

Program

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

Cosponsored by the Parkinson Study Group, Huntington Study Group, Dystonia Study Group, Myoclonus Study Group, Tourette Syndrome Study Group, Cooperative Ataxia Group, Tremor Research Group, and The *Movement Disorder Society*

*To be held on Sunday, 21 September 2008, in the Imperial Ballroom C & D at The Grand America Hotel,
Salt Lake City, UT, USA*

*This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint sponsorship of The Movement Disorder Society and The Parkinson Study Group. The Movement Disorder Society is accredited by the ACCME to provide continuing medical education for physicians. The symposium will consist of peer-reviewed platform and poster presentations designed to communicate recent research advances in the field of Parkinson's disease, Huntington's disease, ataxia, dystonia, myoclonus, Tourette's syndrome, tremor and other Movement Disorders to professionals in neurology and related disciplines. Practitioners, educators, and researchers are invited to attend. Abstracts of platform and poster presentations representing original material will be published in the August 2008 issue of *Movement Disorders*. At the conclusion of this session, participants should be able to: 1) Identify by scholarly review, oral presentation and group discussion the current research into the diagnosis, prevention and treatment of Parkinson's disease and other Movement Disorders; 2) Identify the important advances in research and clinical treatments relating to a variety of Movement Disorders; 3) Discuss new pharmacological and non-pharmacological treatment options available for Parkinson's disease and other Movement Disorders; 4) Identify the mechanisms (genetic, environmental, pathophysiology, neurobiology) linked to Parkinson's disease and other Movement Disorders; and 5) Discuss the diagnostic approaches and tools available for Parkinson's disease and other Movement Disorders.*

8:15 AM-8:30 AM

Introduction and acknowledgements by Andrew Siderowf, MD, MSCE, Chair, PSG Symposia Committee.

8:30 AM – 10:00 AM

KEYNOTE ADDRESSES AND PANEL DISCUSSION:

This session consists of two keynote speakers with a panel discussion to follow. Panel experts will enhance the panel discussions with the participants.

8:30-9:00 AM

KEYNOTE ADDRESS: Prodromal Features of Parkinson's Disease in the Honolulu-Asia Aging Study.

G. Webster Ross, MD. *Pacific Health Research Institute, Honolulu, HI, USA.*

9:00-9:30 AM

KEYNOTE ADDRESS: Biological and Clinical Markers of HD before Diagnosis: The PREDICT-HD Study.

Jane S. Paulsen, PhD. *University of Iowa, Iowa City, IA, USA.*

9:30-10:00 AM

PANEL DISCUSSION: Challenges involved in early detection and potential treatment of Parkinson's disease and Huntington's disease.

G. Webster Ross, MD. *Pacific Health Research Institute, Honolulu, HI, USA.*

Jane S. Paulsen, PhD. *University of Iowa, Iowa City, IA, USA.*

J. William Langston, MD. *The Parkinson's Institute, Sunnyvale, CA, USA.*

Karl Kieburtz, MD, MPH. *University of Rochester Medical Center, Rochester, NY, USA.*

10:00-10:15 AM

BREAK/Poster viewing

10:15 AM – 12:30 PM

PLATFORM PRESENTATIONS:

This session consists of 8 presentations by the following individuals with allotted time for questions and answers after each presenter.

10:15-10:30 AM

LRRK2 prevalence in Sephardic and Ashkenazi Jews.

A.A. Algom,^{1,3} M.J. Rabey,³ Z.K. Wszolek,² M.J. Farrer¹
¹Department of Neuroscience and ²Department of Neurology,
 Mayo Clinic College of Medicine, Jacksonville, FL, USA;
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 Zerifin, Israel.

Introduction: A high prevalence of *LRRK2* G2019S was noted among Ashkenazi Jews. However, there is limited information on prevalence of this mutation in Sephardic Jews. Therefore, we compared the rate of *LRRK2* G2019S mutation among Ashkenazi and Sephardic PD patients and controls.

Methods: DNA was collected through the Ethical Committee approved protocols and consents utilizing standard procedure from Israeli 81 PD and 30 control subjects. DNA was genotyped for the exon 41 *LRRK2* 6055G > A (G2019S) mutation using an ABI 'by-design' probe and analysis was performed using SDS 2.1 software on a 7900ABI.

Results: We studied 50 Ashkenazi PD patients (age 60 ± 12 years), 27 Sephardic PD patients (age 57 ± 11 years), 21 Ashkenazi controls (age 67 ± 10 years), and Sephardic controls (age 66 ± 9 years). We identified G2019S mutation in 4 Ashkenazi PD patients but in none of Sephardic PD patients nor in controls from both groups. We did not have information on the origin of 4 PD and 2 Jewish controls, all were negative for G2019S mutation.

Discussion: The results demonstrate that in our relatively small population sample from Israel, the prevalence of G2019S mutation in Ashkenazi Jews is higher than in Sephardic Jews. We have not found any G2019S mutation carrier in controls. Since there is some controversy regarding the timing of the founding event, our research supports the results derived from the genetic calculation studies that the founding event probably occurred about 700 years ago after the historical separation of Jews to Ashkenazi and Sephardic communities.

10:30-10:45 AM

Role of dopaminergic medications in influencing masked facies in PD: Timing is key.

D. Bowers, U. Springer, A. Mikos, A. Nisenzon, C. Sapienza,
 H.H. Fernandez, M.S. Okun. *University of Florida, Gainesville,
 FL, USA.*

Background: In previous studies we used computer digitizing methods for quantifying dynamic facial expressions and found less robust movement changes in Parkinson Disease (PD) patients compared to controls. The present study investigated what aspects of facial expressivity (i.e., temporal, overall movement) are influenced by dopaminergic deficiency in PD.

Methods: Thirty-nine idiopathic PD patients were videotaped while posing emotional expressions during ON and OFF dopaminergic conditions (12 hour washout). Expressions were digitized and analyzed for dynamic movement changes using custom software (CHEES) that provided indices of initiation time, peak rate of change, and overall movement. On-Off testing order was counterbalanced across different days. Participants were neither depressed nor demented, and in the mid-stages of their disease.

Results: Using repeated measures ANOVA's, we found that dopa medication significantly increased the "peak rate" of facial change ($p < 0.001$) and reduced the *initiation time* of expressions ($p < .001$). However, *total movement* during ON vs OFF conditions failed to reach statistical significance ($p = .09$).

Conclusion: These findings suggest that dopaminergic medications in PD have robust effects on *temporal parameters of facial expressivity* (initiation time, peak rate of change), but not on amount of overall facial movement. More broadly, these findings support the hypothesis of a role for the basal ganglia in modulating facial and other movements. The precise mechanism remains unclear and could involve either diminished activation of frontal cortical regions or movement-based suppression secondary to dopaminergic reduction. Though difficult to appreciate on the UPDRS, clinicians should recognize

there are changes in facial movement, particularly temporal parameters, when comparing ON versus OFF Parkinson medications. Supported by the National Institutes of Health (R01-NS50633, K23-NS44997), the Michael J. Fox Foundation, and the National Parkinson Disease Center of Excellence.

10:45-11:00 AM

Safety and Tolerability of Isradipine, a Dihydropyridine Ca Channel Antagonist, in Patients with Early Parkinson's Disease.

