

Program

Twenty Fourth Annual Symposium on Etiology, Pathogenesis, and Treatment of Parkinson's Disease and Other Movement Disorders

Presented by the Parkinson Study Group, Huntington Study Group, Dystonia Study Group, Myoclonus Study Group, Tourette Syndrome Study Group, Cooperative Ataxia Group, and Tremor Research Group

*To be held on Saturday, 15 May 2010, in the Four Seasons Ballroom at the
Four Seasons Resort, Irving, Texas, 8:30 a.m. to 5:00 p.m.*

The symposium will consist of current issues in genetic and environmental contributions to Parkinson's disease and other movement disorders with peer-reviewed platform and poster presentations designed to communicate recent research advances, including new pharmacological and non-pharmacological treatment options, in the field of Parkinson's disease, Huntington's disease, ataxia, dystonia, myoclonus, Tourette's syndrome, tremor and other movement disorders thereby enhancing patient care.

Current Issues in Genetic and Environmental Contributions to Parkinson's Disease and Other Movement Disorders. This morning session is in honor of the late Clifford W. Shults, MD and hosted by the PSG Genetics and Environmental Risk Working Group.

8:30-8:35 AM

Introduction and acknowledgements by Connie Marras, MD, Chair, PSG Genetics and Environmental Risk Working Group. The following presentations are 20 minutes followed by 10 minutes questions and answers by the audience. The panel discussions are 35 minutes long with 10 minutes for questions and answers by the audience.

8:35-8:55 AM

PRESENTATION: Approaches to Gene Discovery.

David K. Simon, MD, PhD. *Associate Professor of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA.*

9:05-9:25 AM

PRESENTATION: The Spectrum of Genetic Contributions to Parkinson's Disease.

Martha Nance, MD, *Adjunct Professor of Neurology at the University of Minnesota, Medical Director of the Struthers Parkinson's Center and Director of the Hennepin County Medical Center HD Center of Excellence, St. Louis Park, MN, USA.*

9:35-9:55 AM

PANEL DISCUSSION: Melanoma and PD: Association and implications for practice.

Panel Presentation: Epidemiology of melanoma and PD and implications for pathophysiology. Xiang Gao, MD, PhD. *Research Scientist, Harvard School of Public Health, Instructor in Medicine, Harvard Medical School, Associate Epidemiologist, Brigham and Women's Hospital, Boston, MA, USA.*

Panel Presentation: Melanoma and PD: Summary of findings from surveillance studies. Anthony Lang, MD. *Professor of Neurology and Senior Scientist, Division of Patient Based Clinical Research, Toronto Western Research Institute, Toronto, Ontario, Canada.*

ogy and Senior Scientist, Division of Patient Based Clinical Research, Toronto Western Research Institute, Toronto, Ontario, Canada.

Panel Presentation: Implications for practice – should we be making recommendations for screening and what should they be? Karl Kiebertz MD, MPH. *Director, Center for Human Experimental Therapeutics, Professor of Neurology, Preventative Medicine, and Environmental Medicine, Rochester, NY, USA.*

10:05-10:20 AM BREAK

10:20-10:50 AM

PRESENTATION: Update on Environmental Contributions to Parkinson's Disease and Other Movement Disorders.

Alberto Ascherio, MD, PhD. *Professor of Epidemiology and Nutrition, Harvard School of Public Health and Professor of Medicine at the Harvard Medical School, Boston, MA, USA.*

11:00-11:35 AM

PANEL DISCUSSION: Recommendations for Collection, Storage and Use of Genetic and Environmental Data in Parkinson's Disease Clinical Trials.

Introductory remarks by Lin Zhang, MD, Co-chair, PSG Genetics and Environmental Risk Working Group.

Panel Presentation: Genetic Data Collection: Recommendations, Rationale. Tatiana Foroud, PhD. *P. Michael Conneally Professor of Medicine and Molecular Genetics at Indiana University School of Medicine, Indianapolis, IN, USA.*

Panel Presentation: Environmental Data Collection: Current Initiatives, Recommendations, Rationale. Caroline Tanner, MD, PhD. *Director of Clinical Research, The Parkinson's Institute, Sunnyvale, CA, USA.*

Panel Presentation: Considerations of Subject Burden, Implications of Genetic Testing to Subjects. Christine Hunter, RN, CCRC. *Instructor of Neurology, Baylor College of Medicine, Houston, TX, USA.*

Presentations on Parkinson's Disease and Other Movement Disorders. This afternoon session is hosted by the PSG Symposium Organizing Committee. This session consists of a poster session, a guest speaker presentation for 25 minutes with 5 minutes allotted time for questions and answers and 6 platform presentations for 10 minutes with 5 minutes allotted time for questions and answers by the audience.

11:45 AM-12:00 PM

Review and Highlights of Posters by Andrew Feigin, MD, Co-chair, PSG Symposium Organizing Committee.

12:00-1:00 PM

POSTER SESSION: This session consists of presentation of posters by the presenting authors with audience participation.

1:00-1:30 PM

GUEST SPEAKER PRESENTATION: Genetics of Ataxia. Christopher M. Gomez, MD, PhD, Professor and Chair, Department of Neurology, University of Chicago.

1:30-1:45 PM

Serum Cholesterol as a Predictor of the Rate of Clinical Decline in Parkinson Disease: Results from DATATOP.

Xuemei Huang,¹ Peggy Auinger,² Shirley Eberly,³ David Oakes,³ Michael Schwarzschild,⁴ Alberto Ascherio,⁵ Richard Mailman,⁶ Honglei Chen,⁷ for the Parkinson Study Group DATATOP Investigators. ¹Departments of Neurology, Neurosurgery, Pharmacology, Radiology, Kinesiology, and Bioengineering, Pennsylvania State University-Milton Hershey Medical Center, Hershey, PA; ²Center for Human Experimental Therapeutics, University of Rochester School of Medicine and Dentistry, Rochester, New York; ³Department of Biostatistics, University of Rochester, Rochester, NY; ⁴Department of Neurology, Massachusetts General Hospital, Boston, MA; ⁵School of Medical Departments of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA.; ⁶Departments of Neurology, Pharmacology, Pennsylvania State University-Milton Hershey Medical Center, Hershey, PA; ⁷Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA.

Objective: To determine whether serum cholesterol concentrations predict/correlate with clinical progression of PD.

Background: Recent studies (one case control, three prospective studies) have suggested that fasting lower serum cholesterol was positively associated with the occurrence of PD. This led to the hypothesis that higher serum cholesterol would correlate with slower PD progression.

Methods: Eight hundred subjects with early PD enrolled in the Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP) trial. At baseline, the total cholesterol concentration was measured in serum for 774 non-fasting subjects and divided into quintiles. Hazard ratios (HRs) of increasing serum cholesterol concentration for clinical disability requiring levodopa therapy, the pre-specified primary endpoint of the original DATATOP trial, were determined after adjusting for gender, treatment group, baseline age, uric acid concentration, PD subtype, use of antihypertensive meds, use of NSAIDs, BMI, and smoking status. Since only nine subjects reported using cholesterol-lowering agents (two reported statins), this was not adjusted for in the analysis.

Results: The overall mean cholesterol level was 5.6 mmol/L (range 2.6-9.2). The HR of progressing to the primary endpoint decreased with increasing serum cholesterol concentrations. Compared to the lowest quintile, the HRs for each higher quintile (in ascending order) are 0.83 [95% confidence interval (CI), 0.59-1.16]; 0.86 (95% CI, 0.61-1.20); 0.84 (95% CI, 0.60-1.18); and 0.75 (95% CI, 0.52-1.09). The HR for a 1 mmol/L increase = 0.90; 95% CI, 0.80-1.01; one

tail p=0.045 (one-tail p-value is used because this was a hypothesis-driven exploration).

