological dataset has been established to study natural history and clinical diversity. Large multicentric cross-sectional and

longitudinal MR imaging series are being analyzed to provide validated diagnostic and progression markers. We are in the final stage to prepare international guidelines for the clinical diagnosis of PSP based on published evidence. Prospective cohort studies in oligosymptomatic conditions suggestive of PSP are being set up in the US, UK, and continental Europe.

Results: A first retrospective analysis of a large multi-centric original clinico-pathological dataset has been successfully terminated (Respondek et al., Movement Disorders, 2014). Clinico-pathological correlations in the expanding datasets are being performed. Clinical research networks have been set up in the US, UK, France and Germany. A CME Course '50 years of Progressive Supranuclear Palsy' to has been held in October 2014 in Munich.

Conclusions: The MDS PSP Study Group has initiated successfully several measures to improve recognition and treatment of PSP.

SG 2 A non-interventional study to assess the presence of impulsive-compulsive behaviors in an outpatient population with Parkinson's disease

Angelo Antonini 1, Paolo Barone 2, Ubaldo Bonuccelli 3, Karin Annoni 4, Mahnaz Asgharnejad 5, Andreas Fichtner 6, Paolo Stanzione 7

1. IRCCS San Camillo Venice and First Neurology Clinic, University of Padua, Padua, Italy; 2. University of Salerno, Fisciano, Italy; 3. Neurology Unit-Dept. of Clinical & Experimental Medicine, University of Pisa, Italy; 4. UCB Pharma, Milan, Italy; 5. UCB Pharma, Raleigh, NC, USA; 6. UCB Pharma, Monheim am Rhein, Germany; 7. Neurology Clinic, University Roma Tor Vergata, Rome, Italy

Objectives: To assess the presence of impulsive-compulsive behaviors (ICBs) in an Italian outpatient population with Parkinson's disease (PD) over a 2-year period.

Background: ICBs occur in patients with PD, but the relationship with disease characteristics and therapy has not been fully investigated.

Methods: ICARUS (SP0990) was a prospective non-interventional multicenter study in an Italian outpatient population with PD, who had been treated for ≥ 6 months with any approved PD treatment. Study visits occurred at Baseline, Year 1, and Year 2. The primary variable was the presence of ICBs by means of the modified Minnesota Impulsive Disorder Interview (mMIDI): a patient was defined as ICB positive when answering affirmatively to one gateway guestion on the mMIDI plus an affirmative answer to ≥ 1 of the remaining questions in the same module. Prevalence is reported at Baseline, Year 1, and Year 2.

Results: Of 1095 patients enrolled, 1069 (97.6%) patients were included in the full analysis set (all patients who completed the mMIDI, H&Y, and UPDRS at Baseline). Prevalence of ICBs at Baseline was 28.6% (306/1069 patients) (Table 1). A higher proportion of males (32.5%; 223/686 males) screened positive for an ICB vs females (21.7%; 83/383 females). In general, patients who were ICB positive at Baseline were younger (mean±SD age: 63.6±9.5 vs 66.6±9.3 years), younger at diagnosis (mean±SD age: 56.6±10.5 vs 60.8±10.5 years), and had longer disease duration (mean±SD: 6.9±5.2 vs 5.8±4.9 years). Patients ICB positive at Baseline reported more severe non-motor symptoms (NMSS), sleep impairment (PDSS-2), PD-related quality of life (PDQ-8), and depressive symptoms (BDI-II) (Table 1). Although the prevalence of ICBs was similar at Baseline, Year 1, and Year 2 (Table 2), individual patients could have switched their ICB status. The majority of ICB positive patients reported a single ICB subtype (e.g. 66.7%; 204/306 at Baseline) (Table 2). The most prevalent subtype was compulsive eating, followed by punding behavior, compulsive sexual behavior, compulsive gambling, and buying disorder. The prevalence of subtypes generally remained stable across the 3 visits (Table 2).

Conclusions: The results of this study suggest that specific demographic features, disease characteristics, and PD symptoms are associated with the presence of ICBs in patients with PD. The prevalence was stable over the 2-year observation period.

UCB Pharma-funded.

Table 1. Baseline Parkinson's disease sy	ymptom severity by ICB status
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	ICB negative	ICB positive	Wilcoxon/Mann-		
	N=763	N=306	Whitney test		
H&Y stage , mean ± SD (higher score indicates more severe)	2.9 ± 1.2	3.1 ± 1.3	P=0.1270		
NMSS total score , mean ± SD (higher score indicates more severe)	32.2 ± 30.6	45.0 ± 33.4	P=0.0000		
PDSS-2 total score , mean ± SD (higher score indicates more severe)	12.3 ± 8.9	15.1 ± 10.6	P=0.0001		
PDQ-8 total score , mean ± SD (higher score indicates more severe)	21.5 ± 16.2	27.9 ± 17.6	P=0.0000		
BDI-II total score , mean ± SD (higher score indicates more severe)	9.3 ± 7.5	12.6 ± 7.8	P=0.0000		
MMSE adjusted total score, mean ± SD (lower score indicates more severe)	27.6 ± 1.8	27.9 ± 1.6	P=0.0205		
FAB total score , mean ± SD (lower score indicates more severe)	14.9 ± 2.9	15.0 ± 2.7	P=0.9102		
PD-CRS total score , mean ± SD (lower score indicates more severe)	80.7 ± 19.3	80.4 ±17.9	P=0.9513		
H&Y: Hoehn and Yahr scale; MMSE: Mini Mental State Examination; NMSS: Non-motor Symptoms Scale; PDSS-2: Parkinson's Disease Sleep Scale-2; PD-CRS: Parkinson's					

Disease-Cognition Rating Scale; **PDQ-8**: Parkinson Disease Questionnaire-8 items; **BDI-II**: Beck Depression Inventory II; **FAB:** Frontal Assessment Battery

Table 2. Prevalence[†] of ICBs at Baseline, Year 1, and Year 2 by means of the mMIDI as a screening tool

	Baseline	Year 1	Year 2				
	N=1069	N=995	N=925				
	n (%); [% of ICB positive patients]						
ICB Positive	306 (28.6%) 292 (29.3%) 245 (26.5%)						
Number of ICB mMIDI subty	pes						
Single (i.e. 1 mMIDI subtype)	204 (19.1%); [66.7%]	211 (21.2%); [72.3%]	158 (17.1%); [64.5%]				
Multiple (i.e. 2-5 mMIDI subtypes)	102 (9.5%); [33.3%]	81 (8.1%); [27.7%]	87 (9.4%); [35.5%]				
2	77 (7.2%); [25.2%]	57 (5.7%); [19.5%]	63 (6.8%); [25.7%]				
3	16 (1.5%); [5.2%]	17 (1.7%); [5.8%]	19 (2.1%); [7.8%]				
4	6 (0.6); [2.0%]	6 (0.6); [2.1%]	5 (0.5%); [2.0%]				
5	3 (0.3%); [1.0%]	1 (0.1); [0.3%]					
mMIDI modules							
Buying disorder	59 (5.5)	53 (5.3)	55 (5.9)				
Compulsive gambling	76 (7.1)	61 (6.1)	56 (6.1)				
Compulsive sexual behavior	85 (8.0)	79 (7.9)	66 (7.1)				
Compulsive eating	129 (12.1)	128 (12.9)	109 (11.8)				

Punding behavior	96 (9.0)	96 (9.0) 84 (8.4)			
[†] Prevalence of ICBs and subtypes was defined as the number (proportion) of patients who screened positive for ICBs by mMIDI at the particular study visit.					

SG 3

Diagnostic discriminating power of cortical and subcortical MR indices in Multiple System Atrophy: A cross-sectional MODIMSA multicenter study

Weis Luca, Seppi Klaus, Onofrj Marco, Cortelli Pietro, Kaufmann Horacio, Krismer Florian, Wenning Gregor, Nigro Salvatore, Quattrone Aldo, Antonini Angelo on behalf of the MODIMSA neuropsychology and imaging working groups

Department of Parkinson's Disease, IRCCS San Camillo, Venice 30126, Italy; Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; Department of Neuroscience and Imaging, University "G. d'Annunzio", Chieti-Pescara, Italy; Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy/ IRCCS, Institute of Neurological Sciences, Bellaria Hospital, Bologna, Italy; Dysautonomia Center, Department of Neurology, New York University Medical Center, New York, New York, USA; Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; Department of Neurology, National Research Council, Catanzaro, Italy; Institute of Bioimaging and Molecular Physiology, National Research Council, Catanzaro, Italy/Department of Medical and Surgical Sciences, 'Magna Graecia' University, Catanzaro, Italy; Department of Parkinson's Disease, IRCCS San Camillo, Venice 30126, Venice, Italy

Objectives: To investigate the discriminating power of MRI indexes in a large multicentre study comparing an automatic segmentation approach to ROI-drawing based manual measure.

Background: Imaging biomarkers may represent a useful tool to help early identification of patients with multiple system atrophy (MSA).

Methods: Multicenter cohort of 66 MSA patient [mean age 63,6(7,1)] and a single centre cohort of 30 PD [mean age 59,1(7,2)] and 30 healthy subjects [mean age 55,3(8,3)] underwent high-resolution MRI anatomical acquisition at five different academic centres. Discriminant power to detect MSA of manual measures of MRI indexes and automated volume measures of brain sub-cortical volumes averaged between left and right hemispheres was calculated.

Results: Logistic analysis revealed atrophy at the middle posterior part of corpus callosum, cortical and white matter part of cerebellum and putamen and section decrease of the manually measured middle cerebellar peduncle (MCP) provided the best discriminating power (AUC =0.973) and percentage of correct classification (91.4%,) from HC. Moreover bilateral atrophy of the cerebellar white matter and putamen together with the magnetic resonance parkinsonism index (MRPI) reduction significantly discriminated MSA from PD (AUC=0.918). In particular ROC analysis showed that MCP decrease together with globus pallidum bilateral atrophy significantly discriminated MSA-C from PD (AUC=0.966) while putamen, globus pallidum and brain stem bilateral atrophy discriminated MSA-P from PD (AUC=0.946).