T. Simuni,^{1,2} A. Martel,^{1,2} C. Zadikoff,^{1,2} A. Videnovic,^{1,2}
 L. Vainio,^{1,2} F. Weaver,^{1,2} S. Miskevics,² K. Williams,²
 J. Surmeier.² ¹Northwestern University Feinberg School of Medicine,
 Chicago, IL, USA; ²Hines VA Hospital, Hines, IL, USA.

Objective: To evaluate safety and tolerability of isradipine controlled release preparation in patients with early Parkinson's disease (PD).

Background: Recent data suggests that isradipine, a dihydropyridine calcium channel blocker (CCB), is neuroprotective in vitro /in vivo models of PD. Isradipine has not been systematically studied in PD population.

Methods: Normotensive subjects with early PD received isradipine CR daily, for 12 weeks. Initial 5mg dose was escalated by 5mg every 2 weeks up to 20 mg as tolerated. Subjects maintained daily orthostatic blood pressure logs.

Results: 20 study subjects had mean age 59.1 (±7.65) and disease duration 2 years (±1.49). 6/20 subjects were not receiving dopaminergic therapy, and 14/20 were on a single dopaminergic agent. 17/20 subjects completed the study. Early terminations were not directly related to the study drug. 16/20 subjects tolerated 10 mg dose. 13/20 subjects completed the protocol at the maximum dose 20 mg. The most common reason for dose reduction was leg edema (N=3). One subject developed orthostatic hypotension at 15 mg dose. The most common side effects were: leg edema (40%), fatigue (30%) and dizziness (25%). Most of the side effects were mild and did not require dose adjustment. Isradipine was equally well tolerated in subjects with and without concomitant dopaminergic treatment.

Conclusion: Isradipine CR at the daily dose ≤10 mg appears to be well tolerated in normotensive subjects with early PD. Tolerability of the higher dose warrants additional study with a larger cohort. Additional data on tolerability in hypertensive PD subjects will be presented at the meeting.

11:00-11:15 AM

LATE-BREAKING RESEARCH

Does the Placebo Effect Extend to Caregivers?

C. McRae,¹ E. Fazio,¹ G. Hartsock,¹ J. Pinarowicz,¹ D. Colarossi,¹
 D. Russell,² L. Winfield,³ P. Greene,³ S. Fahn.³ ¹University of
 Denver, Denver, CO, USA; ²Iowa State University, Ames, IA, USA;
³Neurological Institute, Columbia University, New York, NY, USA.

The double-blind sham surgery controlled trial to assess the effectiveness of implantation of human embryonic tissue into the putamen of patients with advanced Parkinson's disease included 40 patients and 21 caregivers (19 spouses). Previously published results have demonstrated that the placebo effect was very strong in this study, with both medical and patient ratings being affected by *perceived* treatment, or the type of surgery patients *thought* they received at each assessment point 4, 8, and 12 months post-surgery. Because caregivers rated both patients and themselves at each time period, we examined caregiver ratings to determine if they were also affected by patients' perceived treatment. Independent samples t-tests and repeated measures analyses were used to investigate differences and changes over time. Results indicated there were no differences between *actual* or *perceived* treatment groups at 4 or 8 months. At 12 months in the actual treatment groups, there were differences in caregiver ratings on 2 measures of patient functioning, including the caregiver version of the Hoehn & Yahr (both $P < .05$). Among the *perceived* groups, or those who *thought* they did or did not receive the surgery, there were differences in caregiver ratings on 11 meas-

ures (all $P < .05$); 2 related to caregivers and 9 related to patient functioning. Thus, there were many more differences on caregiver ratings between the *perceived* treatment groups than the *actual* treatment groups. It appears that the strong placebo effect previously observed in this study also extended to caregiver ratings.

11:15-11:30 AM

BREAK/Poster viewing

11:30-11:45 AM

NH004: A Treatment for Sialorrhea in Parkinson's Disease Patients.

E.R. Gamzu, D. Katzman, N.M. Farber. *NeuroHealing Pharmaceuticals Inc, Newton, MA, USA.*

Sialorrhea (excessive drooling) is a major non-motor complaint in PD and can result in psychological and medical disability. Treatments include surgery, Botox and systemic anticholinergic drugs (SAC), all with limitations. SAC are effective but have unacceptable side effects. The ideal agent would be safe and allow patients to control the specific time to obtain relief. NH004 contains tropicamide in an intra-orally, slow dissolving, muco-adhesive thin strip that conveniently adheres to the oral mucosa proximal to the underlying salivary glands. Tropicamide is a quick acting non-selective muscarinic receptor blocker, with a history of safe use in ophthalmic diagnostic procedures. In a pharmacokinetics study comparing NH004 intra-oral strips with ocular and oral administration in rabbits, tropicamide systemic exposure was 40% less for NH004 than by ocular route, supporting a local effect and safety as least as good as in ophthalmic usage. There were no signs of NH004 toxicity on histological examination of the mucosa. A small double-blind, placebo controlled study tested the dryness in the oral cavity in healthy volunteers using NH004 strips (0, 0.3, 1 and 3 mg tropicamide). Based on a visual analog scale, the 1 and 3 mg doses showed a clear effect lasting over one hour. In an exploratory open-label study of 3 mg dose NH004, PD patients reported a reduction of saliva within 10 min of administration that lasted for about one hr, ideal for use in social situations and between meals. No side effects were reported. NH004 is currently being tested in a phase II, dose response, double-blind crossover clinical study.

11:45-12:00 PM

Minimum Incidence of Primary Task-Specific Focal Hand Dystonia.

R.Y. Lo,¹ C.M. Tanner,¹ K.B. Albers,² A.D. Leimpeter,² R. Fross,² K. Comyns,¹ A. Bernstein,² J. Klingman,² S. Goldman,¹ L. Ozelius,³ C. Marras,⁴ S. Bressman,⁵ C. Comella,⁶ N. Risch,^{2,7} L.M. Nelson,⁸ B.S. McGee,² S.K. Van Den Eeden.² ¹The Parkinson's Institute and Clinical Center, Sunnyvale, CA, USA; ²Northern California Kaiser Permanente Medical Care Plan, Oakland, CA, USA; ³Mount Sinai School of Medicine, New York, NY, USA; ⁴Toronto Western Hospital, Toronto, Ontario, Canada; ⁵Beth Israel Medical Center, New York, NY, USA; ⁶Rush University Medical Center, Chicago, IL, USA; ⁷University of California-San Francisco, San Francisco, CA, USA; ⁸Stanford University, Stanford, CA, USA.

Background: In 1988, Nutt et al (Mov Disord 3:188-194) provided the only published estimate of the incidence of writer's cramp, 0.27/10⁵ person-years, based on 4 cases diagnosed over 32 years in Rochester, Minnesota.

Objective: To estimate the minimum incidence of task-specific focal hand dystonia.

Methods: The database of Northern California Kaiser Permanente Medical Care Plan was searched to identify all diagnostic terms consistent with focal hand dystonia during 2006-2007. We reviewed electronic medical records and clinic charts to identify all newly

diagnosed cases meeting criteria for primary task-specific focal hand dystonia.

Results: We identified 36 incident cases of primary task-specific focal hand dystonia in 4.7 million person-years of observation. The age- and gender-adjusted minimum incidence estimate was 0.72 /10⁵ person-years (95% CI 0.49, 0.96) for individuals over age 20. The average age at diagnosis was similar for men (59 years, range: 35-79) and women (57 years, range: 28-76). A nonsignificant male preponderance was observed (M:F = 1.4:1, $p = 0.21$).