Conclusions: The results of this preliminary exploration of the DATATOP dataset are consistent with the hypothesis that higher total serum cholesterol concentrations at baseline may be associated with slower rates of clinical decline. Further investigations with more refined cholesterol assessment (e.g., at fasting; stratified LDL/HDL) are warranted to help our understanding of the role of cholesterol in PD progression.

Supported by the Parkinson Study Group/Parkinson's Disease Foundation datamining grant.

1:45-2:00 PM

Prevalence and Comorbidity of Psychiatric Diagnoses in a Community-based Sample of Patients with Parkinson's Disease (PD). L. Marsh,^{1,2} E.S. Hirsch,² K.E. Anderson,³ SA Goldstein,^{2,4} S. Grill,² S. Lehmann,² J.T. Little,^{2,5} R.L. Margolis,² J. Palanci,² G.M. Pontone,² P.V. Rabins,² H.W. Weiss,² J.R. Williams.^{4,6} ¹Baylor College of Medicine/ Michael E. DeBakey Veterans Affairs Medical Center, (current affiliation); ²Johns Hopkins University School of Medicine, USA; ³University of Maryland School of Medicine, ⁴Food and Drug Administration, (current affiliation); ⁵Georgetown University School of Medicine, (current affiliation); ⁶Johns Hopkins Bloomberg School of Public Health, USA.

Introduction: Psychiatric disturbances are a common and significant source of morbidity in patients with Parkinson's disease (PD), but are frequently unrecognized or undertreated. Previous prevalence estimates have focused on rates of specific symptoms, single conditions, or a limited range of diagnoses. These approaches heighten awareness of psychopathology in PD, but constrain inferences about differential diagnosis, treatment, and disease complexity.

Methods: Two-staged screening and best-estimate diagnostic procedures, applied by a panel of 6 psychiatrists, were used to determine current and lifetime prevalence of DSM-IV-TR and non-standardized DSM psychiatric diagnoses and rates of co-morbid psychiatric diagnoses in a sample of 250 idiopathic PD patients (MMSE > 24) from three community-based movement disorder practices.

Results: 200 subjects (80%) had at least one current diagnosis; 213(85.2%) had at least one lifetime diagnosis, excluding sleep disorders. Mood disorder diagnoses were the most prevalent class (59.2%,n=148) with Major Depressive Disorder most common [38.8% (n=97); 72%(n=70) had an unremitted Major Depressive Episode]. For other diagnostic classes, current prevalence was as follows: Anxiety:41.6%,n=104; Psychosis:25%,n=62; Impulse Control:6.4%,n=16; Substance Use:1.6%,n=4; and Emotionalism: 12%,n=30. Among the 200 subjects with current DSM diagnoses, 125(62.5%) had two or more diagnoses: 64(32%) had two diagnoses, 41 (20.5%) had three, 15 (7.5%) had four, 4 (2%) had 5, and 1 (0.5%) had 7 diagnoses. Non-standardized depression, anxiety and psychotic diagnoses were present in 12%, 22% and 25% of the total sample, respectively.

Conclusions: The high prevalence of psychiatric diagnoses, co-morbid disturbances, and psychiatric conditions that do not conform to standardized diagnostic criteria contributes to the complexity of PD and poses challenges for its management in community-based neurology practices. Concerted efforts to educate mental health professionals about PD and its psychiatric aspects and facilitate their collaboration with the neurological community may reduce the impact of psychiatric morbidity in PD.

2:00 PM-2:15 PM

Psychogenic Symptoms in Patients with Huntington's Disease. K.M. Shannon,¹ J. Jaglin.¹ ¹Rush University Medical Center, Chicago, IL, USA.

Objective: To describe 7 Huntington's disease (HD) patients with psychogenic symptoms.

Background: HD is characterized by protean motor, behavioral, and cognitive symptoms. Repetitive behaviors are common and may

include obsessions about bodily functions, but these only rarely merit diagnostic interventions or hospitalization. Psychogenic disorders in HD have not been reported.

Methods: We reviewed charts of 171 HD patients followed at our center (83 men, 88 women; mean age 52; range 14-71; mean disease duration 8.7 y; range 0-41 years) for psychogenic symptoms that prompted invasive diagnostic testing, emergency room treatment or hospitalization.

Results: Seven patients (2 men, 5 women; mean age 47 y; mean disease duration 6.7 years) had one or more psychogenic symptoms severe enough to require diagnostic testing, emergency room treatment or hospitalization. In 2 patients, psychogenic symptoms preceded the onset of clinically manifest disease, and in 2 patients, symptoms comprised part of the initial disease presentation. In 3 patients, psychogenic symptoms appeared 2-9 years after motor onset. Psychogenic syndromes included pseudoseizures (1), hemi- or diplegia (2), variable trunk jerking (1); aphagia (1); chest pain and shortness of breath (1), and leakage of stool from the rectum (1). In 6 cases, some improvement followed treatment with antidepressant or anxiolytic therapy, behavioral approaches or supportive psychotherapy. But 3 of these had persistent symptoms longer than one year.

Conclusions: Psychogenic complaints are rare in HD, but can lead to unnecessary diagnostic tests, emergency room visits and hospitalizations. Affected patients may be pre-symptomatic or may have mild to moderate clinically manifest HD. Complaints may be neurological or non-neurological. Some patients respond favorably to medications or psychotherapy, but symptoms may be persistent.

[Study supported by: Huntington's Disease Society of America]

2:15-2:30 PM BREAK

2:30-2:45 PM

Antidepressant Treatment May Have Disease Modifying-effects in Early Parkinson's Disease: A Patient-level Meta-analysis.

K.L. Paumier,¹ A.D. Siderowf,² P. Auinger,³ D. Oakes,³ A.J. Espay,⁴ F.J. Revilla,⁴ A. Sahay,⁴ and T.J. Collier,¹ for the Parkinson Study Group Genetics and Environmental Risk Working Group.

¹Department of Neurology, University of Cincinnati, Cincinnati, Ohio; ²Department of Psychiatry, University of Pennsylvania, Philadelphia; ³University of Rochester School of Medicine and Dentistry, Rochester, New York; ⁴The Neuroscience Institute, Department of Neurology, Movement Disorders Center, University of Cincinnati, Cincinnati, OH, USA.

Objective: The objective of this study was to assess the extent to which antidepressants delay the need for dopaminergic therapy or change the degree of motor impairment and disability in a population of early Parkinson's disease (PD) patients.

Background: Preclinical studies indicate that antidepressants modulate the signaling pathways involved in cell survival and plasticity, suggesting they may serve both to treat PD-associated depression and slow disease progression.

Methods: A patient-level meta-analysis included 2064 patients from the treatment and placebo arms of the following trials: FS1, FS-TOO, ELLDOPA, QE2, TEMPO and PRECEPT. Of these, 451 were taking some form of antidepressant. The primary outcome 'time to dopaminergic therapy' was reported as days to initial use of any dopaminergic therapy. The secondary outcome, degree of motor impairment and disability, was reported as annualized change in total UPDRS score from baseline to final visit.