Conclusions: Our findings suggest that MRI specific indices can help discrimination of MSA from PD and healthy controls.

SG 4 Early subthalamic neurostimulation improves quality of life of elderly patients with Parkinson's disease

H. Salimi Dafsari, P. Reker, P. Reddy, M. Silverdale, M. Pilleri, P. Martinez-Martin, A. Rizos, K. Ashkan, M. Samuel, J. Evans, V. Visser-Vandewalle, A. Antonini, K.R. Chaudhuri, L. Timmermann,

On Behalf of EUROPAR and the MDS Non-Motor PD Study Group. Cologne, Germany

Objective: To study the effects of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) in patients with advanced age but short duration of Parkinson's disease (PD).

Background: STN-DBS is a well-established treatment option for patients with PD improving motor symptoms and quality of life (QoL). Since the EARLYSTIM trial, the expansion of the traditional indication for DBS by intervention at earlier stages of PD has re-emerged as a major topic of debate. In EARLYSTIM, patients aged ≤60 years were included (mean age 52.9 years). However, due to an increasing prevalence with advancing age, elderly patients form a relevant part of the PD population.

Methods: We performed a post-hoc analysis of prospective patient data recorded as part of clinical trials or clinical routine in four centers (Cologne, London, Manchester, Venice). Subjects aged ≥61 years with a disease duration of ≤8 years at intervention were included. Motor function, QoL (as measured by the PDQ8), and levodopa equivalent daily doses (LEDD) were compared between baseline and follow-up 3 to 6 months after surgery. Heterogeneous rating instruments (UPDRS, MDS-UPDRS, SCOPA) were harmonized by comparing percentages of the maximum scores. Employing the Wilcoxon test and two-sided t-test when parametric criteria were fulfilled, the Bonferroni method was used to correct for type I errors. Cohen's effect sizes (ES) were calculated for each outcome.

Results: Mean age and disease duration at surgery of the 22 subjects identified were 65.77 (\pm 4.22) and 6.14 (\pm 1.28) years. Motor impairment improved by 48% from baseline to follow-up (40.02% vs. 20.99% of the maximum respective motor score, p<0.001, ES=0.8), QoL improved by 38% (mean PDQ8-SI 29.55 vs. 18.18, p=0.009, ES=0.52) and LEDD was reduced by 51% (mean 957.67mg vs. 464.65mg, p<0.001, ES=0.81). Significance level was reached for all outcomes.

Conclusions: The benefit from STN-DBS was well within the range reported in the literature. Due to the small sample size, different motor scores, and short follow-up period, our findings need to be interpreted with caution. Nevertheless, they are relevant to the debate about selection criteria for STN-DBS and encourage further studies for the group of elderly patients with short disease duration, which is currently underrepresented in the literature but important in daily clinical decision making.

SG 5 Subthalamic stimulation lead coordinates correlate with non-motor effects in Parkinson's disease

H. Dafsari, J.N. Petry-Schmelzer, T. Dembek, A. Rizos, A. Antonini, P. Martinez-Martin, K.R. Chaudhuri, V. Visser-Vandewalle, L. Timmermann.

On Behalf of EUROPAR and the MDS Non-Motor PD Study Group. Cologne, Germany

Objective: To study the influence of lead location in subthalamic nucleus (STN) deep brain stimulation (DBS) on motor and non-motor outcomes.

Background: DBS for patients with Parkinson's disease (PD) improves motor and non-motor symptoms (NMS) with a considerable degree of inter-subject variance, possibly due to individual lead locations. Although DBS targeting is performed visually, we hypothesized that an atlas-based analytic approach could reveal a correlation of lead locations with non-motor effects of DBS.

Methods: 20 patients with PD undergoing bilateral STN-DBS (40 hemispheres) were included in this ongoing study. UPDRS-II (activities of daily living), -III (motor impairment), and -IV (motor complications) and NMS Scale (NMSS), which consists of nine domains covering a wide range of NMS, were collected at preoperative baseline (MedON) and 6 months follow-up (6MFU; MedON/StimON). We used Wilcoxon signed-rank or t-tests, when parametric criteria were fulfilled, to test for significant changes and corrected Type I errors with the Bonferroni method. As we were interested in the influence of DBS lead locations, post-hoc we analyzed Cartesian coordinates of lead tips in respect to the anterior/posterior commissure (AC-PC) line using fused postoperative CT/preoperative MRI images computed with the OPTIVISE software. Left hemispheric leads were mirrored to the right hemisphere. To analyze the relationship between lead tips and change scores (baseline - 6MFU) we employed Spearman-correlations. Results: All outcomes improved significantly from baseline to 6MFU (UPDRS-II: 14.65 vs. 10.60, p=0.004, 27.7% improvement; UPDRS-III: 28.05 vs. 19.42, p=0.016, 30.8% improvement; UPDRS-IV: 6.65 vs. 4.00, p=0.032, 39.9% improvement; NMSS: 58.70 vs. 38.65, p=0.040, 34.2% improvement). Mean (SD) lead tip positions in respect to the AC for all axes were x: 10.91mm (1.28), y: -18.28mm (2.22), and z: -6.04 (2.91). Table 1 shows significant correlations between lead locations and clinical outcomes; all other results were not significant. [figure1]

Spearman-cor	relations		18	왕(
Lead location	correlated to improvement of	correlation coefficient	p	n	
19	UPDRS-II	0.403	0.010	40	
Dorsal	UPDRS-III	0.360	0.027	38	
	NMSS sleep	0.427	0.006	40	
Destaviar	UPDRS-II	0.407	0.009	40	
Postenor	NMSS sleep	0.364	0.021	40	
Lateral	NMSS cardiovascular	0.358	0.023	40	

Conclusions: The results of our cohort are in accordance with the broad agreement that DBS outcomes highly depend on lead locations. This study might provide information for DBS lead positioning in patients with clinically relevant NMS and may encourage further studies including more complex models integrating stimulation parameters to study motor and non-motor effects of DBS.

SG 6

A multicentre study of the patient's perspective: The first Parkinson's disease pain questionnaire (King's PD pain quest)

A.M. Rizos, P. Martinez-Martin, S. Pal, C. Carroll, D. Martino, C. Falup-Pecurariu, B. Kessel, A. Sauerbier, A. Martin, M. Parry, R. Inniss, L. Perkins, D. Trivedi, P. Odin, A. Antonini, K. Ray Chaudhuri

London, United Kingdom

Objective: To develop and validate an "easy to use" novel clinical self-completed Parkinson's specific pain questionnaire (complementary to the King's PD Pain Scale).

Background: Pain is a poorly characterised non-motor symptom of Parkinson's disease (PD) and a determinant of quality of life (Wasner, Deuschl. 2012). We have recently validated the first pain scale specific to PD (King's PD Pain Scale), but there are no patient completed tools to empower patients to self-declare pain related symptoms.

Methods: In a cross-sectional, open, multicentre pilot validation study of the novel PD pain questionnaire (King's PD Pain Quest), which is complementary to the King's PD Pain Scale (Figure 1) we collected data from PD patients with otherwise unexplained pain and controls without PD using the King's PD Pain Quest, addressing the same 14 items as the King's PD Pain Scale in lay English understandable and completed by patients.

Patie	ent ID No:	Initials:			Date of birth:	
Date	of assessment:	Male 🗆	Female		Centre:	
PAI	N IN PARKINSON'S					
The occ spe	e movement symptoms o ur as part of the conditio cific type of your pain, pa	f Parkinson's are we n or its treatment. It articularly if it is trou	ll known. H is importa blesome fo	lowev int the	ver, other problems like pain at the doctor knows about th J.	ca ne
Sev	eral types of pain are list	ed below. Please:				
• 1	Tick the box "Yes" if you h	nave experienced th	is particula	r type	e of pain <u>during the past mor</u>	hth
• 1	f you have <u>not</u> experience	ed the type of pain i	n the past	mont	h tick the "No" box.	
• T	The doctor or nurse may	ask you some additi	onal questi	ons to	o help you decide.	
	ase note that this questie	intuite only relates	o the pull	your	in the more do	12.
HAV	E YOU EXPERIENCED AN	Y OF THE FOLLOWIN	IG IN THE I	AST I	MONTH? Ves	
1. P	ain around the joints (ind	luding pain related	to arthritis)		(
2. Pi	ain related to a specific ir	ternal organ				
(1	for example, pain around	the liver, stomach o	or bowels)			
3. G	eneralised non-specific p	ain in your stomach	area			1
4. N	Ion-specific pain deep wi	thin the body: a gen	eralised co	nstan	nt, dull, aching pain 🗆	
5. P	ain related to abnormal i	involuntary moveme	nts (dyskir	netic p	pain) 🗆	1
6. P	ainful muscle cramps in a	a specific region dur	ng "off" pe	eriods		
(v	when your medication is i	not working)			U	
7. G	Generalised pain during " Dain in the whole body or	off" periods areas that are not a	ffected by	musc	le cramps)	
8. P	ain related to ierking leg	movements during	the night o	r an u	unpleasant burning	
se	ensation in the legs which	improves with mov	ement (res	stless	legs syndrome)	1
9. P	ain related to difficulties	when turning in bea	at night			ſ
10.	Pain when chewing					
11. F	ain related to grinding te	eth during the night				1
12. E	Burning sensation in your	mouth				1
13. E	Burning pain in the limbs	(often associated wi	th swelling	or m	edication)	(
					_	

KINC'S DD DAIN OUEST

Results: 191 patients (mean age 64.2±11.8 years, duration of disease 5.4±4.9 years, median H&Y 2 [range 1-5], 62.8% male) and 174 non PD controls (mean age 56.7±16.0, 55.5% male) were studied. Most patient-reported types of pain were musculoskeletal pain (80.1%), nocturnal (pain while turning in bed, 46.6%), dystonic (46.1%) or radicular pain (39.8%), as shown in Figure 2. Controls also reported mostly musculoskeletal pain (63.8%)%), followed by radicular pain (25.3%), generalized whole body pain (23.0%) and nocturnal pain (22.4%). Differences reached significance level for musculoskeletal, dystonic radicular and nocturnal pain, as well as RLS related pain (p<0.05, chi-square test). [figure2]

KING'S PD PAIN QUEST

Patient ID No:	Initials:		Date of birth:
Date of assessment:	Male 🗆 Female 🗆		Centre:
PAIN IN PARKINSON'S			
The movement symptoms of Park	nson's are we	ll known. Howe	ver, other problems like pain can

Several types of pain are listed below. Please:

- Tick the box "Yes" if you have experienced this particular type of pain during the past month.
- If you have not experienced the type of pain in the past month tick the "No" box.
- · The doctor or nurse may ask you some additional questions to help you decide.