Conclusion: The incidence of task-specific focal hand dystonia in this population is 2.7 times higher than the previous estimate. Because this form of dystonia is often misdiagnosed, this estimate is likely lower than the actual incidence. The suggestion of male predominance resembles the pattern seen in prevalence estimates, but whether this reflects diagnosis bias or a true gender difference is not known. *Supported by grants from NIH 1 RO1 NS046340 to Dr. Tanner.*

12:00-12:15 PM

Neurodevelopment of Dopamine Systems: Insights into the Pathogenesis of Tourette Syndrome.

D.R. Shprecher, R.M. Kurlan. *University of Rochester Medical Center, Rochester, NY, USA.*

Tourette syndrome (TS) is a childhood-onset chronic tic disorder present in up to 3.8% of children. Present in nearly 20% of all children (Neurology 2001;57:1383-1388) at least transient tics may occur during normal childhood central nervous system (CNS) development. In children, persistence of tics may be due to genetically and/or epigenetically mediated errors in the development or maturation of frontal-subcortical inhibitory circuits (Arch Neurol 1997;54:475-483). Developmental and maturational milestones in these dopamine (DA) dependent pathways appear to correlate closely with the natural history of TS. Striatal DA levels reach a plateau between the ages of 2-9 (J Neurochem 2003;87:574-585), the time when most TS children first demonstrate their tics (Arch Pediatr Adolesc Med 2006;160:65-69). Prefrontal gray matter synaptic density peaks between the ages of 11-13 (Nat Neurosci 1999;2:861-863), just as tic severity usually peaks at age 10-11 (Arch Pediatr Adolesc Med 2006;160:65-69). Prefrontal synaptic pruning then ensues and continues beyond age 20. Most TS patients experience a major decline in tic severity between the ages of 15-25 (Ann Neurol 1987;22:383-385; Arch Pediatr Adolesc Med 2006;160:65-69; Pediatrics 1998;102:14-19), the time when prefrontal cortex D1 receptor expression peaks. In some patients with remission in early adulthood, significant recurrence of tics after age 60 can occur (Arch Neurol 1985;42:1079-1080), coinciding with a decline in cortical DA D1 and D2 receptor density and expression (Life Sci 2001;69:1079-1084; Neuroscience 2007;144:1109-1119). Combined with other information implicating disturbances of DA in TS, these close correlations between developmental milestones of the DA system and clinical milestones in the course of TS suggest that careful investigation of all factors influencing DA systems development and maintenance should yield important information on the pathogenesis of the disorder.

12:15-12:30

LATE-BREAKING RESEARCH

Hereditary Diffuse Leukoencephalopathy with Axonal Spheroids (HDLS): A Challenging Diagnosis.

C. Wider,¹ L. Brown,¹ J.Y. Garbern,² E.A. Shuster,¹ A. Tselis,² W. Kupsky,³ C.W. Christine,⁴ S. DeArmond,⁵ D.W. Dickson,⁶ Z.K. Wszolek.¹ ¹Department of Neurology, Mayo Clinic, Jacksonville, FL, USA; ²Department of Neurology, Wayne State University School of Medicine, Detroit, MI, USA; ³Department of Pathology, Wayne State University School of Medicine, Detroit, MI, USA; ⁴Department of Neurology, University of California San Francisco, San Francisco, CA, USA; ⁵Department of Neuropathology, University of California San Francisco, San Francisco, CA, USA; ⁶Department of Neuropathology, Mayo Clinic, Jacksonville, FL, USA.

Objective: To report clinical, imaging and pathological studies of two new families with Hereditary Diffuse Leukoencephalopathy with Axonal Spheroids (HDLS).

Methods: Patients were examined by neurologists and brain tissue by neuropathologists from the University of California (UCSF), Wayne State University and Mayo Clinic. Imaging studies included brain MRI and fluoro-deoxy-glucose PET (FDG-PET).

Results: There were three patients (two women) and four possibly affected individuals in the Michigan family, and two patients (mother and daughter) in the California family. Mean onset age and disease duration in the two families were 39y (five patients; range: 19-57y) and 4y (three deceased patients; range: 3-5y). Michigan family members presented with parkinsonism (postural/gait impairment, asymmetric rigidity, tremor) and initial diagnoses included Multiple Sclerosis (MS) and Parkinson's disease (PD). California family members presented with psychiatric symptoms (depression/suicidal attempts, anxiety, personality changes), followed by dementia and motor impairment (in the mother). Associated findings included syncope, seizures, headache, anorexia, and macrocephaly. Initial diagnoses included several leukodystrophies. MRI studies in both families showed patchy (early stages) or confluent (later stages) white matter signal abnormalities, with cortical atrophy. MR spectrometry and FDG-PET were normal (one patient, early stages). Brain autopsy (one California patient) and biopsy (one Michigan patient) showed patchy white matter disruption with myelin rarefaction and vacuolization, gliosis, and numerous argyrophilic neurofilament-positive axonal spheroids. Spheroids were also seen on electron microscopy.

Conclusion: Our two new pathology-confirmed HDLS families illustrate the phenotypic variability of this condition. HDLS is likely under-recognized as it can mimic PD, MS, and other neurodegenerative or psychiatric diseases.

12:30-12:45 PM

AWARDS PRESENTATION:

Presentation of best abstract awards and closing remarks by Jang-Ho Cha, MD, PhD, Chair, HSG Symposia Committee.

12:45-1:45 PM

POSTER SESSION:

This session consists of a guided tour of the posters by Dr. Andrew Siderowf, Chair of the PSG Symposia Committee and Dr. Jang-Ho Cha, Chair of the HSG Symposia Committee with abstract authors presenting their research.

POSTER 1

Ataxia with Oculomotor Apraxia Type 2 and Neuronopathy in Two Siblings with a Novel Mutation in the Senataxin Gene.

J. Gazulla,¹ I. Benavente,² I. Perez-Lopez,¹ P.J. Modrego,¹ M. Koenig,³ ¹Miguel Servet University Hospital, Zaragoza, Spain; ²Neurophysiology Unit, Hospital San Jorge, Huesca, Spain; ³Institut de Génétique et de Biologie Moléculaire et Cellulaire, CNRS-Université Louis Pasteur UMR7104, Inserm-U596, Illkirch, France.

Background and Objective: Ataxia with oculomotor apraxia type 2 (AOA2) is a rare disease characterized by the following features: onset at an age of 16-22 years, cerebellar atrophy, ataxia, peripheral neuropathy, and elevation of alpha-fetoprotein levels. Its molecular basis is a recessive mutation in the senataxin gene on chromosome 9q34 described firstly in 15 French families. We present two siblings (brother and sister) with the disease and a novel mutation in the senataxin gene.

Observations: Both cases exhibited ataxia, abolished tendon reflexes, limb weakness and hypoesthesia, oculomotor apraxia, elevated levels of serum alpha-fetoprotein (AFP) and creatine-kinase

(CK). The nerve conduction studies were suggestive of a mild sensorimotor neuropathy. Sensory nerve action potentials were absent in the upper and lower limbs. Concentric needle EMG revealed positive sharp waves, fibrillation potentials and fasciculations in proximal and distal muscles. Polyphasic motor unit potentials of large amplitude and increased duration were also recorded. Serum levels of 17-beta estradiol and FSH were indicative of primary ovarian failure in patient 2. Analysis of the SENATAXIN gene by direct sequencing of exons and flanking sequences, demonstrated an homozygous 2755_2756delGT mutation in fragment 1 of exon 8, causing a frame-shift after codon 918 and the occurrence of a stop codon at position 920 (fsVal919Thr920Stop).