Results: Antidepressant-treated subjects showed a lower probability of requiring dopaminergic therapy than those not taking antidepressants (HR=0.6, p=0.0002). This effect was not specific to a particular class of antidepressant as subjects taking tricyclics (HR=0.5, p=0.0009), selective serotonin reuptake inhibitors (HR=0.6, p=0.001) or atypical antidepressants (HR=0.5, p=0.02)

had a slower rate of time to dopaminergic therapy than those not taking antidepressants. Mean change in UPDRS scores over time did not differ significantly between antidepressant-treated subjects and those not taking antidepressants (p=0.15); however, the mean change in UPDRS scores was significantly lower in subjects treated with atypical antidepressants (bupropion, mirtazapine, trazodone, and wellbutrin) (p<0.05).

Conclusions: Regardless of class, antidepressants appear to slow the time to dopaminergic therapy in a population of early PD patients. Also, subjects treated with atypical antidepressants may have a lesser degree of motor impairment and disability than those not taking antidepressants. Combined, these results suggest antidepressant therapy may delay progression of overall disability for early PD patients, thus providing a rationale for early intervention.

Supported by the Parkinson Study Group, the Parkinson's Disease Foundation, and the Udall Center of Excellence in Parkinson's Disease Research at the University of Cincinnati (NS58830).

2:45-3:00 PM

LATE-BREAKING RESEARCH

Using Telemedicine to Conduct New Patient Evaluations for Individuals with Movement Disorders.

L.M. Deuel,¹ N.J. Scoglio,¹ J.I. Reminick,^{2,3} B.P. George,² B. Rajan,³ A. Joseph,⁴ A. Seidmann,³ E.R. Dorsey,¹ K.M. Biglan.¹
¹Department of Neurology, University of Rochester School of Medicine and Dentistry, Rochester, New York; ²University of Rochester School of Medicine and Dentistry, Rochester, New York; ³Simon School of Business, University of Rochester, Rochester, New York; ⁴Presbyterian Home for Central New York, Inc., New Hartford, New York, USA.

Objective: To describe the feasibility of using telemedicine to complete new patient evaluations for individuals with suspected or diagnosed Parkinson disease and other movement disorders

Background: Telemedicine may be useful in providing specialty care to underserved populations, including those in rural areas and nursing homes, as they eliminate burdensome travel requirements. In the context of a pilot trial of telemedicine for individuals with Parkinson disease, we completed in-person baseline assessments and follow-up visits via telemedicine. Opening the program to additional community members and nursing home residents who have never before been seen in-person has created a need to evaluate the feasibility of conducting new patient visits via telemedicine.

Methods: Telemedicine visits occurred every three months from November 2008 to February 2010 between two movement disorder specialists at the University of Rochester (Rochester, New York) and patients at the Presbyterian Home for Central New York, Inc. (New Hartford, New York). New patients were referred by nursing home staff members, the Central New York Parkinson Support Group, and the University of Rochester movement disorders clinic.

Results: A total of thirty-two different patients were seen via telemedicine. Of those individuals, fifteen were new patients that had never before been seen by either investigator in-person at the Presbyterian Home or at the movement disorders clinic in Rochester. Fourteen of fifteen new patients (93%) were managed and followed via telemedicine without issue. Diagnoses included Parkinson disease (13/15), vascular parkinsonism (1/15), and progressive supranuclear palsy (1/15). One patient required an in-person evaluation due to a history and exam suggestive of a multifactorial process. In-person evaluation on this patient revealed parkinsonism and evidence of a peripheral polyneuropathy and spastic paraparesis leading to additional diagnostic testing.

Conclusion: Telemedicine is a feasible means of conducting new patient evaluations for individuals with Parkinson disease and other related conditions.

3:00-3:15 PM

LATE-BREAKING RESEARCH**Dopamine Transporter (DAT) Imaging Predicts Motor and Treatment-Resistant Outcomes in Parkinson Disease.**

K Marek,¹ B. Ravina,² J. Seibyl,¹ D. Jennings,¹ S. Eberly,² D. Oakes,² I. Shoulson,² for the PSG PostCEPT (LABS-PD) Investigators. ¹Institute for Neurodegenerative Disorders, New Haven, CT; ²University of Rochester, Rochester, NY, USA.

Objective: To assess whether DAT imaging predicts treatment-resistant outcomes in patients with PD.

Background: Striatal DAT imaging is reduced by approximately 50% at PD diagnosis and ongoing changes in DAT imaging parallel nigrostriatal degeneration. Early imaging and biological markers that predict progression of motor disability and the eventual onset of PD treatment-resistant clinical outcomes would provide an opportunity to design clinical trials that are enriched for PD sub-types.

Methods: Longitudinal clinical data were analyzed from 537 early, untreated PD subjects enrolled in the PRECEPT trial now in the PostCEPT observational cohort (www.PD-DOC.org database). Both DAT imaging acquired at baseline and the change from baseline at 22 months were examined as potential predictors of selected motor, cognitive, and behavioral outcomes. Separate logistic regressions were adjusted for baseline age, gender, duration of disease and PRECEPT treatment.

Results: The mean (sd) striatal baseline DAT uptake was 3.66 (± 1.03). Among subjects with DAT deficit, a one unit increase in baseline DAT uptake was associated with a statistically significant reduction in the change in motor UPDRS (-2.65 (-4.11, -1.19)) and in the risk of developing an MMSE of < 24 (OR=0.5 (0.2, 1.0)), MoCA of < 26 (OR=0.5 (0.4, 0.7)), MCI (OR=0.4 (0.2, 0.6)), hallucinations (OR=0.3 (0.2, 0.5)), falling (OR=0.6 (0.4, 0.9)), and S/E ADL decline ≥ 15 (OR=0.6 (0.4, 0.9)) after a mean clinical follow-up of 5.5 years. The change in DAT uptake showed further significant relationships with motor UPDRS, MMSE, hallucinations, falling, and QOL decline.

Conclusions: These preliminary analyses suggest that the extent of DAT deficit, both at baseline and over time may predict the development of non-motor as well as motor outcomes in PD. These data highlight the value of longitudinal follow up of clinical trial populations to characterize the relationship between imaging biomarkers and clinical outcomes that are largely refractory to treatment.

[Supported by DOD -TATRC W81XWH-06-1-0679, NIH U01 NS050095, Cephalon, Inc., Lundbeck A/S, Parkinson's Disease Foundation (NYC)]

3:15-3:30 PM

AWARDS PRESENTATION: *Presentation of best abstract awards by the PSG Symposium Organizing Committee.*

3:30-5:00 PM

POSTER SESSION

Additional time for viewing of posters and exhibits.

POSTER 1**Late-onset Neurological Wilson's Disease without K-F Rings or Characteristic MRI Findings.**

E. S. Molho. *Albany Medical College, Albany, New York, USA.*

Objective: Report an unusual case of genetically confirmed Wilson's disease (WD) presenting as late-onset parkinsonism without K-F rings or characteristic brain MRI abnormalities.

Background: The age of onset of WD is variable but, generally occurs in the 2nd or 3rd decade. A neurological presentation is rare beyond 40 years and has not been reported without K-F rings or characteristic brain MRI findings. As a result, screening for WD in patients presenting with a movement disorder is not routine after this age and it remains unclear what the upper limit is for age of neurological phenoconversion.

Methods: Case Report.

