

Program

Twentieth Annual Symposia 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*

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 symposia 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 September 2006 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.

MORNING SESSION: 8:15 AM-NOON

The morning session consists of a keynote speaker and 11 presentations by the following individuals with allotted time for questions and answers after each presenter.

8:15-9:00 AM

KEYNOTE ADDRESS: New Insights Into the Etiology of Parkinson's Disease and Symptom-Linked Adaptations

D. James Surmeier, PhD. *Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.*

9:00-9:15 AM

Gene Therapy for Parkinson's Disease with Subthalamic Nucleus AAV-GAD: FDG PET Results

A. Feigin,¹ C. Tang,¹ M. During,² M. Kaplitt,² D. Eidelberg.¹
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Objective: To assess changes in brain metabolism in a clinical trial of unilateral adeno-associated virus vector delivery of

the glutamic acid decarboxylase gene (AAV-GAD) into the subthalamic nucleus (STN) in Parkinson's disease (PD). *Background:* As part of an open-label trial of unilateral STN AAV-GAD in 12 PD patients (age 58.2 ± 5.7), we performed FDG PET at baseline and after 6 and 12 months. *Design/Methods:* FDG PET scans were analyzed using SPM: 1) To compare regional metabolism at 6 and 12 months versus baseline and 2) To correlate changes in UPDRS ratings at each time point with regional metabolism. We also used network analysis to assess the effects of therapy on the expression of the PD-related covariance pattern (PDRP) on a hemisphere basis. *Results:* Baseline, 6- and 12-month "off" motor UPDRS scores were 38.6 ± 8.4 , 28.7 ± 12.3 ($P = 0.01$) and 29.7 ± 13.6 ($P = 0.02$). Five subjects appeared to respond (UPDRS improvement $> 40\%$, mean $52\% \pm 10\%$), but 7 did not (improvement $< 25\%$, $2\% \pm 21\%$). Brain metabolism declined in internal globus pallidus and ventrolateral thalamus ipsilateral to AAV-GAD. UPDRS improvements correlated with increased metabolism in premotor and supplementary motor regions ($R = -0.84$ $P < 0.001$) ipsilateral to AAV-GAD. Changes in PDRP expression correlated with improvement in UPDRS motor ratings ($R = 0.45$, $P = 0.03$; Bland-Altman within-subject correlation), with greater suppression in the clinical responders ($P < 0.01$). *Conclusion:* These imaging results suggest that

clinical improvements following STN AAV-GAD are generated by alterations in basal ganglia-cortical circuits.

9:15-9:30 AM

Is Pathological Gambling in Parkinson's Disease a Compulsive or Impulsive Disorder?

M.A. Shapiro,¹ Y.-L. Chang,² M. S. Okun,¹ R.L. Rodriguez,¹ F. M. Skidmore,¹ and H. H. Fernandez.¹ ¹Department of Neurology, University of Florida College of Medicine, Gainesville, FL; ²Department of Clinical and Health Psychology, University of Florida, Gainesville, FL, USA.

Background: While pathological gambling in PD is generally thought of as a form of "compulsive" behavior, it may also be a manifestation of an "impulsive" behavior. Previous studies have illustrated that patients with obsessive compulsive disorder (OCD) make more perseverative errors than non-OCD controls (while there is no significant difference in non-perseverative errors). Perseverative errors, seen in frontal lobe dysfunction and compulsive behavior, occur when a participant continues responding in the same manner even after positive reinforcement has been extinguished; whereas a non-perseverative error occurs when a participant responds in an incorrect manner that is different from the previous incorrect response. Non-perseverative errors indicate difficulties related to problem solving. **Methods:** The Wisconsin Card Sorting Test (WCST), which assesses both perseverative and non-perseverative errors, was administered to Parkinson compulsive gamblers (CG: defined as subjects who answered affirmatively to at least four of the questions on a gambling survey derived from the DSM-IV or Gambler's Anonymous that indicated compulsive gambling behavior) and randomly selected Parkinson non-gamblers (NG) while in the "on" state. The Bechara Gambling Task (BGT), which assesses decision-making abilities, was administered in the "on" and "off" state, and the order of the two administrations were counterbalanced between subjects. **Results:** The assessments were administered to 8 CGs and 6 NGs. The two groups were matched on age, gender, education, and illness duration, although the CG group had a tendency to be younger and with a longer disease duration. Statistical analysis revealed no significant differences in the BGT. However, in the WCST, PD CGs surprisingly made significantly more non-perseverative errors than NGs. No difference was seen in perseverative errors between the two groups. **Conclusions:** Our findings suggested that pathological gambling may be less of a compulsive and more of an impulse control behavior.