Conclusions: Patients with AOA 2 should be investigated in order to establish whether a neuropathy might be responsible for the neuromuscular manifestations. Primary ovarian failure may be a feature of AOA 2 and should be searched for in female patients.

POSTER 2

Dopamine Beta-Hydroxylase in Essential Tremor.

A. Rajput, C. Luo. *University of Saskatchewan, Division of Neurology, Saskatoon, SK, Canada.*

Background: Essential tremor (ET) is the most common neurological cause of tremor. Pathological studies have yielded inconsistent results and little is known of the biochemistry of ET. Elevated norepinephrine levels in ET in the cerebellum, including the cerebellar cortex and dentate nucleus, have been reported in a small study of autopsy brain material. Dopamine beta-hydroxylase (DBH) converts dopamine into norepinephrine. We could find no report in the literature on DBH expression in ET.

Hypothesis: We hypothesized that DBH expression would be increased in the cerebellum of ET compared to control brains.

Methods: Autopsy brain samples from 3 controls and 5 essential tremor cases were examined with Western blot for DBH.

Results: DBH immunoreactivity was not detected in cerebellar cortex or dentate nucleus for either ET or control brains. Frontal and temporal cortex were also tested for DBH expression; overall there was no significant difference between ET and controls for average DBH expression. However, the ET cases could be divided into two distinct groups based on DBH expression in the frontal cortex with 2 cases having greater staining density compared to controls and 3 cases having less staining density than controls.

Conclusion: DBH was not expressed in the cerebellar cortex or dentate in controls or ET in this study as determined by Western blot. Overall there was no difference in average DBH expression in frontal and temporal cortex between controls or ET. Two levels of DBH expression were observed in frontal cortex of ET cases.

POSTER 3

Elderly Male with Chorea Secondary to Primary Antiphospholipid Antibody Syndrome.

C. Sengun,¹ J. Maldonado,¹ M. Maldonado,² A. Guevara,¹ C. Singer¹ ¹Miller School of Medicine, University of Miami Department of Neurology; ² Miller School of Medicine, University of Miami Department of Medicine, Miami, FL, USA.

We report a case of primary antiphospholipid antibody syndrome (PAPS) presenting with a complex picture that included dysarthria, dysphagia and chorea with the unusual feature of late onset in life and affecting the male gender. A 73 year old Caucasian male with prior history of coronary artery disease, myocardial infarction, non-insulin dependent diabetes mellitus, hyperlipidemia, and right acoustic neuroma developed a complex progressive neurological syndrome of dysarthria, dysphagia, generalized choreiform movements

(involving face, trunk and limbs) and gait difficulty for the preceding six months. He had recently being diagnosed with left peroneal neuropathy. He had positive anticardiolipin antibodies of IGG and IGM types, positive phosphatidylserine antibodies of IGG type, increased lupus anticoagulant activity, prolonged Russell's Viper venom time, elevated APTT, and positive intrinsic factor antibodies confirming PAPS. Five days of intravenous gammaglobulin provided a significant symptomatic improvement of the involuntary movements and the dysphagia. We conclude that PAPS syndrome should be considered in the differential diagnosis of new onset chorea in the elderly regardless of gender.

POSTER 4

Vitamin B12, Folate and Thyroid abnormalities in Psychogenic Movement Disorders.

R. Simões,¹ A. Constantino,² ¹Neurology Department, Hospital Fernando Fonseca, Amadora, Portugal; ²Movement Disorder Division, Department of Neurology, University of Louisville, Louisville, KY, USA.

Psychogenic Movement Disorders (PMD) are among the most common conversion diseases and account for 2-15% of patients seen at a Movement Disorder Clinic. Mood and anxiety disorders are frequent co morbidities, occurring in up to 78% of patients. Lower percentages (10-15%) of patients have a coexisting organic neurological disorder, which is hardly recognised. The main tendency is to assume that PMD have a psychopathological origin. There are no studies on underlying metabolic or endocrinologic abnormalities. Vitamin B12 and folate deficiencies and thyroid dysfunction are associated with anxiety and mood disorders and may influence response to antidepressant therapy. Movement disorders have been described in patients with both hypothyroidism and hyperthyroidism and also, although more rarely, in adult patients with vitamin B12 deficiency. We report 2 middle-age women with abrupt onset of a tremor-like PMD following a stressful life event and with a co-morbid refractory mood disorder who had low B12/folate levels and thyroid dysfunction. Both had a long term follow-up without remission of symptoms. Vitamin B12 and Folate deficiencies and thyroid dysfunction may play a role in the course, outcome and response to treatment in patients with PMD. Also, one can speculate that induced involuntary movements may eventually expose vulnerable patients to a new disease manifestation that could be psychogenically perpetuated and underrecognized. As these abnormalities may constitute an important confounder, serum levels should be routinely determined in all patients with PMD, even when there are no other signs or symptoms of dysfunction.

POSTER 5

Peak-dose Painful Dystonia – An Unusual Pattern of Levodopa Induced-Dyskinesia.

R. Simões,¹ A. Constantino,² P. Chand,² D. Houghton,² I. Litvan,² ¹Neurology Department, Hospital Fernando Fonseca, Amadora, Portugal; ²Movement Disorder Division, Department of Neurology, University of Louisville, Louisville, KY, USA.

Motor and non-motor fluctuations are commonly experienced by Parkinson's disease patients on chronic dopaminergic therapy. Fluctuating dystonia and pain are common *off*-phenomena that usually involve the side most affected by parkinsonian symptoms and that are usually accompanied by reappearance of rigidity, bradykinesia and tremor, when levodopa effect wears off. Peak-dose dystonia and pain have been described separately but are rare and atypical. We report a middle age PD patient with 3,5 years of slow release formulation levodopa therapy, who described an unusual pattern of *on*-period painful low back dystonia. These painful episodes followed the levodopa effect: they started insidiously as the antiparkinsonian effect, reached a peak of severe pain when better motor status was achieved and then gradually wore off. Peak-dose choreic dyskinesias

were simultaneously present. These episodes lasted for one hour and were followed by parkinsonian symptoms. During these episodes, the patient was rendered immobile and disabled. Lower dose of levodopa was effective in partially relieving the pain. Peak-dose painful dystonia is an unusual phenomenon not explored in the literature. The pain is probably related to the dystonia, but thalamic deregulation may play a role. The reason for its reduced frequency is not clear. The underlying pathophysiological mechanism is complex and involves overactivity of both the direct striatal output pathway and the subthalamic nucleus. The simultaneous occurrence of different peak-dose phenomena whose mechanisms are complementary adds complexity and suggests different parallel nondopaminergic mechanisms.

POSTER 6

Depression and longer duration of care associated with higher burden in caregivers of PD patients.

K.M. Biglan, L. Deuel, A. Chesire, S. Eason, P. Como. University of Rochester Medical Center, Rochester, NY, USA.

Background: Parkinson disease (PD) is associated with progressive disability, and the burden of care is often placed on spouses or other family members. Little is known about the factors associated with caregiver burden in PD. We explored these factors in a practice-based cohort of PD patients and their caregivers.