Please note that this questionnaire only relates to the pain you experienced in the last 30 days.

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING IN THE LAST MONTH?

specific type of your pain, particularly if it is troublesome for you.

Yes	No
1. Pain around the joints (including pain related to arthritis)	\Box
 Pain related to a specific internal organ (for example, pain around the liver, stomach or bowels) 	
3. Generalised non-specific pain in your stomach area	
4. Non-specific pain deep within the body: a generalised constant, dull, aching pain \Box	
5. Pain related to abnormal involuntary movements (dyskinetic pain)	
 Painful muscle cramps in a specific region during "off" periods (when your medication is not working) 	
 Generalised pain during "off" periods (pain in the whole body or areas that are not affected by muscle cramps) 	
 Pain related to jerking leg movements during the night or an unpleasant burning sensation in the legs which improves with movement (restless legs syndrome) 	
9. Pain related to difficulties when turning in bed at night	
10. Pain when chewing	
11. Pain related to grinding teeth during the night \Box	
12. Burning sensation in your mouth	
13. Burning pain in the limbs (often associated with swelling or medication)	
14. Shooting pain/pins and needles down the limbs	

Conclusions: Interim results suggest the Kings PD Pain Quest is an useful and the first self completed tool.

SG 7 Non-motor symptoms profiles of different ethnic groups with Parkinson's disease: A study comparing the UK, Thailand, Nigeria and Kuwait

A. Sauerbier, O. Jitkritsadakul, R. Bhidayasiri, J.Y. Al-Hashel, W.A. Kamel, A. Kilany, T. Farombi, P. Martinez-Martin, R. Brown, M. Parry, A. Martin, R. Inniss, L. Perkins, D. Trivedi, L. Klingelhöfer, A. Rizos, P. Zis, K. Ray Chaudhuri

London, United Kingdom

Objective: To analyse and compare the non-motor symptoms (NMS) profile and burden in people with Parkinson's (PwP) with different ethnic origins: Asian (Thailand), African (Nigeria), Arab (Kuwait) and White Caucasian (UK).

Background: Previously, we reported that NMS profiles might be different in White Caucasians (WC) PwP versus Indian PwP in the UK (Sauerbier et al, 2014; Chaudhuri et al, 2000).

Methods: Clinical data related to Asian (Thai) PwP in Thailand, African PwP in Nigeria, Arab PwP in Kuwait, Syria and Egypt and White Caucasian PwP in UK as part of a NMS naturalistic longitudinal study using the Non motor symptoms scale (NMSS) were analysed. Cross sectional data is presented. **Results:** 60 Thai patients (45% male, mean age 60.49±11.24years, mean duration of disease (DoD) 10.75±5.43 years, age at PD onset 49.73±12.36 years, mean Scopa Motor Score 28.7±14.1), 46 Arab patients (53 % male, mean age 63.16±10.80 years, mean DoD 10.3±5.6 years, age at PD onset 53.17±11.50 years, mean Scopa Motor Score 20.46±10.69), 30 African patients (73 % male, mean age 62.58±10.34 years, mean DoD 2.7±2.2 years, age at PD onset 59.88±9.73 years) and 59 WC (71 % male, mean age 67.95±10.20 years, mean DoD 7.55±6.15 years, age at PD onset 60.32±11.19 years, mean Scopa Motor Score 16.85±9.29) have been compared in this ongoing study.

Applying the Kruskal-Wallis equality-of-populations rank test we found a significant difference between the 4 different ethnic groups in the domains sleep and fatigue (p<0.001), attention and memory (p<0.01), gastrointestinal dysfunction (p<0.01), urinary dysfunction (p<0.001), sexual dysfunction (p<0.001) and miscellaneous (p<0.001). In addition, the NMSS total score was significantly different between the 4 ethnic groups (p<0.001).

Conclusions: This is a first study of its kind and our preliminary results support previous observations that NMS profiles might differ between different ethnic groups. However, given that we present a "snapshot" survey in non-matched populations, the study is expanding to larger sample size to explore the range and nature of these differences.

SG 8

Dopamine transporter scan (DaTscan) and clinical global impression of severity of Parkinson's disease: Data from a non motor natural history study

A. Sauerbier, P. Martinez-Martin, M. Poliis, A. Rizos, N. Troja, N. Mulholland, G. Vivian, B. Cocoran, D. Trivedi, L. Perkins, R. Inniss, M. Parry, A. Martin, R. Brown, K. Ray Chaudhuri

London, United Kingdom

Objective: To analyse and compare the association between DaTscan ratios and duration of disease and the clinical global impression of severity of Parkinson's disease (PD).

Background: The Clinical impression of severity index of PD (CISI-PD) is a valid tool to assess the severity of PD in a comprehensive (motor and cognitive) manner in clinical practice.

Methods: Clinical and CISI data related to PD as well as caudate and putamen uptake ratios with DATScan were analysed. Cross sectional data is presented.

Results: 62 patients (70.97% male, mean age 61.55±12.71 years, mean duration of disease 3.7±3.6 years, age at PD onset 67.84±12.76 years, mean Scopa Motor Score 17.65±9.77, Levodopa equivalent dose 441.86±470.84 mg) showed a low mean uptake caudate (right 1.42±0.59, left 1.45±0.57), putamen (right 0.86±0.47, left 0.93±0.39) and striatum (right 1.14±0.52, left 1.20±0.47) in this ongoing study.

A moderate association between the caudate uptake and the duration of disease (right caudate r = -0.49, left caudate r = -0.41) and CISI-PD total score (right caudate r = -0.46, left caudate r = -0.45) was noted while there was a strong association between the duration of disease and putamen uptake (r = -0.56/ - 0.51). Association between putamen uptake and CISI (r = -0.48/ -0.48) was moderate. Overall, a moderate to strong association between the striatum uptake and the duration of disease (right striatum r = -0.54, left striatum r = -0.48) and the total score of the CISI-PD (right striatum r = -0.48, left striatum r = -0.48, left striatum r = -0.48) was noted. Furthermore, cognitive impairment as indicated by Mini Mental State Examination and CISI-PD correlated significantly with putaminal and caudate uptake ratios.

Conclusions: This first study addressing CISI-PD and DaTscan suggests that CISI-PD could function as a marker of disease severity and progression as indicated by striatal and putaminal DaT uptake values in PD. In addition, striatal DaTscan uptake could be a marker for aspects of cognitive impairment in PD.

SG 9

Effect of acute non-oral dopaminergic (apomorphine and levodopa) treatment on non-motor symptoms in Parkinson's disease

L. Perkins, M. Politis, F. Niccolini, A. Sauerbier, R. Inniss, A. Martin, D. Trivedi, K. Ray-Chaudhuri

London, United Kingdom

Objective: To analyse the Non-motor symptoms (NMS) of Parkinson's disease (PD) using the NMS Scale (NMSS) in acute non-oral dopaminergic response tests.

Background: Global and domain based aspects of NMS of PD can be assessed using the NMSS and it is recognised that some NMS could be dopaminergic in origin (Chaudhuri and Schapira, 2009). Previous studies have shown that some NMS are more susceptible to improvement with Apomorphine (Apo) and Intrajejunal levodopa infusion (IJLI) (Martinez-Martin, Reddy et al, 2014).

Methods: In two separate ongoing studies NMS have been documented before and after a standard Apo challenge test and also after IJLI pump (off and on) in a cohort of advanced PD undergoing Apo or IJLI therapy. In the Apo arm, a modified NMSS addressing only severity of NMS was used while in the IJLI group NMSS was used as a whole. In the Apo arm, assessments were performed at baseline (OFF) and after 15 and 30 minutes post Apo, whilst in the IJLI group, NMS were measured at 4, 7 and 10 hrs after pump was switched on.

Results: Apomorphine patients (age (mean +/-SD), 66.5+/-9, disease duration 7.4+/-5.9, HY range 3-4) showed a reduction in NMS severity after challenge, specifically the sleep / fatigue (66.7%), mood and anxiety (66.7%) domains were improved.

In the IJLI arm (age (mean +/-SD) 56.7+/-9.2, disease duration 16.3+/-3.7, HY range 4-5) sleep and fatigue domain (38%), gastrointestinal (40.7%), urinary (45.5%) improved and this was sustained as long as the infusion was continued at 4, 7 and 10 hrs.

Conclusions: Although not matched, these acute challenge based studies suggest that the non-oral agonist (Apo) and non-oral levodopa therapies can lead to improvements in NMS. This supports theories of some NMS being of dopaminergic origin.