9:30-9:45 AM

Assessment of Compulsive Behaviors in Parkinson's Disease

J.S. Hui,¹ G. Murdock,¹ J. Moon,² D. Fly,² M. Gomez,¹ M. Langille,¹ S. Christensen,¹ M.D. Welsh.¹ ¹University of Southern California, Los Angeles, CA; ²Fuller Theological Seminary School of Psychology, Pasadena, CA, USA.

Objective: To validate a novel screening method for the diagnosis of new-onset compulsive behaviors (CB) in Parkinson's disease (PD), and to determine the prevalence of CBs using these standardized criteria. **Background:** Compulsive behaviors, including pathological gambling, hypersexuality, and binge eating, are increasingly reported in PD. However, there are no standardized criteria for the diagnosis of these behaviors. Existing DSM-IV (Diagnostic and Statistical Manual of Mental

Disorders-IV) criteria do not reflect the diversity, severity, or temporal presentation of these behaviors. **Methods:** 48 consecutive PD patients were interviewed by a clinical psychologist using a semi-structured questionnaire, screening for impulse-control disorders and obsessive-compulsive traits. Identified behaviors were ranked as possible, probable, and definite CBs, based on whether the behavior was a distinct change from their baseline personality, interfered with daily life, and whether there was an urge to perform the behavior. Predictive value positive (PVP), predictive value negative (PVN), sensitivity, and specificity for the CB rating system were calculated against corresponding DSM-IV criteria to test for validity. **Results:** 13/48 (27%) of subjects exhibited a total of 29 new-onset CBs. Seven subjects exhibited 1 CB, and 6 subjects exhibited 2 or more behaviors. Of the 29 CBs, 14 were categorized as "definite" (48.3%). Among all subjects with CBs, PVP and PVN of the CB rating criteria were 31% and 99.6%, respectively. Sensitivity and specificity were 81.8% and 95.7%, respectively. Two CBs meeting DSM-IV criteria were pre-existing behaviors, and did not meet criteria for new-onset CBs. **Conclusions:** Compulsive behaviors are common in PD. Standardized criteria for the identification of new-onset CBs may allow for more accurate identification and earlier treatment of these behavioral abnormalities.

9:45-10:00 AM

Deep Brain Stimulation for Treatment of Parkinson's Disease: Longitudinal Perspectives of Quality of Life among Patients and Caregivers

C. McRae,¹ E. Sullivan,¹ G. Hartsock,¹ L.M. Winfield,² R.R. Goodman,² G.M. McKhann,² S.L. Pullman,² B. Ford.² ¹University of Denver, Denver, CO; ²Center for Movement Disorders Surgery, Columbia-Presbyterian Medical Center, New York, NY, USA.