Methods: Demographics, disease-specific features, and behavioral assessments were collected in a practice-based cohort of PD patients and their caregivers. The Zarit Caregiver Burden Score (0-88, with higher scores associated with higher burden) was collected in all caregivers. Multiple linear regression methods were used to evaluate those factors associated with increasing caregiver burden.

Results: Thirty-six patients and their caregivers participated; with one exception all caregivers were spouses. Twenty four (66.7%) of the caregivers were female (n=24). PD patients had a mean age of 65.4 (10.2), mean Hoehn and Yahr of 2.4 (0.7), mean Schwab and England (SEADL) of 90.3 (19.8) in non-fluctuators (n=15) and mean "off" SEADL of 65.0 (17.1) in fluctuators (n=21). Caregivers' fear for the patients' futures and the feeling that the patients are dependent upon them most contributed to their burden. Caregivers cited most frequently the transporting to appointments or other outings as their most time consuming task. In the multiple regression model, greater duration of caregiving (p<0.0001) and caregiver depressive symptoms (p=0.06) were associated with higher caregiver burden.

Conclusion: PD caregiver burden is associated with duration of caregiving and caregiver depression. Efforts to reduce caregiver burden could include respite care and treatment of caregiver depression.

POSTER 7

The Effects of Gait Impairment with and without Freezing of Gait in Parkinson's Disease.

A.P. Finkbiner, A.L. Gruber-Baldini, K.E. Anderson, P.S. Fishman, W.J. Weiner, S.R. Reich, L.M. Shulman. University of Maryland School of Medicine, Baltimore, Maryland, USA.

Objective: To compare the impact of gait impairment without freezing of gait (FOG) versus FOG without gait impairment in Parkinson's disease (PD).

Background: FOG increases the risk of falls and disability in PD. However, gait impairment is often present in the absence of FOG, resulting from other PD features (bradykinesia, imbalance).

Methods: PD patients were assessed with the UPDRS and OARS Disability scale. Responses to UPDRS Items #14 (Freezing) and # 29 (Gait) were used to create 4 subgroups: 1) No FOG or gait impairment, 2) FOG, no gait impairment, 3) Gait impairment, no FOG, and 4) Both FOG and gait impairment. Disease severity and disability were compared across the subgroups with ANOVAs, and between subgroups with t-tests.

Results: 916 PD patients were divided into 4 subgroups (N= #1: 213, #2: 41, #3: 323 and #4: 339). Total UPDRS progressively increased from Group 1 through Group 4 (1=25.2, 2=33.7, 3=39.2, 4=59.2; $p<0.001$). Motor UPDRS also progressively increased (1=17.4, 2=19.7, 3=26.9, 4=36.5; $p<0.0001$). Similarly, disability progressively increased (Total OARS: 1=15.3, 2=17.2, 3=18.9, 4=28.4; $p<0.001$). Group 4 was associated with greater disease severity and disability than Groups 2 or 3 ($p<0.001$). Group 3 had greater disease severity than group 2 ($p=0.03$) but not greater disability.

Conclusions: Gait impairment without FOG was associated with greater disease severity than FOG without gait impairment. The combination of gait impairment and FOG was associated with the greatest disease severity and disability. These results show that FOG only partially explains gait-related disability in PD.

POSTER 8

Efficacy and Safety of Low Level Electromagnetic Fields Treatment in Parkinson's Disease.

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Background: Small case series suggest extremely low level (10^{-12} -Tesla) electromagnetic fields (EMF) may be useful in the treatment of Parkinson's disease (PD). No controlled studies have been previously reported.

Design/Methods: A single center, double blind, randomized, placebo controlled trial of EMF as an adjuvant to standard medical therapy in PD patients with motor fluctuations was performed in 12 subjects (6 per group). 24 sessions of 1.5 hour of total body EMF were administered over 8 weeks. Standardized motor and non-motor assessments were performed prior to treatment, at endpoint, and monthly for 3 months.

Results: The treatment group demonstrated significant improvement over placebo after 8 weeks of therapy as follows: *Scale, absolute point reduction, % improvement vs % improvement placebo* (unless noted all results $p<.05$): UPDRS II(ON) 5.5, 56% vs 28%; UPDRS III(ON) 9.5, 40% vs 20%, $p=.054$; PDQ-39(SI) 8.4, 42% vs 7%; PDQ-39(MOB) 11.67, 47% vs 6%; PDQ-39(ADL) 15.97 pts, 64% vs 9%; PDQ-39(BD) 8.33 pts, 30% vs -13%; Beck Depression Inventory II 5.73 pts, 47% vs 1%; Fatigue Severity Scale 7.66 pts, 22% vs 5%, $p=.12$; Finger Taps (ON) 67 taps, 25% vs -5%. Importantly, improvement on several scales persisted up to 2 months post treatment. No treatment related adverse events reported.

Conclusions: Low level EMF may improve motor and non-motor features of PD beyond that achieved with standard medical therapy. These effects are long-lasting. Larger placebo-controlled studies should be undertaken to confirm and further investigate the benefit of this unique, noninvasive and potentially promising therapy.

POSTER 9

A Demonstration of Filterable Nocardiae in the Midbrain in Patients with Parkinson's Disease; The Histochemical and Immunohistochemical Study.

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To confirm or refute the proposed link between nocardiae and Parkinson's disease (PD), we studied the presence of filterable nocardiae at the midbrain nigral lesion of six PD patients. The examination of PD tissues, immunostained for filterable nocardiae, revealed as follows; 1) Several Lewy bodies were immunopositive in stage 2 and 3 PD patients. In stage 3 PD patient, immunopositive and PAS-positive substance was localized in non melanin-pigmented neuron. Nearby the neuron, PAS-positive inclusion within melanin-pigmented neuron was observed. 2) A large number of round structures, immunopositive for filterable nocardiae, was observed in six PD patients. They were vari-

able in size and PAS-positive. They were densely distributed through the ventromedial to the center of ventral region. 3) In one inpatient among four inpatients without neurologic disorders, several Lewy bodies were observed. Lewy body was immunopositive. Round structures, immuno- & PAS-positive and similar to that observed in PD patients, were moderately distributed through the ventromedial region. In other three inpatients, no Lewy body was observed. We concluded that filterable nocardiae might invade the midbrain to be involved in the formation of Lewy body and in the loss of neurons.

POSTER 10

Time Course of Cortical Facilitation Following Subthalamic Deep Brain Stimulation (STN DBS) in Parkinson's Disease.

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Little is known about the time course and effects of STN stimulation on motor cortical circuits. We studied 6 Parkinson's disease patients with chronically implanted STN DBS electrodes. We first identified the latencies of cortical evoked potentials from STN stimulation, then performed single pulse STN DBS followed by TMS to M1 at intervals of 0 to 15 ms and latency of the recorded evoked potential around 23ms. Surface EMG was recorded from the contralateral first dorsal interosseous muscle. TMS was delivered to the M1 ipsilateral to DBS with induced currents in three directions: lateral-medial (LM) to activate corticospinal axons directly, posterior-anterior (PA) to activate corticospinal neurons through one interneuron, anterior-posterior (AP) to activate corticospinal neurons through three interneurons. STN DBS did not change the responses to LM TMS. For PA TMS, MEP facilitation was observed at 2, 3, 7-15ms after STN DBS and at the latency of the long latency evoked potential (~23 ms). For AP TMS, MEPs were significantly larger than control responses at 2 and 3 ms after STN DBS. Single pulse STN stimulation facilitates the M1 at short, medium and long latencies at the level of cortical interneurons but not corticospinal axons. Short latency facilitation (2-3 ms) occurs at the level of interneurons in M1, likely due to antidromic excitation of the cortico-STN fibers. Medium latency facilitation (7-15 ms) may be due transmission through the basal-ganglia thalamocortical pathway. Long latency facilitation (~23 ms) may involve thalamic projections to premotor and parietal areas, subsequently reaching the M1.