SG 10 Sleep assessment in Parkinson's disease – The use of Parkinson's KinetiGraph

L. Klingelhoefer, M. Horne, A. Rizos, A. Sauerbier, S. McGregor, D. Trivedi, L. Perkins, K. Ray Chaudhuri

Dresden, Germany

Objective: In this prospective controlled study we examine whether the Parkinson's KinetiGraph (PKG) can be used as an objective marker of nighttime sleep in patients with Parkinson's disease (PD). **Background:** Sleep disturbances as an important non-motor symptom (NMS) in patients with PD are multifactorial and disturbed nighttime sleep can be expressed with excessive daytime sleepiness (EDS). The PKG, a system consisting of algorithms operating on wrist worn accelerometry, can be used as an objective measure of different motor states. Furthermore, periods of immobility during daytime and nighttime can be measured by PKG and it is thought that these periods represent episodes of sleep.

Methods: A total of 63 PD patients (43 male) were studied and divided to a sleepy and non sleepy group based on Epworth Sleepiness Scale (ESS). 33 patients have been evaluated as controls (PD-C, ESS < 10) while 30 patients had EDS (PD-EDS, ESS > 10). The groups were matched for age, gender and Hoehn and Yahr state. Data from 24-hour PKG recordings over six consecutive days are compared with Hauser diaries and scales of motor state, sleep and health related quality of life (HRQoL).

Results: Both patient groups are comparable in their motor disability and depression as well as medication side effects were not confounders (hospital anxiety and depression scale (HADS) scores and levodopa equivalent dose (LED) were not significant different between the control and study group). Nighttime sleep markers such as the duration of sleep and wake periods measured by PKG showed a significant correlation with the total score of the non motor symptoms questionnaire (NMSQuest) (p=0.002), single items of the NMSQuest, the total score of the Parkinson's disease sleep scale (PDSS) (p=0.002) and a HRQoL scale (p=0.002) in the PD-EDS group alone.

Conclusions: Our preliminary and pilot data suggests that the PKG may be a useful marker for assessment of nighttime sleep. Further studies with comparative nighttime polysomnographic studies would be useful.

SG 11 PD-MCI : Application of the level I criteria and prediction of PDD

J.A. Boel, J. Hoogland, R.M.A. de Bie, J.G. Goldman, B. Schmand, A.I. Tröster, D.J. Burn, I. Litvan, G.J. Geurtsen

The MDS PD-MCI Validation Study Group. Amsterdam, Netherlands

Objective: To evaluate the prognostic value of Level I MDS PD-MCI criteria using Parkinson's disease dementia (PDD) as the primary outcome.

Background: Mild cognitive impairment (MCI) is considered a transitional stage between normal cognitive functioning and dementia. Mild cognitive impairment in Parkinson's disease (PD-MCI) is of potential importance in the early identification and management of patients at risk for the development of

dementia. A clear definition of PD-MCI is essential for future research on etiology, disease course, and disease modifying or causative treatment of cognitive decline in PD.

The International Parkinson and Movement Disorder Society (MDS) proposed diagnostic criteria for PD-MCI, comprising two operationalizations: Level I (abbreviated neuropsychological assessment) and Level II (comprehensive neuropsychological assessment).

Methods: Level I PD-MCI criteria will be retrospectively applied to several databases provided by the MDS Study Group "Validation of Mild Cognitive Impairment in Parkinson's disease". These databases include PD patients with longitudinal neuropsychological assessment and available PDD status. Level I PD-MCI criteria will be applied in several forms: namely by, 1) scales for global cognitive abilities, 2) varying numbers of tests per domain, and 3) different cut-offs for cognitive impairment. Analyses include survival analysis while correcting for relevant demographic variables (e.g. age and years of education) and clinical variables (e.g. symptom duration and UPDRS-III scores).

Results: Longitudinal data on approximately 1400 patients fulfilling level I PD-MCI criteria will be analyzed. Follow-up duration ranges from 1 to 8 years. The results will include the prognostic value of Level I PD-MCI for PDD.

SG 12 Predictive validity of level II PD-MCI criteria for PDD

J. Hoogland, J.A. Boel, R.M.A. de Bie, J.G. Goldman, B. Schmand, A.I. Tröster, D.J. Burn, I. Litvan, G.J. Geurtsen

The MDS PD-MCI Validation Study Group. Amsterdam, Netherlands

Objective: To assess the predictive validity of Level II MDS PD-MCI criteria using Parkinson's disease dementia (PDD) as the primary outcome.

Background: Mild cognitive impairment in Parkinson's disease (PD-MCI) represents a stage of cognitive decline between normal cognition and PDD. Diagnostic criteria for PD-MCI were proposed by the International Parkinson and Movement Disorder Society (MDS). They comprise two operationalizations: level I (abbreviated assessment) and level II (comprehensive neuropsychological assessment). Both can be used as a descriptive entity and are of potential value as a risk factor in studies on the etiology, disease course, and treatment or prevention of cognitive decline in Parkinson's disease. The current study focused on level II PD-MCI.

Methods: Level II criteria were retrospectively applied to four large databases of PD patients with comprehensive and longitudinal neuropsychological assessments. Conversion to dementia was the main outcome. We used a Cox model to evaluate whether level II PD-MCI at baseline adds to the risk of PDD as estimated by age, gender, level of education, disease duration, UPDRS-III, and MMSE score. **Results:** Follow-up data on 470 PD patients were available. The mean age was 68.7 years (SD 8.8), median duration since PD symptom onset was 4.0 years (IQR 2.0-8.0), median UPDRS-III total score was 20 (13-27) and median MMSE score was 28 (27-29). Fourteen percent developed PDD during 1573 person-years of follow-up. Adjusting for the other variables, preliminary analyses indicated an increased risk for PDD with increasing age, a lower MMSE and level II PD-MCI (using a cut-off of -1.5 SD for neuropsychological performance).

Conclusions: Level II PD-MCI increases the risk of PDD beyond the risk estimated by demographic and PD-specific measures.

SG 13 Benign progressive supranuclear palsy : A clinico-pathological analysis of cases with prolonged survival G. Respondek, C. Kurz, M. Stamelou, L.W. Ferguson, A. Rajput, W.Z. Chiu, J.C. Van Swieten, C. Troakes, S. al Sarraj, E. Gelpi, C. Gaig, E. Tolosa, S. Wagenpfeil, A. Giese, T. Arzberger, G. Hoeglinger

Munich, Germany

Objective: To report the clinical and pathological characteristics of patients with Progressive Supranuclear Palsy (PSP) with a disease duration of \geq 10 years, compared to patients with shorter survival.

Background: PSP has been recognized as a rapidly progressive neurodegenerative disease with a mean survival of 5 to 8.6 years (De Bruin et al., 1994; Birdi et al., 2004). However, several studies reported cases of autopsy-confirmed PSP that survived longer than 10 years (Birdi et al., 2004; Litvan et al., 1996; Respondek et al., 2014).

Methods: Clinical charts of autopsy-confirmed PSP cases from five brain banks were systematically reviewed and multiple brain areas were centrally analysed.

Results: Of 137 PSP patients with sufficient clinical data, 37 had a disease duration of \geq 10 years (mean: 14.0 [10 – 27]). Compared to cases with a survival of <10 years, these patients were younger at disease onset (63.6 years [41 – 78] vs. 66.2 years [52 – 91]), presented less frequently with supranuclear gaze palsy and showed a higher prevalence of tremor, asymmetric onset, and initial L-dopa response. Only 38 % of patients with long disease duration qualified for the diagnosis of PSP-P. Although the frequency of falls, cognitive impairment frontal dysfunction, and dysphagia did not differ at final record, the time to onset of these clinical milestones was significantly prolonged in patients that survived \geq 10 years, indicating a slower progression of disease. The primary cause of death in both patient groups was aspiration pneumonia. Histopathologically, patients with a disease duration of \geq 10 years had more Lewy body and ß-amyloid co-pathology, a greater extent of neuronal loss in the caudate nucleus and substantia nigra, less tau pathology in the occipital cortex, and more tau pathology in the striatum, thalamus and medulla oblongata.

Conclusions: A surprisingly high percentage of cases survived longer than 10 years after disease onset. The natural history of this benign PSP variant is characterized by younger age at disease onset, and the late development ofclinical milestones. Due to the assimilation of the clinical picture at final record, histopathological differences present during the early disease course might be abolished at post-mortem examination. Yet, neuropathological analysis revealed regional differences in neuronal loss, tau pathology and co-pathology.

GUIDED POSTER TOUR ABSTRACTS

GUIDED POSTER TOUR 1 -PARKINSON'S DISEASE: PHENOMENOLOGY

1220 Do distribution and co-existent myoclonus and dystonia aid in the identification of SGCE mutations? R. Zutt, J.M. Dijk, K. Peall, H. Speelman, Y.E.M. Dreissen, M.F. Contarino, M.A.J. Tijssen (Groningen, Netherlands)

1185 Modulation of dystonia during sleep

E. Antelmi, R. Ferri, K. Bhatia, F. Mignani, C. Scaglione, F. Provini, P. Martinelli, R. Liguori (Bologna, Italy)

1196 4-year longitudinal changes in clinical rating, medication and quantitative motor assessment in mild and moderate Parkinson's disease: Results from the MODEP study

S. Heinzel, F. Bernhard, M. Maechtel, T. Heger, S. Nussbaum, W. Maetzler, D. Berg (Tuebingen, Germany)

1202 Impact of different baseline motor features on prognosis in Parkinson's disease

A.D. Macleod, C.E. Counsell (Aberdeen, United Kingdom)

1191 A simple approach to monitoring of Parkinson's disease state using a Smart phone platform

J.M. Dean, M. Silverman (Boulder, CO, USA)

1194 Physical activity correlates with disease severity among new onset Parkinson's disease patients

P. Gonzalez-Latapi, J.D. Ciolino, T. Simuni (Boston, MA, USA)

1211 Non-motor symptoms profiles of different ethnic groups with Parkinson's disease: A study comparing the UK, Thailand, Nigeria and Kuwait