Results: A 50 year old man presented with a 15 month history of left hand tremor, left arm stiffness, insomnia and anxiety. Examination showed predominantly left sided parkinsonism with resting tremor, rigidity and bradykinesia. K-F rings were absent. Quetiapine and olanzapine were briefly used to treat anxiety after the onset of motor symptoms but, were discontinued at least 2 months prior to presentation. Parkinsonism was subsequently unresponsive to ropinirole, pramipexole and only minimally responsive to levodopa up to 200mg TID. Investigation included a normal brain MRI and normal EEG. Two years later, a low serum ceruloplasmin of 4.1 was unexpectedly found as part of a research project. Repeat studies at a commercial lab were ceruloplasmin 7.4 mg/dL (25-63), serum copper 28 g/dL (70-150), urine copper 65 g/24 hours (3-35). Iron studies and LFTs were normal. Formal ophthalmological exam did not reveal K-F rings. ATP7B gene sequencing (Mayo Clinic) revealed 2 different known pathogenic WD mutations (compound heterozygote). The patient was treated with zinc for 6 months without improvement. A liver biopsy revealed increased copper without cirrhosis and a repeat slit lamp examination at an academic medical center failed to reveal K-F rings. Current treatment is Trientine.

Conclusions: The diagnosis of WD was made fortuitously after a low serum ceruloplasmin was found as part of a research project. This case suggests that late-onset WD is more common than previously thought and expands the range of phenotypic expression to include parkinsonism presenting in later adulthood without the presence of K-F rings or MRI abnormalities. Screening for WD with a serum ceruloplasmin should be routine in patients presenting with parkinsonism, tremor or dystonia in later life.

POSTER 2**The Effect of Onabotulinumtoxin (Botox[®]) Treatment on Restless Legs Syndrome.**

P. Agarwal,¹ C. Sia,² N.K. Vaish,³ ¹Booth Gardner Parkinson's Center, Kirkland, WA and University of Washington, ²Booth Gardner Parkinson's Center, Kirkland, WA; ³Biotechnology company, Bothell, WA, USA.

Background: Restless Legs Syndrome (RLS) is a sensorimotor disorder characterized by an urge to move the legs and often associated with pain and paresthesias. While individual case reports suggest botulinum toxin type A may improve RLS, there have been few systematic investigations into this use.

Objectives: To determine if onabotulinumtoxin is a safe, effective treatment for moderate to severe RLS.

Methods: An open label, single-arm, pilot trial (funded by an unrestricted grant from Allergan, Inc.) was conducted at a tertiary movement disorders center to study the effect of onabotulinumtoxin on moderate to severe RLS. At the initial visit, after screening, patients received 50 units of onabotulinumtoxin (25 units injected into each tibialis anterior muscle). Severity and improvement in RLS were evaluated at subsequent visits (weeks 8 and 12). The primary outcome measure was improvement in International RLS Scale (IRLSS) score. Clinical Global Impressions of Severity and Change (CGIS, CGIC), Patient's Global Impressions of Severity and Change (PGIS, PGIC), Visual Analog Scale (VAS), and the Epworth Sleepiness Scale (ESS) comprised the secondary outcome measures.

Results: Eight patients were enrolled and completed the study. No adverse events or significant side effects were noted. IRLSS improved at visit 2 ($\Delta = -5.75$, $p = 0.0292$) relative to baseline (visit 1). In addition, VAS at visit 3 (~ 5 22.625; $p = 50.0289$) and PGIS ($\Delta = -0.75$, $p=0.047$) improved compared with baseline.

Conclusion: Patients receiving a single dose of onabotulinumtoxin showed improvement in some RLS measures and tolerated the drug well. A larger dose spread over more muscle groups may increase the duration of action without causing side effects such as muscle weakness. A larger pilot study may elucidate the potential for use of this drug in RLS.

POSTER 3

Brain Magnetic Resonance Imaging in Atypical Parkinsonism.

R. Malkani,¹ A. Videnovic,¹ C. Zadikoff,¹ T. Simuni,¹ M. Walker.¹
¹Northwestern University, Chicago, IL, USA.

Objective: To characterize and quantify abnormal brain MRI findings in atypical parkinsonism applying reported MRI findings.

Background: Definitive diagnosis of an atypical parkinsonian disorder requires neuropathological confirmation. Sensitivity of the clinical criteria remains low, especially early in the disease process. Brain Magnetic Resonance Imaging (MRI) may increase the diagnostic accuracy. Only a few standardized imaging criteria have been published and may be underutilized in routine clinical practice.

Methods: A spectrum of brain MRI findings in atypical parkinsonism was identified based on a detailed literature review. A retrospective review of brain MRIs of patients with multiple systems atrophy (MSA), progressive supranuclear palsy (PSP), and corticobasal syndrome (CBS) was thereafter done by a neuroradiologist blinded to the clinical diagnosis and applying reported MRI findings. Findings of our review were subsequently compared with the original MRI reports.

Results: Nineteen subjects with atypical parkinsonism (MSA=12, PSP=2, CBS=5) who had brain MRI after onset of the disease were identified. The most common MRI finding in MSA was putaminal T2 gradient echo hypointensity (n=7). In PSP, midbrain anteroposterior diameter ≤ 17 mm was the most common finding (n=2). In CBS, posterior frontal and superior parietal cortical atrophy (n=3) and T2 hyperintensity in the motor cortex and subcortical white matter were the most frequent findings (n=3). We report the distinguishing imaging findings for MSA and CBS but did not identify any for PSP. All syndromes had overlapping findings on brain MRI. Available initial brain MRI reports recognized abnormal findings in 7/18 (39%) scans.

Conclusions: Although brain MRI findings may assist in the diagnosis of atypical parkinsonism, a significant overlap of abnormal imaging findings exists among these syndromes. Increased awareness of imaging findings among neurologists and radiologists may improve diagnostic utility of brain MRI in atypical parkinsonism.

POSTER 4

Differences in Motor and Cognitive Function in Patients with Parkinsonism with and without Orthostatic Hypotension.

T. Ellis,^{1,3} A.D. Hohler,^{2,3} D. I. Katz,^{2,3} T. J. DePiero,^{2,3}
 C. L. Hehl,³ A. Leonard,³ V. Allen,³ J. Dentino,³ M. Gardner,³
 H. Phenix,³ M.H. Saint-Hilaire.^{1,2} ¹Boston University: College of Health & Rehabilitation Sciences; Sargent; ²Boston University School of Medicine; ³Braintree Rehabilitation Hospital, USA.

Objective: To investigate differences in motor and cognitive function in patients with Parkinson's disease (PD) and Atypical Parkinsonism (APD) with and without orthostatic hypotension (OH).

Background: Patients with PD or APD may present with OH due to side effects of pharmacological management and/or autonomic dysfunction.

Methods: Sixty-one patients with a diagnosis of PD (N=44) or APD (N=17) were admitted to an inpatient rehabilitation hospital to participate in an interdisciplinary movement disorders program from January 2009 to December 2009. The Functional Independence Measure (FIM), the Mini Mental Status Examination (MMSE), the Berg Balance Test (BBT), the Two Minute Walk (TMW), the Timed Up & Go (TUG) and the Finger Tapping (FT) tests were administered within 3 days of admission. Blood pressure (BP) was also recorded during this period. Orthostasis was defined as a drop in systolic BP of 20 mmHg or in diastolic BP of 10 mmHg from sitting to standing.

Results: Of 61 patients admitted, 29 (48%) were determined to be orthostatic (17 with PD, 12 with APD). Patients with OH had significantly lower scores in the Total FIM (p=.006), Motor FIM (p=.04), Cognitive FIM (p=.0007), BBT (p=.03) and the MMSE (p=.001)

compared to patients without OH. No significant differences between groups were found for the TMW, TUG and FT.

Conclusions: Orthostatic hypotension was present in almost half of patients with PD and APD admitted to a rehabilitation hospital. Those with OH had significantly lower gross motor, balance and cognitive function compared to those without OH; walking function and finger tapping were similar between groups. The results suggest that patients with PD and APD should be routinely screened for OH as it commonly occurs and may negatively impact gross motor, balance and cognitive function.