POSTER 11

Comparing the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) in Parkinson's Disease.

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Introduction: The Montreal Cognitive Assessment (MoCA), a brief screening tool for cognitive dysfunction, has the same number of points as the more widely used Mini-Mental State Examination (MMSE), but may be more sensitive to early cognitive changes in Parkinson's disease (PD).

Methods: Both tests were administered in counterbalanced order to 63 subjects with PD (mean age=71.3, mean education=14.7) and 70 age-matched controls (NC) (mean age=72.2, mean education =15.2). Associations between MoCA and MMSE with other clinical variables were evaluated by Spearman rank correlations.

Results: Scores on the MoCA (PD $M=22.4$, range=11-30; NC $M=26.5$, range=21-30) were consistently lower with greater range than those on the MMSE (PD $M=27.3$, range=18-30; NC $M=28.6$, range=23-30) in both patient groups ($p<0.001$). Compared to NC, PD subjects had significantly lower scores on the MoCA ($p<0.001$), but not on the MMSE. For PD subjects, MMSE score

correlated with UPDRS I ($r=-.425$; $p=0.012$), UPDRS III ($r=-.560$; $p=0.001$), and UPDRS total ($r=-.456$; $p=0.007$). MoCA score, on the other hand, correlated with UPDRS I ($r=-.497$; $p=0.003$), UPDRS II ($r=-.374$; $p=0.029$), UPDRS III ($r=-.495$; $p=0.003$), UPDRS total ($r=-.465$; $p=0.006$), and a structured evaluation of non-motor symptoms, the NMS Quest ($r=-.455$; $p=0.007$).

Conclusions: Our results suggest that the MoCA may be more effective than the MMSE in screening for cognitive impairment in PD. Larger studies will be needed to confirm and extend these findings.

POSTER 12

Cognitive Declines One Year after Unilateral STN and GPI Deep Brain Stimulation Surgery in Parkinson's Disease.

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Conflicting research suggests that deep brain stimulation (DBS) surgery, an effective treatment for medication-refractory Parkinson's disease, may lead to selective cognitive declines, particularly in verbal fluency. We compared cognitive performance of 22 PD patients who underwent unilateral STN or GPi DBS to 19 medically-treated PD controls of similar age at baseline and 12 months. We hypothesized that compared to PD controls, DBS patients would decline on tasks involving dorsolateral prefrontal cortex circuitry (verbal fluency and working memory) but not on other tasks (semantic knowledge), and that a greater proportion of DBS patients would fall below Reliable Change Indexes (RCIs). Compared to controls, DBS patients declined only on the fluency tasks (i.e., FAS and Animals). RCI and chi-square analyses classified more DBS patients than controls as decliners (50% vs. 11%). T-tests revealed that DBS decliners experienced less motor improvement than non-decliners. Pearson chi-square tests revealed a significant association between left-sided surgery and semantic fluency decline. Our findings provide evidence that unilateral DBS surgery is associated with verbal fluency declines. While results suggest these changes may not be systematically related to age, cognitive or depression status at baseline, semantic fluency declines are more common after left-sided surgery and amongst patients who show less motor improvement. The present study adds to the literature through its hypothesis-driven method of task selection, inclusion of a control group, longer-term follow-up and use of Reliable Change, which highlights the impact of individual variability and indicates that fluency declines likely reflect significant changes in a subset of patients who may demonstrate less robust surgical outcome.

POSTER 13

Declines in Memory and Processing Speed after Deep Brain Stimulation Surgery for Parkinson Disease.

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Background: Although Deep Brain Stimulation (DBS) surgery is an effective treatment for medication-refractory Parkinson disease (PD), it may lead to certain cognitive declines. The present study investigated the effects of unilateral DBS on memory, processing speed, executive functioning and visuospatial abilities. Additionally, we examined the clinical significance of effects using reliable change indices and predictors of decline using regression analyses.

Methods: We used the University of Florida Movement Disorders Center research database to compile data from 25 unilateral DBS patients and 19 PD controls of similar age, education, and disability level. Neuropsychological testing took place before DBS and 15 months after surgery.

Results: Compared to PD controls, the DBS group declined on a processing speed composite but not on the other neuropsychological tests. Reliable change analyses revealed that 24% of DBS patients experienced significant declines on list learning compared to 0% of controls. Additionally, a small but significant proportion of DBS patients declined relative to controls on tests of story memory, processing speed, and response inhibition. Presurgical performance on the list learning task was a significant predictor of decline, but no other predictors (i.e., age, general cognitive status, side of surgery, depression) were significant.

Conclusions: This study suggests that despite minimal group-level changes following unilateral DBS surgery, a small but significant proportion of DBS patients show clinically significant individual declines on memory, processing speed, and response inhibition tasks. Potential mechanisms, including changes in frontally mediated organization/retrieval strategies, will be discussed.

POSTER 14

Safety and Tolerability of Research Lumbar Punctures in Patients with Parkinson's Disease.

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Objective: To establish the frequency of adverse events (AE) related to research lumbar punctures among patients with Parkinson's disease (PD).

Background: Cerebro-spinal fluid (CSF) analysis is a critical element in biomarker research for PD. No data have been published on the safety of research lumbar puncture (LP) in patients with PD or PD with Dementia (PDD). Motor symptoms of PD/PDD and dyskinesia resulting from treatment could complicate collection of CSF.

Methods: Data was obtained from a database of approximately 1181 patients with neurological disorders and normal controls who underwent research LP. From this we selected 39 patients with confirmed diagnosis of PD/PDD to investigate the incidence and severity of procedure-related AE. All patients underwent bedside LP using a 24-gauge atraumatic Sprotte needle or had LP performed under fluoroscopy guidance. Concurrent Unified Parkinson's Disease Rating Scale (UPDRS) scores assessed the severity of resting tremor, rigidity and dyskinesia.

Results: Among PD/PDD patients ($n=39$), 6 experienced AEs (15.3%); all were 'mild' or 'mild-moderate' in severity and all resolved the same day as LP. Site pain/shooting pain during the procedure was the most frequent event (10.1%). One case of headache (2.6%) and one case of nausea/lightheadedness (2.6%) were reported. Of the six who reported an AE, one patient had moderate dyskinesia and one patient had tremor and rigidity rated '2' on the UPDRS. The others had no tremor, rigidity, or dyskinesia.

Conclusions: Research LPs can be done safely in patients with PD/PDD. The incidence of AEs, including post-LP headache, is acceptably low.

POSTER 15

Putative biomarkers which differentiate pulsatile and continuous dopaminergic stimulation (CDS).