A. Sauerbier, O. Jitkritsadakul, R. Bhidayasiri, J.Y. Al-Hashel, W.A. Kamel, A. Kilany, T. Farombi, P. Martinez-Martin, R. Brown, M. Parry, A. Martin, R. Inniss, L. Perkins, D. Trivedi, L. Klingelhöfer, A. Rizos, P. Zis, K. Ray Chaudhuri (London, United Kingdom)

1195 New observations in the Fragile-X associated tremor/ataxia syndrome (FXTAS) phenotype

D.A. Hall, A.Y. Fraint, P. Vittal, A. Szewka, B. Bernard, E. Berry-Kravis (Chicago, IL, USA)

1208 Clinical features of late-stage earlyonset Parkinson's disease: 38 years of follow-up

B. Pinter, A. Diem-Zangerl, G.K. Wenning, W. Oberaigner, K. Seppi, W. Poewe (Innsbruck, Austria)

1219 Comparing wearable activity sensors and self-report measures of mobility

L.F. Zhu, P. Boissy, C. Lavigne-Pelletier, M. Jog, R. Edwards, C. Duval, M. Speechley (London, ON, Canada)

GUIDED POSTER TOUR 2 - SLEEP DISORDERS AND RLS

1254 Periodic leg movements of sleep under general anesthesia

N. Vanegas, M. Hallett, K.A. Zaghloul, C. Lungu (Bethesda, MD, USA)

1245 Deep brain stimulation (DBS) of the subthalamic nucleus (STN) improves restless leg syndrome (RLS) in patients with Parkinson's disease (PD)

O.S. Klepitskaya, Y. Liu, S.H. Sillau, J. Tsai, A.S. Walters (Aurora, CO, USA)

1240 The prevalence of RLS and severity of symptoms in patients with Idiopatic Parkinson's disease in the Republic of Macedonia

A. Doneva, S. Mancevska, V. Donev (Skopje, Macedonia)

1242 Decision making in Parkinson's disease with and without REM sleep behavior disorder

M.L. Fantini, P. Beudin, M. Figorilli, A.R. Marques,

T. Vidal, B. Debilly, P. Derost, U. Miguel, M. Puligheddu, F. Durif (Clermont-Ferrand, France)

1252 Familial impulse control disorders associated with dopaminergic agonist therapy for RLS

M. Schonberger, C. Sidiropoulos, P. LeWitt (West Bloomfield, MI, USA)

1241 Acute restless legs syndrome and kleptomania after liposuction surgery G. Fabiani, H.A.G. Teive (Curitiba, Brazil)

1097 Pilot study to evaluate transcranial direct current stimulation (tDCS) during sleep for the treatment of Parkinson's disease

D.A. Heldman, C.L. Pulliam, L.M. Blassucci, J.P. Giuffrida, C.L. Comella (Cleveland, OH, USA)

926 Sleep architecture observed in the patients with SCA 10

E. London, A.C. Crippa, H.A.G. Teive, A. Moro, M. Moscovich, T. Ashizawa (Curitiba, Brazil)

1009 Motor and non-motor features of Parkinson's disease in idiopathic REM sleep behaviour disorder

M. Rolinski, L. Griffanti, K. Szewczyk-Krolikowski, R.A. Menke, T. Quinnell, Z. Zaiwalla, C.E. Mackay, M.T.M. Hu (Oxford, United Kingdom)

GUIDED POSTER TOUR 3 – TREMOR

1459 Climbing fiber-Purkinje cell synaptic changes correlate with clinical features in essential tremor

S. H. Kuo, R.J. Louis, C.Y. Lin, A.H. Koeppen, P.L. Faust, E.D. Louis (New York, NY, USA)

1470 Elderly onset essential tremor and cognitive impairment

H.A. Shill, J.G. Hentz, J.N. Caviness, E. Driver-Dunckley, S. Jacobson, C. Belden, M.N. Sabbagh, T.G. Beach, C.H. Adler (Sun City, AZ, USA)

1455 The efficacy of electrical muscle stimulation in various tremor syndromes: An open-label, pilot study including 68 patients

O. Jitkritsadakul, C. Thanawattano, C. Anan, R. Bhidayasiri (Bangkok, Thailand)

1444 Rate-controlled syllable repetitions improve comparability of DBS-induced dysarthria between on- and off-state in patients with essential tremor

J. Becker, D. Mücke, A. Hermes, T.A. Dembek, A.F. Josten, I. Meister, V. Visser-Vandewalle, M. Grice, L. Timmermann, M.T. Barbe (Cologne, Germany)

1454 Different features of iron deposition in subcortical nuclei between essential tremor and tremor-dominant Parkinson's disease

L. Jin, J. Wang, G. Fei, C. Zhong (Shanghai, China)

1465 Functional connectivity in the sensorimotor cortex in Parkinson's patients with and without tremor S.E. Qasim, C. de Hemptinne, N. Swann,

P.A. Starr (San Francisco, CA, USA)

1469 Improvement of repeated Archimedes spirals in essential tremor: Evidence for a learning effect?

N. Schuhmayer, C. Weber, M. Kieler, W. Pirker, E. Auff, D. Haubenberger (Vienna, Austria)

1445 Smartphone apps provide a simple, accurate bedside screening tool for orthostatic tremor

D. Bhatti, R. Thompson, A. Hellman, C. Penke, J.M. Bertoni, D. Torres-Russotto (Omaha, NE, USA)

1449 Hypertrophic olivary degeneration does not reduce essential tremor

A. Elkouzi, J.C. Kattah, R.J. Elble (Springfield, IL, USA)

1463 Non-motor symptoms of essential tremor are independent of tremor severity and have an impact on quality of life

T. Musacchio, V. Purrer, A. Papagianni, A. Fleischer, D. Mackenrodt, C. Malsch, G. Gelbrich, F. Steigerwald, J. Volkmann, S. Klebe (Würzburg, Germany)

GUIDED POSTER TOUR 4 -PARKINSON'S DISEASE: NON-MOTOR FEATURES

489 Depression and nighttime-sleep problems in Parkinson's disease

K. Zhu, J. Marinus, J.J. van Hilten (Leiden, Netherlands)

379 Delineating non-motor symptoms in early Parkinson's disease and first-degree relatives

F. Baig, M. Lawton, M. Rolinski, C. Ruffmann, K. Nithi, S.G. Evetts, H.R. Fernandes, Y. Ben-Shlomo, M.T.M. Hu (Oxford, United Kingdom)

427 The contribution of the insula in Parkinson's disease: A quantitative metaanalysis study

M. Marion, L. Christopher, P. Boulinguez, B. Ballanger, A.E. Lang, S.S. Cho, A.P. Strafella (Toronto, ON, Canada)

487 Visual exploration in Parkinson's disease

D.F. Ye, N. Vanegas-Arroyave, P. Lauro, M. Hallett, C. Lungu (Bethesda, MD, USA)

482 Antipsychotic use in Parkinson's disease is associated with increased mortality

D. Weintraub, C. Chiang, H.M. Kim, J. Wilkinson, C. Marras, B. Stanislawski, E. Mamikonyan, H.C. Kales (Philadelphia, PA, USA)

376 Constipation preceding Parkinson's disease – Systematic review and metaanalysis

K.L. Adams-Carr, A. Schrag, S. Shribman, J.P. Bestwick, A. Lees, A.J. Noyce (London, United Kingdom)

431 Elevated salivary DJ-1 in Parkinson's disease is associated with altered salivary secretion

J.M. Masters, A.J. Noyce, G. Giovannoni, T.T. Warner, G.B. Proctor (Herts, United Kingdom)

419 Clinical analysis of the non-motor symptoms of Parkinson's patients with diabetes

Y. Liu, C. Liu, J. Zhang, M. Wang, S. Chen, C. Zhao (Jinan, China)

446 Emaciation and life prognosis in Parkinson's disease

K. Park, T. Oeda, A. Umemura, M. Kohsaka, S. Tomita, H. Sugiyama, H. Sawada (Kyoto, Japan)

378 Aspiration pneumonia in a hospitalized Parkinson's disease cohort

L. Almeida, D. Martinez-Ramirez, K.W. Hageland, J.C. Giuni, C. Little, J.P. Chapman, B. Ahmed, E. Monari, M. Troche, M.S. Okun (Gainesville, FL, USA)

GUIDED POSTER TOUR 5 - LEWY BODY DEMENTIA & DEMENTIAS

1274 Characteristic of cognitive and emotional personality disorders in patients with essential tremor

R.J. Matmurodov, K.K. Khalimova (Tashkent, Uzbekistan)

1273 Parkinson's disease and cognitive reserve

F. Mancini, S. Guzzetti, L.G. Manfredi, A. Caporali, R. Daini, A. Antonini (Milano, Italy)

1271 Pallidal deep brain stimulation improves memory in patients with cervical dystonia: Is the effect on the nucleus basalis of Meynert?