Subthalamic nucleus deep brain stimulation (STN DBS) is considered a most promising and effective treatment for advanced Parkinson's disease (PD). Although changes in quality of life have been examined for limited periods following surgery, this is the first empirical study to address changes in the physical and psychosocial domains of quality of life for both PD patients and caregivers following DBS over a 36-month period. Research objectives were to examine change in patients, as rated by patients and caregivers, in two domains of QOL (physical and psychological functioning), and to examine change in caregiver burden based on changes in patient status. Participants included 52 patients and 31 caregivers who completed assessments at baseline, 12, 24, and 36 months after surgery. Assessments included the patient and caregiver versions of the Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr, S & E, and PDQ-39. Caregivers completed the Caregiver Burden Scale. Growth curve modeling was used to investigate change over time. Results indicated that a number of QOL ratings by patients and caregivers improved significantly ($P < 0.05$) from baseline to 12 months. There were few changes in scores from 12 to 36 months, indicating that initial improvements were maintained over the follow-up period of 36 months. These results are notable because of the decline of QOL typically observed over time in PD. No changes were reported in Caregiver Burden over 36 months, suggesting that despite improvement in several areas of patient functioning, these changes were not enough to affect burden.

10:00-10:15 AM

BREAK

10:15-10:30 AM

Assessment of Brain Iron and a Neuronal Marker in Patients with Parkinson's Disease Using Novel MRI ContrastsS. Michaeli, D. Sorce, G. Öz, K. Ugurbil, M. Garwood, P. Tuite. *University of Minnesota, Minneapolis, MN, USA.*

Increased iron in the substantia nigra (SN) is a well appreciated postmortem finding in Parkinson's disease (PD). It is thought that this iron may facilitate free radical injury that is intrinsic to PD pathogenesis. However, to date, Magnetic Resonance Imaging (MRI) scanning has not demonstrated an in vivo difference of iron between PD and control subjects. This may be due to the limitations of the conventional MRI techniques employed. Here, novel T2 ρ and T1 ρ MRI relaxation methods were used to measure iron load and distribution [1,2,3]. T2 ρ appears to be indicative of tissue iron content and distribution and measure molecular motion in local susceptibility gradients. T1 ρ , on the other hand, may assess cellular loss. When applied at high magnetic fields these two methods could provide a non-invasive means to assessing iron accumulation and neuronal loss in PD. In our 4 Tesla study, we found a significant change of the T1 ρ and T2 ρ relaxation time constants in the PD group versus controls. Relaxogram analysis of the T2 ρ and T1 ρ measurements demonstrated increased water and iron content, as well as changes in iron distribution in the SN. Therefore high-resolution MRI with T2 ρ and T1 ρ provide unique information in PD as compared to conventional T1 and T2 measurements. This information may prove useful in evaluating the pathogenesis and severity of PD.

10:30-10:45 AM

Does Perceived Cognitive Dysfunction on the PDQ-39 Correlate with Actual Cognitive Dysfunction in Parkinson's Disease?

M.S. Okun,¹ A. Roy,² C.W. Garvan,² D.Bowers,³ H.H. Fernandez,¹ C. Jacobson,¹ R.L. Rodriguez,¹ D. Loring,¹ K. Meador.¹ ¹Department of Neurology, University of Florida Movement Disorders Center, McKnight Brain Institute, Gainesville, FL; ²Division of Biostatistics, University of Florida Movement Disorders Center, McKnight Brain Institute, Gainesville, FL; ³Department of Clinical and Health Psychology, University of Florida Movement Disorders Center, McKnight Brain Institute, Gainesville, FL, USA.

Objective: To evaluate patients' perceived cognition in Parkinson's disease (PD) and to investigate possible links with cognitive function, and depression. **Background:** Perceived cognition is related to depression more than actual memory dysfunction in epilepsy, but the relation in PD is unknown. **Methods:** A battery of tests was used in subjects with idiopathic PD to evaluate general cognitive function (Mini Mental State Examination and Dementia Rating Scale total scaled score), frontal function (Controlled Oral Word Association, Stroop Task Interference-t score, Trail Making Test- B timed section), memory (Hopkins Verbal Learning Test- delayed T score), depression (Geriatric Depression Scale [GDS]), and perceived cognition/memory dysfunction (items on subscale of the PDQ-39). Spearman correlations were used to test for significant associations among numerical measures. The Wilcoxon rank sum test was used to test for gender differences in perception of