POSTER 5

Utility of the NeuroTrax Computerized Battery for Cognitive Screening in Parkinson's Disease: Comparison to the MMSE and MoCA.

B. Hanna-Pladdy,^{1,2} A. Enslein,^{1,3} M. Fray,^{1,3} B.J. Gajewski,⁴
 R. Pahwa,³ K.E. Lyons.³ ¹Landon Center on Aging, ²Department of Psychiatry & Behavioral Sciences, University of Kansas Medical Center, Kansas City, KS; ³Parkinson's Disease and Movement Disorders Center, Department of Neurology, University of Kansas Medical Center, Kansas City, KS; ⁴Department of Biostatistics, School of Nursing, University of Kansas Medical Center, Kansas City, KS, USA.

Objective: To determine the utility of a predefined computerized battery (NeuroTrax) in providing cognitive profiles in Parkinson's disease (PD) compared to other commonly used screening measures.

Background: Cognitive impairment is an increasingly recognized symptom of PD, although evaluation may be compromised as screening measures may have limited utility in early identification, and comprehensive neuropsychological assessment may not always be practical.

Methods: The cognitive performance of 50 patients with idiopathic PD on the NeuroTrax was compared to the Mini Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA).

Results: The results revealed fair agreement between cognitive impairment identified by the NeuroTrax and the MMSE (kappa =.291, p =.031), but only slight agreement between the NeuroTrax and MoCA (kappa=.138, p=.054) and MoCA and MMSE (kappa=.168, p=.069). The NeuroTrax identified 52% of the sample as average or above, 40% as below average, and 8% as impaired. The MoCA identified 54% of the sample as impaired and 46% as average or above, while the MMSE identified 66% as average or above. Several step-wise regressions revealed that executive functions, and verbal functions were the best predictors of cognitive functioning on the NeuroTrax, while memory recall and working memory were the best predictors on the MoCA. **Conclusions:** These results suggest that the MMSE may lack sensitivity, while the MoCA may be too stringent with a lack of graduated classifications in the below average to mild range of impairment possibly related to heavy weighting of memory and working memory functions. Conversely, the NeuroTrax may provide a better classification of cognitive impairment and provide good utility for cognitive screening in PD because of inclusion of the executive subtest. Future studies should evaluate the agreement between the NeuroTrax and comprehensive neuropsychological assessment in PD.

POSTER 6

Clinical Validation of Diagnostic Procedures for Parkinson's Disease Dementia (PD-D).

B. R. Barton,¹ D. Grabli,² B. Bernard,¹ V. Czernecki,² J. Goldman,¹
 G. Stebbins,¹ B. Dubois,² C. G. Goetz.¹ ¹Rush University Medical Center, USA; ²Hôpital de la Salpêtrière, Paris, France.

Objective: To evaluate proposed diagnostic procedures for detecting Parkinson's disease dementia (PD-D).

Background: Dementia occurs in up to 48-78% of Parkinson's disease (PD) patients. Diagnostic procedures for PD-D based on recent clinical criteria have been proposed by a Movement Disorders Soci-

ety (MDS) Task Force. A brief, practical, bedside eight-item screening checklist derived from simple assessments with suggested cutoff points has not yet been validated in comparison to results of more extensive neuropsychological testing.

Methods: Subjects were recruited from those scheduled for neuropsychological testing at two specialty PD centers, administered by a neuropsychologist as part of routine clinical care. Independent and blinded clinical neurologists also administered the screening checklist. Kappa coefficient was used to compare outcomes of the checklist and the neuropsychological battery.

Results: We tested ninety-one PD subjects, with mean age 66.3 (SD=9.7) and mean disease duration 8.8 years (SD=6.1). Seven subjects (7.7%) met all eight checklist criteria for probable PD-D, as compared to 15 (16.5%) with probable PD-D using the full neuropsychological assessment. There was moderate agreement between these two methods for determination of PD-D (Kappa=0.59, $p < 0.001$). The screening checklist showed 100% specificity and 46.7% sensitivity for diagnosing PD-D as compared to the full neuropsychological assessment. The missed PD-D cases were largely due to two checklist items (positive depression screening and Mini Mental State Examination (MMSE) scores ≥ 26).

Conclusions/Relevance: Where subjects met screening checklist criteria, the designation of PD-D was 100% specific. However, for cases that did not meet these criteria, full neuropsychological testing was still needed to differentiate PD-D from milder cognitive impairment. The screening checklist may therefore be used with confidence that cases included under the designation of PD-D are accurate. Modification of cutoff values for the problem items on the checklist may allow adjustments to optimize sensitivity.

POSTER 7

Effects of Acute Medication Challenge on Quantitative Measures in Standard Movement Tests in Parkinson Disease.

X.K. Gao, K.A. Bonnet. *Eastern Neurologic Services, New York, NY, USA.*

Objective: To assess the effects of acute medication challenge on quantitative measures of standard movement tests in Parkinson disease.

Background: Objective measures of standard movement tests have not yet matched experienced clinician examination.

Methods: Image analyses were applied to video of patients performing standard movement tests (MDS-UPDRS items 3.2,3.4-3.12,3.15-3.17). Quantization of movement parameters was compared in morning "baseline" and in acute (maintenance medication) "challenge". Subjects: 36 adult outpatients (69.90xx +/-10.88xx years, 17 male and 19 female, 77% Chinese-American) with Hoehn-Yahr level 1-3 Parkinson disease. Patients voluntarily provided informed consent and were maintained on carbidopa-levodopa ("CL", 25/100 x1 or x2 daily) for 39-52 months, or on CL-entacapone ("CLE", 25/100/200) for 2-3 weeks after long-term CL, prior to video study. Recording under controlled, in-office conditions, 8:45-9:15 AM, prior to routine morning medication administration ("challenge") and 1 or 2.5 hours later. Age-matched controls (n=15) providing informed consent were recorded under the same conditions.

Results: CL (25/100 x2) challenge produced significant decreases at 1 hour in quantization values for tremor activity, for latency in sit-stand, for head sway upon arising, for head-body sway (standing in place), and for other measures (paired $t > 3.81$, $p < 0.01$ with Bonferroni correction). Arm swing and gait values were significantly improved acutely. Acute challenge effects differed slightly, quantitatively, across individuals within severity levels. CLE (25/100/200 x2) produced similar qualitative effects at 2.5 hours with slightly greater net quantitative effect. Azilect acute challenge data are comparable.

Conclusion: Acute medication challenge short latency effects reflected in quantitative data from controlled recording of video of outpatients in-office can be a useful clinical adjunct for individual treatment. MDS-UPDRS items 3.1,3.3,3.13,3.14, 3.18 and chorea and dystonia are least amenable to quantization in video image analysis.

Quantification data of the variables within the remaining Part 3 motor test items compares with clinical interrater reliability (0.73).

POSTER 8

The Washington State Parkinson Disease Registry.

J.B. Leverenz,^{1,3,4,5,6} H.M. Kim,^{1,5} A. Samii,^{1,4,5} B. Gerton,^{1,5} M. Baca,¹ J. Pate,¹ E. Martinez,¹ S. Thomas,¹ D.W. Tsuang,^{1,3,6} C.P. Zabetian.^{1,2,4,5} ¹VA-Puget Sound Health Care System, ²Geriatric, ³Mental Illness, and ⁴Parkinson Disease Research, Education, and Clinical Centers. Departments of ⁵Neurology and ⁶Psychiatry and ⁶Behavioral Sciences, University of Washington, Seattle, WA, USA.

Objective: To describe the design and characteristics of the Washington State Parkinson Disease Registry (WPDR), and to present WPDR as a resource for movement disorder investigators.