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Objective: Parkinson's disease is initially treated successfully with oral administration of compounds that substitute dopamine or stimulates dopamine neurotransmission. Complications in terms of motor fluctuations and mental disturbances appear after various years of treatment. There is strong clinical evidence that CDS give reduced

“off”-time and dyskinesias but also significant decrease of non-motor disturbances, as demonstrated by duodenal administration of levodopa which acts continuously throughout the day. The biochemical background to this difference between CDS and pulsatile stimulation is poorly understood and difficult to monitor.

There is a need for further studies which answers how CDS operates in a more comprehensive way including action on compensatory mechanism stabilizing serotonergic/noradrenergic circuits.

Patient study: In a randomized clinical trial (RCT) with parallel/double dummy technique provide different way of administration of dopaminergic stimulation; oral, subcutaneous, transcutaneous, intestinal and intravenous. Besides clinical evaluations also measurements from serum/CSF: of synaptic proteins, neuropeptides, neurotrophic factors, proteins implicated in neurodegeneration, monoamines and their metabolites.

Animal study: Development of a rat model for studies of CDS through duodopa infusion in order to study locomotion, presence of dyskinesia-like behavior and identification of genes and/or proteins in dopamine receptive brain region.

Investigator-initiated studies with an unrestricted grant from Solvay Pharma AB, Sweden.

Conclusion: The main purpose is to identify biomarkers which differentiate treatment by pulsatile and continuous dopaminergic stimulation and is combined with favorable outcome. We will present and discuss these intentional studies and give some preliminary data.

POSTER 16

The Dose Finding Study - Nasointestinal Infusion of Levodopa (Duodopa) as a Dose Finding Tool in Parkinsonian Patients with Fluctuations.

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Objective: A dilemma in the treatment for PD with motor fluctuations is to recognize the optimal treatment. PD patients' denial of the conditions of the disease and less motivation for changes makes individual titrations complex and time consuming. These difficulties led to formulation of an alternative strategy for optimization of individual treatment strategies.

Method: PD patients with motorfluctuations optimized with available oral combinations of antiparkinsonian treatment were selected. Motor- and nonmotor status were registered and a nasointestinal tube was placed in the jejunum. Individual titration of levodopa (Duodopa) started and proceeded for 3-5 days. Re-examination after optimized on/off relations and the tubing was removed. The dosing schedule (morning-, maintenance- and extra-dose) were converted to an optional oral treatment regime.

Result: In this pilot study the patients obtained, during the test phase, a significant improvement of UPDRS II-III- IV) ($p < 0.05$) and of QoL (PDQ 39) ($p < 0.01$) which could be maintained. An investigator-initiated study.

Conclusion: This scheme will give an objective standard for comparison and an awareness of potential clinical improvement. Improved Quality of Life will encourage better compliance to oral treatment.

POSTER 17

Vitamin D levels in men with Parkinson's disease (PD).

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La Jolla, CA, USA; ⁶University of Alabama, Birmingham, Birmingham, AL, USA.

Objective: To measure the prevalence of vitamin D deficiency in older men with and without PD.

Background: PD increases risk for falls, fractures, and low bone mass density as compared to controls. Vitamin D has beneficial effects on bone, muscle cells, appears to decrease falls, and may improve balance. A Japanese study reported lower vitamin D levels in persons with PD.

Methods: The Osteoporotic Fractures in Men (MrOS) study is a geographically diverse U.S. cohort of men aged 65 and older. At baseline vitamin D levels were measured in a subset ($n=2309$) of participants including 22 of 52 men who identified themselves as having physician-diagnosed PD.

Results: Vitamin D levels were deficient (< 20 ng/mL) in 41% of men with PD, insufficient (20-29 ng/mL) in another 41%, and sufficient (> 30 ng/mL) in only 18%. In race matched non-diseased men 28% were deficient, 46% insufficient and 26% sufficient. Vitamin D levels were lower in men with PD compared to those without; 22.8 (± 6.7) ng/mL vs. 24.4 (± 7.9) ng/mL; but this difference was not statistically significant ($p=0.4$). Similar results were obtained when adjusted for age, season, physical activity, and BMI.

Conclusion: Our results suggest vitamin D deficiency is common in community dwelling men with and without PD. The prevalence of vitamin D deficiency was higher in those with PD, but this difference did not reach statistical significance.

POSTER 18

Intact Global Cognition on the DRS-2 in Parkinson Disease may be Misleading.

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The Dementia Rating Scale-2nd edition (DRS-2; Jurica, et al., 2001) is commonly used to assess global cognitive function in PD. Our study's purpose was to examine the type and frequency of neurocognitive impairment in a cohort of idiopathic PD patients with “average” or better DRS-2 scores. Participants included 142 idiopathic PD patients (U.K. Brain Bank Criteria, Hughes et al., 1992) from the University of Florida's Movement Disorders Center, with a DRS-2 total raw score of 130 or better when measured in the “on” state. The mean age was 64.68 \pm 9.95 and patients had no other significant neurological comorbidity. From a set of 12 neuropsychological tests completed by all patients, a factor analysis identified 5 cognitive test domains explaining 75% of the variance: visual-motor processing, inhibition, structured learning, unstructured learning, and verbal fluency. Standard deviation cut-offs were used to grade cognitive impairment as absent to minimal (less than -1.0SD), moderate (between -1.0 to -2.0 SD), or severe (-2.0 or more SD). Of the 142 patients, moderate impairment was observed in 16 (11.3%) for visual-motor processing, 20 (14.1%) for inhibition, 19 (13.4%) for structured learning, 37 (26.1%) for unstructured learning, and 27 (19.0%) for verbal fluency. Severe impairment was most common for unstructured learning (9.2%; all other domains \leq 4.2%). Correlation analysis showed a negative relationship between raw DRS scores and number of domains impaired [$r = -0.344$; $p < .001$]. These findings suggest PD patients may have significant impairment in a variety of neurocognitive domains even with “average” or better DRS-2 scores.

POSTER 19

Metoclopramide – Induced Encephalopathy in Parkinson's disease.

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Objective: To report a metoclopramide-induced prolonged encephalopathy in a patient with Parkinson's disease.

Background: Metoclopramide is a dopamine receptor antagonist prescribed for gastrointestinal disorders. It is associated with tardive dyskinesia and drug induced parkinsonism.

Methods: Case Report – A 71 year old man with stable Parkinson's disease was treated with levodopa/carbidopa and trihexypenidyl. Prior to the introduction of metoclopramide, his UPDRS motor score was 17, MMSE 28, and Hohen & Yahr Stage II. He was started on metoclopramide 10 mg t.i.d. This resulted in markedly increased motor symptomatology, personality changes, agitation and aggressiveness. One week following cessation of metoclopramide examination revealed a wheelchair bound severely parkinsonian man who was encephalopathic. Two weeks later, his mental state improved slightly, but his personality was entirely altered and he was markedly apathetic. Two months following cessation of metoclopramide, impaired cognitive function remained. Six months after metoclopramide was discontinued, his cognitive state and personality returned to baseline, however, his parkinsonism remained markedly exacerbated (UPDRS – motor score = 57).

Conclusions: This patient with Parkinson's disease and no evidence of cognitive dysfunction was treated with metoclopramide. This induced a severe encephalopathy which resolved very slowly over a six month period. Marked exacerbation of motor symptomatology also occurred and failed to resolve after six months. This illustrates two unusual features of metoclopramide administration in a patient with Parkinson's disease – prolonged exacerbation of parkinsonism and the induction of a very slowly resolving encephalopathy.