M. Chung, R. Huh, I.U. Song (Incheon, Korea)

1272 Age-dependent distribution change of amyloid-beta protein in macaque brains K. Kimura, K. Inoue, F. Tanaka, M. Takada (Yokohama, Japan)

1279 Learning effect plays a significant role in performance on the Montreal cognitive assessment in patients with Parkinson's disease

J.P. Squires, E. Nosova, K. Co, A. Book, O. Yu, V. Silva, C. Thompson, V. O'Neill, S. Yardley, S. Burden, M. McKeown, A.J. Stoessl, S.A. Cresswell (Vancouver, BC, Canada)

1277 Status of working memory in patients of Parkinson's disease

A. Pal, M. Behari, R. Sharma (New Delhi, India)

1278 Cerebral microbleeds in dementia with Lewy bodies and Alzheimer disease and their influence on cognitive decline T. Poliakova, N. Trusova, A. Arablinskiy, O. Levin (Moscow, Russia)

1275 Effects of early iron deficiency on catecholaminergic transporters in rat brain

W. Mohamed (Shebin el Kom, Egypt)

18 Attentional modulation of activity in the nucleus basalis of Meynert in patients undergoing deep brain stimulation for Parkinson's disease dementia and Lewy body dementia

J. Gratwicke, A. Oswal, S. Little, M. Beudel, V. Litvak, L. Zrinzo, M. Hariz, P. Brown, M. Jahanshahi, T. Foltynie (London, United Kingdom)

GUIDED POSTER TOUR 6 - HD AND OTHER CHOREIFORM DISORDERS

1375 First time use of SD-809 in Huntington disease (first-HD) S. Frank, Huntington Study Group/First-HD Investigators (Boston, MA, USA)

1384 Safety of pridopidine when taken with antidepressants or antipsychotics: Pooled analysis from two Huntington's disease clinical trials

G.B. Landwehrmeyer, S. Zhao, V. Abler (Ulm, Germany)

362 Clinical characteristics and genetic testing of a Huntington mutation negative cohort

K.J. Peall, H.R. Morris, M. Wardle (Cardiff, United Kingdom)

1382 Objective measurement of gait abnormalities in Huntington disease using a shoe-worn inertial sensor

P. Hogarth, A. Lenahan, A. Portillo, R.K. Ramachandran, K.A. Stenson, A.T.R. Legedza, M.C. Botfield, F.B. Horak, J. McNames, M. El-Gohary (Portland, OR, USA)

1380 Using a brief balance assessment to estimate disease onset in Huntington's disease

A. Herndon, J. Corey-Bloom, A. Lam, C. Heil, S.K. Nam, P. Gilbert, D. Goble (La Jolla, CA, USA)

1395 Abnormal electrophysiological motor responses in Huntington's disease:

Evidence of premanifest compensation L.M. Turner, R. Croft, A. Churchyard, J.C.L. Looi, D. Apthorp, N. Georgiou-Karistianis (Canberra, Australia)

1397 Callosal thickness progressively changes in Huntington's disease: 30 month IMAGE-HD data

F.A. Wilkes, M. Walterfang, C. Adamson, J.C.L. Looi, M.L. Seal, D. Velakoulis, J. Stout, A. Churchyard, P. Chua, G.F. Egan, N. Georgiou-Karistianis (Canberra, Australia)

1387 Metabolic brain correlates of apathetic symptoms in pre-manifested Huntington's disease: An 18-FDG PET study

S. Martinez-Horta, J. Perez-Perez, F. Sampedro-Santalo, R. Fernandez-Bobadilla, M. Carceller, J. Pagonabarraga, A. Campolongo, B. Gomez-Anson, B. Pascual-Sedano, V. Camacho-Marti, D. Lopez-Mora, J. Kulisevsky (Barcelona, Spain)

1390 Gait speed modulation in prodromal and early manifest Huntington's disease: Role of internal and external cues

A.K. Rao, F. Porciuncula, J. Uddin, K.S. Marder (New York, NY, USA)

GUIDED POSTER TOUR 7 - RATING SCALES

1088 A multicentre study of the patient's perspective: The first Parkinson's disease pain questionnaire (King's PD pain quest) A.M. Rizos, P. Martinez-Martin, S. Pal, C. Carroll, D. Martino, C. Falup-Pecurariu, B. Kessel, A. Sauerbier, A. Martin, M. Parry, R. Inniss, L. Perkins, D. Trivedi, P. Odin, A. Antonini, K. Ray Chaudhuri (London, United Kingdom)

1075 Handling missing values in the MDS-UPDRS

C.G. Goetz, S. Luo, L. Wang, B.C. Tilley, N.R. LaPelle, G.T. Stebbins (Chicago, IL, USA)

1082 Automatic spiral analysis for objective assessment of motor symptoms in Parkinson's disease

M. Memedi, A. Johansson, F. Bergquist, D. Nyholm (Borlänge, Sweden)

1089 How to screen for dysphagia in Parkinson's disease? The Munich dysphagia test (MDT-PD) – A patient reported outcome questionnaire J.A. Simons, A. Waldmann, U.M. Fietzek (Lübeck, Germany)

1073 UPDRS motor subscales provide a measure of key locomotor function

C. Curtze, J.G. Nutt, P. Carlson-Kuhta, M. Mancini, F.B. Horak (Portland, OR, USA)

1086 PDSS-2 cut-off scores for the severity of sleep disturbances in PD Patients

M.L. Muntean, H. Benes, F. Sixel-Döring, C. Trenkwalder (Kassel, Germany)

1076 Predictive validity of facial masking for experienced stigma in Parkinson's disease

S.D. Gunnery, M. Saint-Hilaire, C.A. Thomas, L. Tickle-Degnen (Medford, MA, USA)

1080 Inter-rater reliability of the hemifacial spasm severity scale (HFS-SS)

E.C. Lim, A.M. Quek, L.L. Yeo, L. Shen, A.W. Chow, R.C. Seet (Singapore)

1071 Correlation between the functional independence measure (FIM) and the scale for assessment and rating of ataxia (SARA) for the evaluation of spinocerebellar ataxia

F.M. Branco Germiniani, T.V. Canelossi Rosa, R. Nickel, P.B.N. Liberalesso, H.A.G. Teive (Curitiba, Brazil)

1077 Minimal clinically important difference on the Parkinson's disease sleep scale 2nd version (PDSS-2)

N. Kovács, Z. Aschermann, P. Ács, G. Deli, J. Janszky, S. Komoly, B. Faludi, K. Horváth (Pécs, Hungary)

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1159 LRRK2 and GBA variants influence rate of motor progression in Parkinson's disease

M.Y. Davis, C. Johnson, J.B. Leverenz, D. Weintraub, J.Q. Trojanowski, A. Chen-Plotkin, V.M. Van Deerlin, S. Factor, C. Wood-Siverio, J.F. Quinn, K.A. Chung, A.L. Peterson-Hiller, L.S. Rosenthal, T.M. Dawson, M.S. Albert, J.G. Goldman, G.T. Stebbins, B. Bernard, D. Yearout, S. Hu, B.A. Cholerton, T.J. Montine, K.L. Edwards, C.P. Zabetian (Seattle, WA, USA)

1162 Novel recruitment strategy to enrich for LRRK2 mutation carriers

T. Foroud, D. Smith, J. Jackson, J. Verbrugge, C. Halter, L. Wetherill, K. Sims, W. Xin, V. Arnedo, S. Lasch, K. Marek (Indianapolis, IN, USA)

1164 Exon dosage analysis of parkin gene in Chinese sporadic Parkinson's disease J.-F. Guo, X. Dong, X.X. Yan, B. Tang (Changsha, China)

1029 Using a GBA deficient drosophila model to understand pathogenic mechanisms in PD

M.Y. Davis, K. Trinh, R. Thomas, B. Whittley, T. Montine, L. Pallanck (Seattle, WA, USA)

1154 Glucocerebrosidase activity in Parkinson's disease with and without GBA mutations

R.N. Alcalay, O.A. Levy, C. Waters, S. Fahn, B. Ford, S.H. Kuo, P. Mazzoni, M.W. Pauciulo, W. Nichols, Z. Gan-Or, G.A. Rouleau, W.K. Chung, P. Wolf, P. Oliva, J. Kreutzer, K.S. Marder, X.K. Zhang (New York, NY, USA)

1167 The impact of rare variants in FUS and HTR2A in essential tremor

F. Hopfner, G. Stevanin, S.H. Müller, E. Mundwiller, M. Bungeroth, A. Durr, M. Pendziwiat, M. Anheim, S.A. Schneider, L. Tittmann, S. Klebe, D. Lorenz, G. Deuschl, A. Brice, G. Kuhlenbäumer (Kiel, Germany)

1234 Dystonia-spasticity in a patient with a novel *SLC25A12* mutation

M. Parnes, L. Robak, J.M. Shulman, A. Stocco, J. Jankovic (Houston, TX, USA)

1223 Drug response to zinc and Dpenicillamine in ATP7B mutant hepatic cell lines

G. Chandhok, J. Horvath, A. Aggarwal, M. Bhatt, A. Zibert, H.H.J. Schmidt (Münster, Germany)

1060 Leucine-rich repeat kinase 2 (LRRK2) impairs function of the retromerassociated WASH complex

K. Venderova, D. Kaing, R. Eismati, R. Joseph, L. Radek, H. Yu-Ju, H. Emily, T. Ariel, F. Ryan, F. Derek (Stockton, CA, USA)

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302 Updated long-term safety from ongoing phase 3 trials of levodopacarbidopa intestinal gel in patients with advanced Parkinson's disease

R.L. Rodriguez, N. Schmulewitz, D. Stein, W.Z. Robieson, C.M. Hall, S. Eaton, K. Chatamra, J.A. Benesh, A.J. Espay (Gainesville, FL, USA)

260 Inhaled levodopa (CVT-301) provides rapid motor improvements after administration to Parkinson's disease patients when OFF

P.A. LeWitt, M.-H. Saint-Hilaire, D.G. Grosset, R. Hauser, F. Stocchi, M.I. Freed, T. DeFeo-Fraulini, M. Leinonen, K. Kieburtz (West Bloomfield, MI, USA)

312 The profile of the hospitalized and rehospitalized Parkinson's disease patient: 5 year data from the National Parkinson's Foundation L. Shahgholi, S. De Jesus, S. Wu, Q. Pei, A. Hassan, P. Schmidt, M. Okun (Gainesville, FL, USA)

181 Clinical predictors of functional decline in early treated Parkinson's disease: NET-PD LS1 cohort

D. Bega, S. Kim, Y. Zhang, J. Elm, J. Schneider, R. Hauser, A. Fraser, T. Simuni, On Behalf of the NET-PD LS1 Investigators (Chicago, IL, USA)