Background: Disease specific registries are often used as an epidemiologic tool. However, registries can also be utilized to promote other kinds of research by connecting well-characterized patients and investigators.

Methods: In collaboration with advocacy groups and the Washington State Department of Health, the WPDR was established in 2007 to recruit PD patients who are willing to be contacted about research participation. A validated screening questionnaire is administered in person or by phone to exclude cases with a low likelihood of PD. Detailed personal and medical information are then collected and updated on a yearly basis. Applications to use WPDR are reviewed by an executive board.

Results: A total of 1004 PD patients are fully enrolled in the WPDR. Mean age of registrants is 69.6 years (± 9.8) with a duration of disease of 8.6 years (± 5.8). Ninety percent of registrants were diagnosed by a movement disorders specialist or neurologist. Most registrants (93%) live in Washington State, but the remainder lives in 21 other states and two other countries. Frequency of common motor and non-motor symptoms include 95% with bradykinesia, 85% with tremor, 89% with gait disturbance, 66% with cognitive impairment, and 49% with depression. Active treatment includes levodopa in 85%, dopamine agonists in 48%, and DBS in 12%. Nine research projects have applied and been approved to use the WPDR.

Conclusions: Surprisingly, the WPDR registrants approximate the demographics of community PD. However, unlike epidemiologically oriented PD registries, WPDR provides ready access to a well-characterized sample of PD subjects who are highly motivated to participate in research. We believe the WPDR fulfills a previously unmet need for researchers and PD patients.

POSTER 9

Vascular Diseases and Cerebral Angiopathy in Patients with Parkinson's Disease and Parkinsonian Syndrome.

R. A. Norman, E. Motta. *Silesian Medical University, Katowice, Poland.*

Background and purpose: The cause of Parkinson disease is still unknown. Changes in cerebral blood flow are considered as one of important pathogenetic factors. On the other side cerebral angiopathy plays role in etiology of Parkinsonian syndrome. Non-invasive neurosonology methods are known to be convenient tool in the assessment of vascular changes. The aim of this study was to assess the character and frequency of comorbid vascular diseases in patients with Parkinson disease and Parkinsonian syndrome. The second aim was the comparison of changes in cerebral blood flow between these groups.

Material and Methods: Eighty eight patients (36 women and 52 men, mean age 68.3+- 8.1 years) were included into the study. Parkinson disease was diagnosed in 66 patients and Parkinsonian syndrome in 22 of them. All patients underwent internal and neurological examination, transcranial doppler evaluation (mean blood flow velocity and pulsatility index in middle cerebral artery),

computed tomography and magnetic resonance imaging of head, neuropsychological examination.

Results: Mean blood flow velocity and pulsatility index in patients with Parkinson disease were in normal range, while in patients with extrapyramidal syndrome mean blood flow velocity in middle cerebral artery was significantly lower and pulsatility index was significantly higher in patients with Parkinsonian syndrome.

Conclusions: 1. Vascular diseases and cerebral angiopathy are more frequent in patients suffered from Parkinsonian syndrome than from Parkinson disease. 2. Transcranial doppler examination is useful in differential diagnosis in patients with extrapyramidal damage.

POSTER 10

Accumulation of Co-morbidities Worsens Functional Mobility and Motor Deficits in Persons with PD.

K.B. Foreman,¹ J.T. Cavanaugh,² G.M. Earhart,³ T.D. Ellis,⁴ M.P. Ford,⁵ L.E. Dibble.¹ ¹University of Utah, Salt Lake City, UT; ²University of New England, Portland, ME; ³Washington University, St Louis, MO; ⁴Boston University, Boston, MA; ⁵University of Alabama at Birmingham, Birmingham, AL, USA.

Objective: To examine the influence of co-morbidities on gait and motor deficits.

Background: While Parkinson disease (PD) results in functional decline and worsening of motor deficits, the influence of co-morbidities on PD-related gait and motor deficits has not been examined. The presence of PD and other conditions contribute to sedentary behavior and we hypothesized that co-morbidities potentiate the burden of PD and are related to greater functional limitations and motor deficits.

Methods: Participants were recruited from samples of convenience at 4 US sites. Medical data were gathered via personal interview. Gait data were collected using the Freezing of Gait (FOG) Questionnaire, 6-Minute Walk Test (6MW), and the Berg balance scale. Motor deficits were quantified using the MDS-UPDRS motor subsection. Self-reported co-morbidities were categorized by number (0-2, 3-4, >5) and used as the independent variable. One-way ANOVAs ($\alpha = 0.05$) were used to evaluate differences between co-morbidity categories for each outcome variable.

Results: Data from 205 participants were analyzed (age: 40-84y; duration of PD: 1-25y; Hoehn and Yahr (HY) score: 1-4). Overall number of co-morbidities ranged from 0-8. There were no between-group differences in duration of PD. In participants with greater than 5 co-morbidities, HY and FOG scores were higher, 6MW distances were shorter, and balance was worse relative to individuals with 0-2 co-morbidities. The severity of motor deficits increased monotonically with co-morbidity number (MDS_UPDRS for 0-2 co-morbidities = 32, >5 = 38).

Conclusions: Greater numbers of co-morbidities appear to be associated with greater PD disease severity, functional limitations, and motor deficits. Many of the co-morbidities examined may be exacerbated by sedentarism and lack of exercise. Future research is needed to examine if exercise interventions targeted at reducing the impact of co-morbidities on functional mobility may have a beneficial impact on persons with PD.

POSTER 11

Perisaccadic Gamma Lateralization with Voluntary Saccades in Parkinson Disease and Controls.

M.A. Javaid,¹ S. Glazman,¹ I. Bodis-Wollner.¹ ¹SUNY Downstate Med Center, Brooklyn, NY, USA.

Background: Scalp recordable gamma range oscillations represent neuronal ensemble properties associated with a number of cognitive processes. Bodis-Wollner et al (2002) and Forgacs et al (2008) emphasized on the importance of peri- especially intrasaccadic (ISG) gamma modulation associated with voluntary saccades. Gamma

power increases over parieto-occipital scalp sites during the saccade and lateralizes with its direction.

Saccades may be away or toward central fixation. Using BOLD imaging, Rieger et al (2003) found an anatomical/functional hemispheric separation of cortical activity for 'towards body center/centripetal CP saccades' and 'away from body center/centrifugal CF'.

Objectives:

1. Quantify perisaccadic gamma lateralization in healthy subjects and PD patients
2. Evaluate perisaccadic gamma for 'CP' and 'CF' saccades.

Method: The EEG was recorded with Electro-cap in 13 healthy subjects (age 23-30 yrs, 3 females) and in 14 PD patients (age 60-70 yrs, 5 females, H-Y stage 1-3). EOG and ISCAN recorded eye movements. Subjects executed saccades to a mark at right on a screen and back to fixation point/midline and vice versa. 2 minute EEG was obtained from each subject for each of the eight possible saccades (rightwards and leftwards, centripetal and centrifugal x 2 distances; 15 and 30 degrees). Each perisaccadic EEG segment was subjected to continuous wavelet transform (cWT). Single trial results were averaged after WT.

T-test was used for gamma power comparisons.

Results:

1. ISG power was higher over contralateral hemisphere to saccade direction for both 'CP' and 'CF'
 2. ISG power is higher for 'CP' than for 'CF'.
 3. ISG is not evident in PD.
- "Parkinsonian" saccades are often "multistep". ISG and saccade kinetics in PD is under investigation.

A lack of hemispheric separation of perisaccadic gamma may be due to the fact that these studies were performed in the light.