cognition. *P* values less than 0.05 were considered significant. **Results:** There were no significant gender differences in perception of cognition, and no association with age or duration of symptoms (19 women and 39 men with an average age of 68.3 years [SD = 8.5], and disease duration of 6.9 years [SD = 5.1]). Perceived cognition was significantly correlated with GDS (Spearman's $r = 0.56, P < 0.0001$). Perceived cognition was not found to correlate significantly with measures of general cognitive, memory, or frontal function. **Conclusion:** Perceived cognition in PD seems to be strongly associated with depression, but not with cognitive function. Clinicians should be aware that depression may significantly impact subjective ratings of cognitive dysfunction.

10:45-11:00 AM

The POETRY Study: The Safety, Tolerability and Efficacy of Estrogen Replacement Therapy in Post-Menopausal Women with Parkinson's Disease (PD)

Parkinson Study Group¹ (L.M. Shulman,² presenting on behalf of the POETRY Steering Committee, Investigators and Coordinators). ¹University of Rochester School of Medicine, Rochester, NY; ²University of Maryland School of Medicine, Baltimore, MD, USA.

Objective: To assess safety, tolerability and efficacy of estrogen replacement therapy (ERT) in post-menopausal women with PD. **Background:** Previous studies of estrogen's effects in PD have resulted in contradictory results including beneficial and detrimental effects. **Methods:** A multi-center, double-blind, randomized placebo-controlled pilot study lasting 8 weeks of 0.625 mg/d of conjugated equine estrogens (CEE; Premarin) or matching placebo was conducted in post-menopausal women with PD and motor fluctuations. Outcome measures included: UPDRS, diaries and neuropsychological tests. ANCOVA was used to compare the mean changes from baseline to Month 2 in the treatment and placebo groups in the various outcomes, adjusting for the baseline value. **Results:** Twenty-three post-menopausal women (age 63 \pm 6, TUPDRS 25 \pm 13, 9 \pm 6 yrs since symptom onset, 70% \pm 10% "on" time) were enrolled. There were no serious adverse events. One subject withdrew due to worsening of tremor and dystonia. The CEE group showed improved total and motor UPDRS scores although these did not reach significance (changes from baseline, ERT vs. placebo: TUPDRS -5.1(6.4) vs. 3.1(14.9), $\Delta = -7.8, P = 0.10$; motor UPDRS -3.4(5.4) vs. 3.1(12.3), $\Delta = -5.4, P = 0.16$). There were no treatment effects on change in "off" time or any neuropsychological test measure. **Conclusions:** ERT was safe and well-tolerated in post-menopausal women with advanced PD. The data suggest that ERT may be associated with improvement in motor symptoms. While larger studies of longer duration are necessary to determine the effects of ERT in PD, the complex risk/benefit profile and continued controversy surrounding estrogen are obstacles to clinical trials.

11:00-11:15 AM

Ropinirole 24-Hour Prolonged Release Improves Sleep but Does Not Increase Daytime Sleepiness when Used as Adjunctive Therapy in Patients with Parkinson's Disease Not Optimally Controlled by L-Dopa