297 A randomized controlled pilot study to evaluate the effect of rotigotine on Parkinson's disease-associated pain

O. Rascol, T. Zesiewicz, K.R. Chaudhuri, M. Asgharnejad, E. Surmann, E. Dohin, S. Nilius, L. Bauer (Toulouse, France)

326 Assessing the burden of osteoporosis in a population of patients with idiopathic Parkinson's disease

M.P. Sritharan, S.J. Jackson (Exeter, United Kingdom)

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oxycodone/naloxone (OXN PR) is associated with treatment benefits in patients with severe Parkinson's disease (PD)-related pain: Results from a randomised, controlled trial C. Trenkwalder, P. Martinez-Martin, O. Rascol, M. Lomax, J. DeCesare, M. Hopp, K.R. Chaudhuri (Kassel, Germany)

321 Safety and clinical effects of NTCELL® [immunoprotected (alginateencapsulated) porcine choroid plexus cells for xenotransplantation] in patients with Parkinson's disease (PD): 26 weeks follow-up

B.J. Snow, K.M. Taylor, J.A. Stoessl, A. Bok, M. Simpson, D. McAuley, L. Macdonald, K.J. Durbin, J. Lee, H. Lin, V. Sossi, K. Dinelle, J. McKenzie (Auckland, New Zealand)

221 Efficacy of opicapone as adjunctive therapy to levodopa in patients with Parkinson's disease and motor fluctuations: Analysis of pooled phase III studies

J. Ferreira, A. Lees, A. Santos, N. Lopes, R. Costa, C. Oliveira, R. Pinto, T. Nunes, J.F. Rocha, P. Soares-da-Silva (S. Mamede do Coronado, Portugal)

196 24 hour levodopa-carbidopa intestinal gel may reduce falls from unresponsive freezing of gait in Parkinson's disease F.C.F. Chang, D.S.Y. Tsui, N. Mahant, N. Wolfe, S.D. Kim, A.D. Ha, J.M. Griffith, M. Drury, V.S.C. Fung (Westmead, Australia)

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1339 Neurochemical and behavioral dysfunction in a new mouse model of dopa-responsive dystonia S.J. Rose, X.Y. Yu, H.A. Jinnah, E.J. Hess

(Decatur, GA, USA)

1343 Neural correlates of GNAL mutation in laryngeal dystonia

K. Simonyan, G. Putzel, T. Fuchs, E. Rubien-Thomas, A. Blitzer, S.J. Frucht, L. Ozelius (New York, NY, USA)

1348 Embouchure dystonia: Phenomenology, natural history and mimicks

P. Termsarasab, S.J. Frucht (New York, NY, USA)

1302 Primary writing tremor is a dystonic trait: Evidence from a single family

R. Erro, M. Ciocca, A. Batla, J. Rothwell, K.P. Bhatia (London, United Kingdom)

1353 Botulinum toxin modulates motor cortical potentiation and depotentiation in focal hand dystonia

K. Udupa, N. Phielipp, R.F.H. Cash, C. Gunraj, R. Pellicciari, T. Hoque, R. Chen (Toronto, ON, Canada)

1290 Correlation between Tsui tremor scores and the Toronto western spasmodic torticollis rating scale (TWSTRS): An analysis of data from the ongoing INTEREST IN CD2 study C. Colosimo, D. Charles, V.P. Misra, P. Maisonobe, S. Om (Rome, Italy)

1355 Task specific oromandibular dystonia secondary to chewing khat (cantha edulis)

P.M. Wadia, J.N. Khanna (Mumbai, India)

1292 Characteristics of dystonia in multiple system atrophy

E.A. Coon, J.E. Ahlskog, M. Suarez, P.A. Low, W. Singer (Rochester, MN, USA)

1325 Sun exposure is an environmental factor for the development of blepharospasm

A. Molloy, L. Williams, O. Kimmich, J. Butler, I. Beiser, E. McGovern, S. O'Riordan, R.B. Reilly, C. Walsh, M. Hutchinson (Dublin, Ireland)

1303 The role of TorsinA in developing neurons

B. Fabry, K. Bretzel, T. Ott, K. Grundmann-Hauser, O. Rieß (Tübingen, Germany)

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662 Progressive ataxia under thalamic neurostimulation in essential tremor, neurostimulation effect or disease progression?

M.M. Reich, J. Brumberg, F. Steigerwald, G. Marotta, T. Musacchio, D.A. Kirsch, L. Müller, K. Herrmann, A. Buck, J. Volkmann, I.U. Isaias (Wuerzburg, Germany)
647 Impedance fluctuations in patients undergoing thalamic deep brain

stimulation for essential tremor and their effect on clinical outcome

J. Eskenazi, E. Tan, A.N. Mamelak, M. Tagliati (Los Angeles, CA, USA)

638 Deep brain stimulation in rare movements disorders

I. Beaulieu-Boire, C.C. Aquino, A.E. Lang, R.P. Munhoz, Y.Y. Poon, A. Valencia, M. Fallis, S. Kalia, M. Hodaie, E. Moro, A.M. Lozano, A. Fasano (Sherbrooke, QC, Canada)

652 Deep brain stimulation for dystonia: A programming algorithm evaluated by long-term results of the German multicentre study for generalized or segmental dystonia

A.D. Kirsch, A.A. Kühn, J. Müller, J. Volkmann for the Deep-Brain Stimulation for Dystonia Study Group (Würzburg, Germany)

651 Functional assessment and quality of life in essential tremor following treatment with bilateral or unilateral deep brain stimulation and unilateral focused ultrasound thalamotomy

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646 Update on deep brain stimulation for refractory Tourette syndrome: 10 patients with CM-Pf/Voi stimulation

R.S. Dowd, M.H. Pourfar, A.Y. Mogilner (New York, NY, USA)

655 Therapeutic deep brain ablation via implanted DBS leads: Technique and potential complications

A. Mantovani, A.R. Bona, M.S. Okun, K.D. Foote (Gainesville, FL, USA)

641 The efficacy of VIM and VIM/ZI DBS in treatment of various tremors

M. Bonello, J. Osman-Farah, P.R. Eldridge, B. Hammersley, L. Lowry, P. Byrne, N.A. Fletcher, S.H. Alusi (Liverpool, United Kingdom)

658 Reversal of acquired hepatocerebral degeneration with live donor liver transplant

A.H. Qavi, S. Hammad, A.I. Rana, M. Salih, N.H. Shah, F.S. Dar, A. Ahmad (Islamabad, Pakistan)

644 Target correlated mapping of therapeutic effects in deep brain stimulation using voxel-based estimations of neuroanatomical structures and volumes of tissue activated

T.A. Dembek, M.T. Barbe, M. Åström, V. Visser-Vandewalle, L. Timmermann (Cologne, Germany)

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105 Association between locus coeruleus pathology and gait dysfunction in Parkinson's disease: A clinicalpathological preliminary analysis K.A. Mills, Z. Mari, C. Bakker, G.M. Pontone, J.C. Troncoso, L.S. Rosenthal (Baltimore, MD, USA)

69 Dopaminergic fibers from the substantia nigra to the olfactory bulb in the rat

D. Alvarez-Fischer, O. Arias-Carrion, C. Klein, W.H. Oertel, G.U. Hoeglinger (Luebeck, Germany)

120 Alpha-synuclein immunohistochemistry studies in gastrointestinal tissue from preclinical Parkinson's disease patients

M.G. Stokholm, E.H. Danielsen, S.J. Hamilton-Dutoit, P. Borghammer (Aarhus, Denmark)

71 Staining for unphosphorylated alphasynuclein in the colon mucosa. No difference between patients with

Parkinson's disease and healthy controls L. Antunes, S. Frasquilho, M. Ostaszewski, J. Weber, L. Longhino, P. Antony, A. Baumuratov, P. Derkinderen, R. Balling, N.J. Diederich (Luxembourg-City, Luxembourg)

119 Isradipine rescues alpha-synuclein toxicity in a zebrafish model of Parkinson's disease by upregulating autophagy

M.C. Stahl, S. Prabhudesai, A. Lulla, J. Bronstein (Hershey, PA, USA)

113 Mid-life milk consumption and substantia nigra neuron density at death

G.W. Ross, R.D. Abbott, H. Petrovitch, K.H. Masaki, L.J. Launer, L.R. White, J. Nelson, C.M. Tanner (Honolulu, HI, USA)

88 Insights into freezing of gait from wearable sensors

F.B. Horak, J.G. Nutt, M. Mancini (Portland, OR, USA)

100 Gait outcomes characterize people with Parkinson's disease who transition to falling within the first year

S. Lord, D. Burn, L. Rochester (Newcastle upon Tyne, United Kingdom)

507 Efficacy of high-frequency repetitive transcranial magnetic stimulation on depression in Parkinson's disease H.-W. Shin, S.J. Chung, Y.H. Sohn (Seoul, Korea)

121 Premorbid exercise engagement and motor reserve in Parkinson's disease M.K. Sunwoo, J.E. Lee, J.Y. Hong, B.S. Ye, H.S. Lee, J. Oh, J.S. Kim, P.H. Lee, Y.H. Sohn (Seongnam, Korea)

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772 Prevalence of depression in atypical Parkinsonian disorders versus Parkinson's disease

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833 Benign progressive supranuclear palsy: A clinico-pathological analysis of cases with prolonged survival

G. Respondek, C. Kurz, M. Stamelou, L.W. Ferguson, A. Rajput, W.Z. Chiu, J.C. Van Swieten, C. Troakes, S. al Sarraj, E. Gelpi, C. Gaig, E. Tolosa, S. Wagenpfeil, A. Giese, T. Arzberger, G. Hoeglinger (Munich, Germany)