Conclusion: Cortical saccade control is impaired in PD.

POSTER 12

Early Clinical Predictors of Treatment-Resistant Outcomes in Parkinson Disease.

R. Kurlan,¹ B. Ravina,² S. Eberly,² D. Oakes,² I. Shoulson,² for the PSG PostCEPT (LABS-PD) Investigators. ¹Atlantic Neuroscience Institute, Overlook Hospital, Summit, NJ; ²University of Rochester, Rochester, NY, USA.

Objective: To identify early clinical predictors of treatment-resistant outcomes in patients with Parkinson disease (PD).

Background: During the initial decade of PD, treatment-resistant outcomes, such as cognitive impairment and balance problems, emerge and become increasingly disabling. The ability to operationally define these outcomes and identify their clinical and biological precursors will enable the design of trials enriched by these precursors and employing early interventions to ameliorate or delay the disabilities.

Methods: We analyzed longitudinal data from 491 early, untreated PD subjects who enrolled in the PRECEPT trial, had dopamine transporter (DAT) deficit on baseline SPECT, and have continued in the PostCEPT observational cohort (www.PD-DOC.org database). Baseline clinical precursors were examined as potential predictors of selected cognitive, motor and behavioral outcomes that are refractory to treatment. Separate logistic regressions, adjusted for baseline age, gender, duration of disease and PRECEPT treatment, were carried out for the frequency of each outcome at the last PostCEPT visit.

Results: Subjects were 65% men with baseline mean age of 59.8 years, duration since diagnosis of 0.8 years and were followed prospectively for an average of 5.5 years. Both freezing of gait and more impaired Schwab & England Activities of Daily Living (S/E ADL) scores at baseline predicted subsequent hallucinations, postural instability and falling. Subjects with more impaired baseline S/E ADL and motor UPDRS scores were more likely to develop cognitive impairment/dementia. More impaired baseline motor UPDRS also predicted subsequent hallucinations and lower quality of life. Walking problems at baseline were predictive of subsequent falling, postural instability, and lower quality of life.

Conclusions: These preliminary analyses support the value of longitudinal follow-up of clinical trial populations to identify early clinical precursors of treatment-resistant outcomes. The strength of these associations should increase as additional longitudinal data are accrued and the frequencies of outcomes increase.

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POSTER 13

Genetic Polymorphisms of the Cholecystokinin (CCK) System in Parkinson's Disease Patients with and without Hallucinations.

J.G. Goldman,¹ D. Marr,² L. Zhou,¹ B. Ouyang,¹ S.E. Leurgans,¹ E. Berry-Kravis,¹ C. G. Goetz,¹ ¹Rush University Medical Center, Chicago, IL, USA; ²University of British Columbia, Canada.

Objective: To determine whether cholecystokinin (CCK) gene and receptor polymorphisms are associated with Parkinson's disease hallucinations (PD-H).

Background: The neuropharmacology of PD-H, a troublesome complication affecting 1/3 of patients on chronic dopaminergic therapy, is not fully understood. CCK, a CNS neuropeptide, influences dopaminergic modulation. Increased hallucination risk has been associated with the CCK -45 C/T locus in Chinese PD patients (Wang J, et al, *Pharmacogenetics* 2003;13:365-9). In a matched case-control study, we previously detected a trend toward more frequent representation of the CCK T allele in Caucasian PD-H patients, particularly when combined with the CCK-A C allele (Goldman JG, et al, *Arch Neurol* 2004;61:1280-4). This study investigates CCK polymorphisms in a larger sample of well-matched Caucasian PD-H patients with PD patients who never hallucinated (PD-NH).

Methods: We studied 88 pairs of PD-H cases and PD-NH controls, matched for age, dopaminergic medications, and PD duration. Genomic DNA was analyzed for CCK polymorphisms by PCR. Genotypic and allelic frequencies were compared using Mantel-Haenszel and Chi-square tests. The numbers of index alleles in cases and controls were compared with Wilcoxon signed rank tests.

Results: The CCK T allele was modestly represented in our Caucasian PD population (overall 15%; PD-H 16%, PD-NH 14 %). Comparing matched pairs, we did not find significant differences in genotype or allele frequencies for the CCK gene, or CCK-A or CCK-B gene receptor polymorphisms. Combined CCK T and CCK-A C genotype did not influence hallucination status. PD hallucinators, however, had worse cognitive function and greater motor impairment.

Conclusions: Our study did not reveal an association between CCK polymorphisms and hallucinations in a large sample of well-matched Caucasian PD patients. The CCK T allele was much less common in our population compared to the Chinese sample reported previously, and thus highlights important racial differences in allele frequencies that contribute to the effects of CCK polymorphisms on PD hallucination risk.

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POSTER 14

Significance and Confounders of Peripheral DJ-1 and α -synuclein in Parkinson Disease.

M. Shi,¹ C.P. Zabetian,¹ K.A. Chung,² J.F. Quinn,² E.R. Peskind,¹ D. Galasko,³ J. Jankovic,⁴ J.B. Leverenz,¹ and J. Zhang,¹ ¹University of Washington, Seattle, WA; ²Oregon Health and Science University, Portland, OR; ³University of California, San Diego, CA; ⁴Baylor College Medicine, Houston, TX, USA.

Objective: Define biomarkers for Parkinson disease.

Background: DJ-1 and α -synuclein are leading biomarkers for Parkinson disease diagnosis and/or disease progression monitoring. A few recent investigations have determined DJ-1 and α -synuclein levels in plasma or serum, a more convenient sample source than cere-

brospinal fluid, but with inconsistent results. Besides limitations in detection technology and limited number of cases in some studies, inadequate control of several important confounders likely has contributed to the variable or even contradictory results obtained to date.

Methods: The relative contribution of each blood components to blood DJ-1 and α -synuclein was evaluated first, followed by quantification of plasma levels of both markers in a larger cohort of patients/subjects (~300 cases) whose DJ-1 and α -synuclein levels have been determined recently in their matching cerebrospinal fluid samples.

Results: DJ-1 and α -synuclein in blood resided predominantly in red blood cells (>95%), followed by platelets (1-4%), white blood cells and plasma (<1%), indicating that variations in hemolysis and/or platelet contamination could have a significant effect on plasma/serum DJ-1 and α -synuclein levels. Nonetheless, after adjusting for the age, although there was a slight decrease in DJ-1 or α -synuclein in patients with Parkinson and Alzheimer disease compared with healthy controls, no statistical difference was observed in this cohort between any groups, even when the extent of hemolysis and platelet contamination were controlled for. Additionally, no correlation between DJ-1 or α -synuclein and disease severity was identified.

Conclusion: Unlike in cerebrospinal fluid, total DJ-1 or α -synuclein in plasma alone is not useful biomarker for Parkinson disease diagnosis or progression/severity.

POSTER 15

NIC-PD - A Randomized, Placebo-controlled, Double-blind, Multi-centre Trial to Assess the Disease-modifying Potential of Transdermal Nicotine in Drug-naïve, Early Parkinson's Disease in Germany and the USA.

M. M. Unger,¹ J. C. Möller,¹ K. Kiebertz,² W. H. Oertel,¹ ¹Philipps-University Marburg, Department of Neurology, Marburg, Germany; ²University of Rochester, Department of Neurology, Rochester, USA.

Background: Currently available pharmacotherapy for Parkinson's disease (PD) is symptomatic. No treatment is available that retards or stops disease progression. Epidemiological and experimental data suggest that nicotine represents a promising substance for disease-modification in PD. Due to the availability and safety of transdermal nicotine treatment, this approach could (if proven to be effective) be easily translated in routine care.