POSTER 20

Glucosidase Beta Variations and Lewy Body Disorders.

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Introduction: Heterozygous inheritance of glucosidase- β (GBA) mutations has been postulated to increase susceptibility to different forms of parkinsonism, ranging from classic levodopa-responsive PD to rapidly progressive dementia with Lewy Bodies (DLB). We examined the frequency of GBA mutations in a sample of neuropathologically confirmed Lewy body disease (LBD) cases and controls.

Subjects and methods: The 101 cases and 99 controls brains were obtained from the Mayo Clinic Jacksonville Brain Bank, University of Saskatoon and University of Miami/NPF Brain BankTM. Cases were selected based on pathologic features consistent with LBD including 34 brainstem, 14 transitional and 50 diffuse LBD cases. DNA was obtained from a frozen cerebellum. Long-range PCR was employed to amplify the functional GBA gene, in three fragments ranging from 1.7 kb to 3 kb in length encompassing exons 1-5, 5-7 and 8-11. PCR products were purified using a Biomek FX and Agencourt bead technology. Products were directly sequenced with internal primers adjacent to all exon and exon-intron boundaries. Electropherograms were analyzed with SeqScape v2.5, and independently viewed by two people.

Results: We found 3 cases of GBA in our collection of neuropathologically defined LBD, and 1 case in control population. All three affected carriers were pathologically classified as diffuse Lewy body disease. Although an increased frequency was observed, our study suggests GBA mutations have a minor role to play in susceptibility to Lewy body disease in the North America population. *The study was*

funded by M.K Udahl PD center of excellence grant given to the Mayo Clinic, Jacksonville.

POSTER 21

Multidisciplinary Fall Prevention Program Associated with Reduced Falls in Individuals with Parkinson Disease.

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Objective: Determine if a multidisciplinary fall prevention program reduces falls in PD individuals.

Background: Falls in PD are common and disabling. Although multidisciplinary interventions reduce falls in the general population, their effect in PD has not been assessed.

Methods: We performed a retrospective analysis using data from the Parkinson Disease Program provided through Home Care of Rochester. The program provides a comprehensive evaluation including environmental assessment, gait and balance testing, skilled nursing evaluation and medication review. Based on individual needs, patients receive skilled nursing and therapy interventions (physical, occupational, and speech). Among other variables, we collected demographics, fall history, disease duration, and medications.

Results: Of the patients referred to the program from June 2006 through January 2008, 72 had data available on prior fall history. Mean participant age was 81 (range 53-95), 67% were male, the average disease duration was 6.6 years (range 1-23), and 29% had sustained a fall-related injury at any point. In the month prior to program entry, 61% had sustained a fall. The average falls per week was 0.52 ± 0.99 (range 0-7). During the program, the average fall rate was 0.15 ± 0.34 (range 0-2). The change in fall rate was 0.37 (95% CI 0.18, 0.56, $p = 0.0003$). In univariate analyses, longer disease duration was associated with higher baseline fall rate; both factors were associated with increased change in fall rate during the program.

Conclusions: A multidisciplinary intervention appears to reduce falls in PD. The validity and durability of these findings will need confirmation.

POSTER 22

Depression and Self-Efficacy Among Family Caregivers of Parkinson Patients.

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Caregivers of persons with Parkinson's disease (PD) often become depressed over the years of caring for the patient. While research has shown that a variety of factors contribute to the development of depression, no research known to the authors has been conducted regarding factors related to positive mood, or less depression among PD caregivers. The purpose of this study was to investigate such predictors. The sample included 70 caregivers (74% female) from a regional PD association who were currently living with the patient. Questionnaires were sent through the mail with a 39% response rate. Standard assessment instruments were used to measure depression, perceived social support, caregiver self-efficacy, and demographic variables related to both patients and caregivers. Questions associated with arranging respite care for the patient and taking time for self-care were also included. Results of regression analyses indicated that six variables accounted for 74% of the variance in predicting less depression ($P < .001$). Significant individual predictors were caregiver age ($P = .001$) and perceived self-efficacy ($P < .001$). Older caregivers reported less depression as did those with higher self-efficacy, or greater certainty that they could manage common caregiving situations. Arranging for respite care was marginally significant ($P = .08$). It appears that increasing self-efficacy regarding caregiving issues may decrease depression. Because previous research has shown a strong relationship between patient and caregiver well-being, improving the mood of caregivers may lead to more positive outcomes for patients.

Providing opportunities to increase self-efficacy could be done during caregiver support group meetings.

POSTER 23

LATE-BREAKING RESEARCH

Predictors of the Placebo Effect at 4, 8, and 12 Months in the Double-blind Sham Surgery Trial for the Treatment of Parkinson's Disease.

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A double-blind sham surgery-controlled trial was conducted to determine the effectiveness of implantation of human embryonic dopamine neurons into the putamen of patients with advanced Parkinson's disease (PD). Forty persons participated in the study, with 20 receiving neural implantation and 20 receiving sham surgery. Neurological assessments were completed 4, 8, and 12 months after surgery by medical personnel who were blind to the treatment condition of each patient. Patients were asked which surgery they thought they received before each assessment. Patients completed quality of life (QoL) measures sent through the mail immediately after inpatient evaluations at each time. Because results of previous analyses have shown a strong placebo effect in this study, we used logistic regression analyses to investigate both neurological and QoL variables to determine the strongest predictors of the placebo effect at each time point. Results indicated that Optimism was a significant predictor of perceived treatment early in the study, at 4 and 8 months (both $P < .05$). Depression predicted perceived treatment at all three time points (all $P < .05$), with more depression linked with perceived sham surgery. Neurological variables (UPDRS, Hoehn & Yahr, and Schwab & England) were significant predictors only at 12 months (all $P < .05$). Results suggest that Optimism was effective for the first 8 months as a predictor of the type of surgery patients thought they received. By 12 months physical changes as measured by neurological variables became stronger predictors of the type of surgery patients thought they received.

POSTER 24

LATE-BREAKING RESEARCH

Evaluation of Gastric Emptying in Familial and Sporadic Parkinson's Disease.

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Objective: To assess for the presence of gastric dysmotility in familial and sporadic Parkinson's disease.

Design: Case-control study.

Setting: Tertiary care movement disorders center.

Patients: 10 cases with familial Parkinson's disease (FPD), 20 cases with sporadic Parkinson's disease (SPD), and 15 controls. Parkinsonism was graded by the Hoehn & Yahr scale.

Interventions: Gastric emptying was assessed by dynamic abdominal scintigraphy over 92 minutes following ingestion of a solid meal containing ^{99m}Tc- labeled colloid of 40 MBq activity.

Main Outcome Measures: Gastric emptying half-time and radio-tracer activity over the gastric area at 46 and at 92 minutes.

Results: Gastric emptying time was delayed in 60% of subjects with PD. In comparison to mean $t_{1/2}$ of 38.4 ± 7 min in controls, mean $t_{1/2}$ was 58.4 ± 24 min in FPD ($p > 0.006$) and 48.2 ± 25 min in SPD (NS). Both FPD and SPD groups included subjects with delayed gastric emptying at an early stage of disease.

Conclusions: Patients with familial PD showed significantly delayed gastric emptying in comparison to normal age-matched individuals. Further studies of gastrointestinal dysfunction in PD, particularly familial PD, are warranted.

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