826 Highly specific radiographic marker predates clinical diagnosis in progressive supranuclear palsy

E.K. Owens, K.N. Krecke, J.E. Ahlskog, R.D. Fealey, A. Hassan, K.A. Josephs, B.T. Klassen, J.Y. Matsumoto, J.H. Bower (Rochester, MN, USA)

814 The contribution of cerebellar cortex to cognitive impairment in multiple system atrophy using a probabilistic MR atlas-based topographic analysis

J.J. Lee, D.K. Lee, J.H. Ham, J.M. Lee, Y.H. Sohn, P.H. Lee (Seoul, Korea)

823 Underlying dopaminergic deficit in suspected drug-induced Parkinsonism is associated with olfactory impairment J.F. Morley, G. Cheng, J. Bubroff, J.R. Wilkinson, J.E. Duda (Philadelphia, PA, USA)

837 Clinicopathological features and diagnostic criteria for progressive supranuclear palsy with predominant cerebellar ataxia

T. Shimohata, M. Kanazawa, H. Takahashi, M. Nishizawa (Niigata, Japan)

789 Longitudinal follow-up and neurophysiological findings in two Chinese siblings with compound heterozygote mutations in ATP13A2 (PARK9) causing juvenile onset Parkinsonism (Kufor-Rakeb syndrome) H.L. Chiang, D.S.Y. Tsui, S.D. Kim, V.S.C. Fung (Sydney, Australia)

815 American multiple system atrophy natural history study

P.A. Low, S.G. Reich, J. Jankovic, C.W. Shults, M.B. Stern, P. Novak, C.M. Tanner, S. Gilman, F.J. Marshall, F. Wooten, B. Racette, T. Chelimsky, W. Singer, S. May, D.M. Sletten, P. Sandroni, J. Mandrekar (Rochester, MN, USA)

817 The visual estimation of midbrain to pons ratio combined with cerebrospinal fluid biomarkers improves the diagnostic accuracy of PSP

N. Magdalinou, H. Ling, A. Noyce, L. Massey, R. Paterson, J. Schott, I. Davagnanam, C. Micallef, N. Fox, T. Warner, H. Zetterberg, A. Lees (London, United Kingdom)

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548 Interventional MRI (iMRI) guided DBS: Factors affecting lead placement accuracy R.R. Coleman, J.L. Ostrem, P.A. Starr, A.J. Martin, S.E. Qasim, N. Ziman, P.S. Larson (San Francisco, CA, USA)

557 Electrode lead induced white matter changes in patients treated with deep brain stimulation

R. Erasmi, O. Granert, D. Zorenkov, O. Jansen, D. Falk, G. Deuschl, K. Witt (Kiel, Germany)

543 Subthalamic nucleus deep brain stimulation (STN-DBS) reduces freezing of gait in Parkinson's disease in the

VANTAGE prospective, multi-center trial M.T. Barbe, C. Stummer, N. Van Dyck, R. Jain, L. Chen, T. Brücke, F. Seijo, E. Suarez San Martin, C. Haegelen, M. Verin, M. Amarell, S. Gill, A. Whone, M. Porta, D. Servello, F. Alesch, B.R. Bloem, L. Timmermann (Cologne, Germany)

633 Role of the frequency of STN stimulation on bradykinesia in Parkinsonian patients

A. Zacharia, I. Sastre, D. Georgiev, M. Hariz, L. Zrinzo, T. Foltynie, M. Jahanshahi, J. Rothwell, P. Limousin (London, United Kingdom)

563 Differential effects of subthalamic nucleus stimulation frequency on speech intelligibility and verbal fluency in patients with Parkinson's disease

T. Grover, D. Georgiev, R. Kaliola, L. Zrinzo, M. Hariz, T. Foltynie, M. Jahanshahi, P. Limousin, J. Candelario, E. Tripoliti (London, United Kingdom)

596 The maintenance of motor function with unilateral electrode dysfunction in Parkinson's disease after bilateral subthalamic nucleus deep brain stimulation

H. Park, B.S. Jeon, H.J. Kim, W.W. Lee, C.W. Shin (Seoul, Korea)

582 Parkinson's disease (PD) patient experience with deep brain stimulation (DBS) surgery using asleep interventional MRI (iMRI)-guided versus awake physiology-guided implantation techniques

S.C. LaHue, J.L. Ostrem, N.B. Galifianakis, M. San Luciano, N. Ziman, S. Wang, C. Racine, P.A. Starr, P.S. Larson, M. Katz (San Francisco, CA, USA)

550 Motor cortex stimulation for gait disorders in advanced Parkinson's disease

E.U. da Silva, L.A. Nilton, Jr., J.C.E. Veiga, J.M.d.A. Silva, H.C. de Souza (Sao Paulo, Brazil)

618 Effect of STN deep brain stimulation on autonomic functions in patients with Parkinson's disease

P. Surathi, A. Lenka, K.R. Jhunjhunwala, A. Zafar, T.N. Sathyaprabha, R. Yadav, M. Nethravathi, D. Srinivas, A. Arivazhagan, P.K. Pal (Bangalore, India)

632 Hesitation in deciding-deep brain stimulation of Parkinson's disease

J.Y. Yun, M.R. Kim, Y.H. Lim, K.R. Kim, S.H. Paek, B.S. Jeon (Seoul, Korea)

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888 Pattern of working memory deficit in REM sleep behaviour disorder is the same as in Parkinson's disease M. Rolinski, N. Zokaei, C.E. Mackay, M. Husain, M.T.M. Hu (Oxford, United Kingdom)

867 Predictive validity of level II PD-MCI criteria for PDD

J. Hoogland, J.A. Boel, R.M.A. de Bie, J.G. Goldman, B. Schmand, A.I. Tröster, D.J. Burn, I. Litvan, G.J. Geurtsen, The MDS PD-MCI Validation Study Group (Amsterdam, Netherlands)

902 Long-term outcomes for Parkinson's disease patients with normal cognition

D. Weintraub, K. Pigott, J. Rick, S.X. Xie, H. Hurtig, A. Chen-Plotkin, J. Duda, J. Morley, L. Chahine, N. Dahodwala, R. Akhtar, A. Siderowf, J. Trojanowski (Philadelphia, PA, USA)

858 Visual hallucinations in Parkinson's disease with mild cognitive impairment do not imply a more severe cognitive deficit but a more severe cerebral hypometabolism

C. Gasca-Salas, P. Clavero, D. García-García, R. González-Redondo, J. Obeso, M.C. Rodríguez-Oroz (Toronto, ON, Canada)

846 Validation of predictors of dementia in Parkinson's disease

J.B.M. Anang, S.R. Romenets, T. Nomura, R.B. Postuma (Montreal, QC, Canada)

865 Substantia nigra hyperechogenicity and cognitive functions: Results from the TREND study

S. Heinzel, R. Yilmaz, I. Liepelt-Scarfone, B. Roeben, R. Niebler, G.W. Eschweiler, A.J. Fallgatter, F.G. Metzger, W. Maetzler, D. Berg (Tuebingen, Germany)

859 Using virtual reality to investigate the deficits in voluntary gait initiation and cessation in patients with Parkinson's disease and freezing of gait

M.J. Georgiades, M. Gilat, J.M. Shine, S.J.G. Lewis (Sydney, Australia)

877 Does prolonged use of anticholinergic medication contribute to cognitive impairment in early Parkinson's disease? R.A. Lawson, A.J. Yarnall, G.W. Duncan, D.P. Breen, T.K. Khoo, D. Brooks, R.A.

Barker, D. Collerton, J.-P. Taylor, D.J. Burn (Newcastle upon Tyne, United Kingdom)

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237 F15599, a 5-HT1A biased agonist with preferential affinity for post-synaptic receptors, reduces dyskinesia without impairing the anti-Parkinsonian effect of L-DOPA, in the MPTP-lesioned macague P. Huot, T.H. Johnston, A. Newman-Tancredi, S.H. Fox, J.M. Brotchie (Montreal, Canada)

170 Pharmacokinetics, safety and tolerability of sub-lingually administered APL-130277 compared to subcutaneous apomorphine in healthy volunteers

A. Agro, J. Dubow, L. Toong-Chow, A. Giovinazzo (Toronto, ON, Canada)

281 Pharmacokinetic factors and levodopa-induced dyskinesia in Parkinson's disease

T. Oeda, A. Umemura, S. Tomita, M. Kohsaka, K. Park, Y. Mori, H. Sawada (Kyoto, Japan)

322 BDNF rs6265 met allele confers suboptimal response to medication in early Parkinson's disease subjects

C.E. Sortwell, M.L. Hacker, P.E. Konrad, T.L. Davis, J.S. Neimat, L. Wang, Y. Song, Z.R. Mattingly, A. Cole-Strauss, J.W. Lipton, D. Charles (Grand Rapids, MI, USA)

331 Single oral treatment with the 5-HT1A/B agonist, eltoprazine, counteracts L-dopa-induced dyskinesias in Parkinson's disease: A phase I/IIA, double-blind, randomized, placebocontrolled, dose-finding study P. Svenningsson, C. Rosenblad, K. af

Edholm Arvidsson, K. Wictorin, C. Keywood, B. Shankar, D.A. Lowe, A. Björklund, H. Widner (Stockholm, Sweden)

259 Predictability of response to apomorphine subcutaneous injections: **Responder analyses from the AM-IMPAKT** trial

M. Lew, S. Isaacson, F. Pagan, W. Ondo (Los Angeles, CA, USA)

241 Analysis of the incidence of supine hypertension with droxidopa

S. Isaacson, W.B. White, G.J. Rowse, L.A. Hewitt (Boca Raton, FL, USA)

207 Efficacy of IPX066, an extendedrelease formulation of carbidopalevodopa, in advanced Parkinson's disease patients with troublesome dyskinesia

R. Dhall, L. Struck, R. Rubens, V. Shah, S. Gupta (Phoenix, AZ, USA)



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