Methods: We developed a study design for evaluation of the disease-modifying potential of transdermal nicotine in early PD patients - the NIC-PD trial. The objective of the NIC-PD trial is to demonstrate that transdermal nicotine treatment retards disease progression in very early-stage PD as measured by change in total UPDRS (part I, II, III) score between baseline and 12 months of transdermal nicotine treatment plus 2 months of wash-out.

The NIC-PD trial has three unique features: 1) The trial assesses for the first time the disease-modifying potential of transdermal nicotine (max. 28 mg /day) over a treatment period of 12 months. 2) For the first time a population of very early-stage (Hoehn and Yahr stage I), drug-naïve PD patients is enrolled in a large prospective trial. This patient population is a.) particularly amenable to disease-modifying effects due to partially intact nigrostriatal projections b.) was chosen as most likely the majority of these patients is only mildly affected and thus patients will not require a symptomatic treatment during the 12 months. By this means, it will be possible to avoid confounding effects of dopaminergic drugs. 3) NIC-PD is a randomized, placebo-controlled, double-blind multicenter trial and the first investigator-initiated transatlantic collaboration between PD networks in Germany and the USA.

The study design will be presented and discussed at the meeting.

[The NIC-PD trial is funded by the Michael J. Fox Foundation for Parkinson Research and resources of the German Competence Network on Parkinson's Disease.]

POSTER 16

Hereditary Parkinson's Disease of Unknown Genetic Cause in Two Families from Southern Sweden.

A.J. Puschmann,^{1,2,3} S. Lindskov,⁴ C. Marktorp,⁴ C. Nilsson,^{2,3} K. Nilsson,^{2,3} J. Reimer,^{2,3} D. van Westen,² E. Persson,² H. Widner,² S. Lincoln,¹ S. Cobb,¹ O. Ross,¹ C. Vilariño-Güell,¹ M. Farrer,¹ Z.K. Wszolek,¹ ¹Mayo Clinic Jacksonville, USA; ²Lund University, Sweden; ³Swedish Parkinson Academy, Sweden; ⁴Central Hospital Kristianstad, Sweden.

Background: The presently known mutations in PD-related genes are found in fewer than 10% of families with hereditary PD. We studied two Southern Swedish families with hereditary PD. The major known genes/mutations for autosomal dominant PD were excluded.

Methods: Seven affected members from 2 families were examined clinically. Data from the medical records were compiled, and two members underwent MRI of the brain and ¹²³I-MIBG scintigraphy.

Results: In **Family F 003**, three siblings have PD. Age at onset was between 50 and 64 years. All three have tremor, bradykinesia and rigidity, a positive response to L-dopa and self-reported anosmia. All three suffered from frequent fainting caused by cardiac arrhythmias, necessitating cardiac pacemaker implantation and sympathectomy in one individual each. MRI of two individuals was normal. Cardiac ¹²³I-MIBG scintigraphy (not performed in the sympathectomized sibling) revealed signs of functional sympathetic denervation. The three siblings' maternal uncle developed PD at age 77. In **Family F 081**, four cousins (two pairs of siblings) developed PD between 57 and 63 years of age. They shared the maternal grandmother, who reportedly had PD since age 55 years, and a maternal aunt with PD. Only one of the 6 affected family members had resting tremor. All six had bradykinesia. Rigidity and positive L-dopa response were noted in the four family members who are still alive. Three had orthostatic hypotension. Cognitive dysfunction became evident in one affected individual after a disease duration of 10-12 years, and eventually, dementia was diagnosed. In **both families**, no pathogenic mutations in *SNCA* (including multiplication), *LRRK2*, *ataxin-2* or *ataxin-3* were detected. Both families originate from the same village.

Conclusions: Further genetic analyses may identify the gene(s) responsible for the PD phenotype in these families. Genealogical studies are also pending to determine if both families share common ancestors.

POSTER 17

Let's Dance! Gait and QOL after Dance Therapy in PD.

L.M. Daniel, E.A. Murray, C.H. Jung, J. Millar, E. Talles, S.R. Dunlop, D. Solomon, R. von Coelln, Z. Mari, and S.H. Ying. *Johns Hopkins University, Baltimore, MD, USA.*

Objective: To evaluate dance therapy for QOL and gait in patients with PD.

Background: The use of dance as movement therapy has been emerging in PD, but data to support efficacy are lacking.

Methods: Nine patients with idiopathic PD participated in a modern dance class. One neurologically normal subject who had taken the class and another normal subject who had not taken the class were also included for comparison. There were two consecutive series of movement therapy instructions, each consisting of 8 weekly on hour dance classes. At the end of each series, patients self-reported on quality of life (SF-36), comparing their status at the end to their status at the beginning of the series. Patients also underwent gait exami-

nation (GAITRite mat, CIR Systems, Havertown, PA, USA). Of the 9 patients tested, 6 patients participated in both sessions. As steadily progressive decline is expected with PD, therapy was considered successful if patients' quality of life or function was the same or better after the series of dance classes.

Results: On both occasions the majority of patients self-reported being the same or better on all 8 domains of QOL measured by the SF-36 (physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health). Of the 6 patients who had repeated quantitative gait measures, a majority performed the same or better on velocity, cadence, stride length, swing percentage, stance percentage, single support percentage, and double support percentage.

Conclusions: A cross-sectional pilot study of dance as movement therapy in PD showed objective improvement gait and quality of life. Dance is a promising method of socially engaging movement therapy for PD as reflected in gait and QOL improvements. A randomized, controlled study is warranted.

POSTER 18

Quantitative Electroencephalography as a Predictor for Parkinson's Disease Dementia.

B. Klassen,¹ J. Hentz,¹ C.H. Adler,¹ H. Shill,² E. Driver-Dunckley,¹ V. Evidente,¹ M. Sabbagh,² J. N. Caviness,¹ ¹Mayo Clinic, Scottsdale, Arizona; ²Sun Health Research Institute, Banner Health System, Sun City, Arizona, USA.

Objective: Evaluate quantitative electroencephalographic (QEEG) measures as predictive biomarkers for dementia incidence in Parkinson's disease (PD).

Background: Reliable biomarkers for PD dementia (PDD) are needed to study the natural course and treatment of PD cognitive decline. Preliminary work shows that certain QEEG measures do correlate with current PD cognitive state. A reliable predictive QEEG biomarker for PDD incidence is not yet identified but would be valuable for the study of PDD, including treatment trials aimed at preventing PD cognitive decline.

Methods: Our brain and body donation program utilizes premortem longitudinal clinical, motor, and neuropsychological evaluation. All PD subjects undergo EEG recording during relaxed wakefulness using standard 10-20 placement. The QEEG measures were analyzed offline to determine background frequency (BF) and relative power in delta, theta, alpha, and beta bands. The incidence of dementia was calculated by using the Kaplan-Meier method. The relationship between the time to onset of dementia and the possible predictors was assessed by using Cox regression.

Results: The hazard of developing dementia was 13 times higher for those with low BF (lower than the grand median of 8.5 Hz) than for those without low BF (95% CI 4.4 to 38, $P < .001$). The incidence of dementia within 5 years was 63% for those with low BF versus 7.5% for those without low BF. The hazard of developing dementia was 2.8 times higher for those with high relative EEG power in the theta band than for those without high theta power (95% CI 1.30 to 6.2, $P .009$). The incidence of dementia within 5 years was 48% for those with high theta power versus 20% for those without high theta power.

Conclusion: The QEEG measures of BF and relative power in the theta band are potential predictive biomarkers for dementia incidence in PD.