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Introduction: Ropinirole is efficacious in treating motor symptoms of Parkinson's disease (PD). A 24-hour prolonged release (PR) formulation allows a simple, once-daily dose-titration regimen. The effect of ropinirole 24-hour PR adjunctive therapy on sleep and daytime sleepiness is presented. **Methods:** In this study (EASE-PD Adjunct), patients with PD not optimally controlled with L-dopa were randomized to adjunctive ropinirole (n = 202) or placebo (n = 191), once daily, for 24 weeks. Initial dose was 2.0 mg/day, titrated to maximum 24 mg/day. At 8.0 mg/day, and with each subsequent increase, L-dopa dose reduction was required. Secondary endpoints included change in PD Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS) total scores. Primary endpoint was mean change from baseline in awake time "off" at Week 24 last observation carried forward (LOCF). **Results:** Baseline PDSS and ESS total scores were similar between treatment groups. At Week 24 LOCF, PDSS total score was statistically significantly improved (increased) in the ropinirole group versus placebo; adjusted mean change from baseline: 1.3 versus -3.3 (adjusted mean treatment difference [AMTD]: 4.7; $P = 0.0196$). Ropinirole treatment was not associated with significant change in ESS total score at Week 24 LOCF (AMTD: 0.3; $P = 0.3692$). At Week 24 LOCF, there was a significant treatment benefit for ropinirole for change in awake time "off" (AMTD: -1.7 hours; $P < 0.0001$). At Week 24, mean dose of ropinirole was 18.8mg/day. **Conclusions:** Ropinirole 24-hour PR leads to statistically significant improvements in sleep without increasing measured daytime somnolence, compared with placebo, in patients with PD not optimally controlled with L-dopa. Study supported by GlaxoSmithKline and SkyePharma.

11:15-11:30 AM

LATE-BREAKING RESEARCH

ACP-103 Reduces Psychosis Without Impairing Motor Function in Parkinson's Disease

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A Phase II multi-center, double-blind, placebo-controlled study to evaluate antipsychotic efficacy and motoric tolerability of ACP-103 in patients with Parkinson's disease (PD) suffering from treatment-induced psychosis was conducted. This study was designed to demonstrate that ACP-103, a 5-HT_{2A} inverse agonist/antagonist, would reduce psychosis while not worsening motoric function in patients with Parkinson's disease undergoing dopamine replacement therapy. **Methods:** Sixty patients were administered oral ACP-103 or placebo once-daily for 28 days. The starting dose of ACP-103 was 20 mg with dose escalations to 40 mg and 60 mg permitted at Day 8 and Day 15, respectively. **Results:** Fewer patients on ACP-103 were escalated to higher doses as compared to placebo-treated patients and the mean total dose of ACP-103 was significantly less than the mean total dose of placebo ($P = 0.05$). Antipsychotic efficacy of ACP-103 was assessed using Part I of the UPDRS, which includes measures of the severity of psychosis, and the Scale for the Assessment of Positive Symptoms (SAPS). ACP-103 significantly reduced the UPDRS Part I score compared to placebo ($P < 0.05$). In addition, the percent change from baseline in the SAPS score was significantly greater with ACP-103 than placebo ($P = 0.05$); analysis of the absolute change from baseline in the SAPS score showed a trend to

significance ($P < 0.09$). ACP-103 did not worsen motor symptoms in PD as assessed by the UPDRS Parts II and III. **Conclusions:** ACP-103 reduced psychotic symptoms in patients with PD suffering from treatment-induced psychosis without impairing motor function.

11:30-11:45 AM

LATE-BREAKING RESEARCH

Exercise Induced Behavioral Recovery and Plasticity in the MPTP-Mouse Model of Parkinson's Disease

G.M. Petzinger,^{1,3} P. Arevalo,² M. Vuckovic,² P. Turnquist,² E. Hogg,² J. Walsh,² G. Akopian,² C. Meshul,⁴ A. Abernathy,¹ M. Ramirez,¹ B. Fisher,^{1,3} and M.W. Jakowec.^{1,3,7} ¹Dept. Neurology; ²Davis School of Gerontology; ³Dept. Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA; ⁴VA Medical Center, OHSU, Portland, OR, USA.

To better understand the beneficial effects of exercise in patients with Parkinson's disease, we investigated the application of intensive treadmill exercise training in the MPTP mouse model of basal ganglia injury and dopamine depletion. Mice were administered MPTP (4 × 20 mg/kg each) and subjected to intensive treadmill running for 30 days starting 4 days after the last injection of MPTP (when cell death is complete) at a speed up to 20 m/min for 1 hour. Mice were investigated for improvement in behavioral motor features. Harvested brain tissues were analyzed by HPLC for levels of dopamine and its metabolites, and glutamate and the pattern of expression of genes and proteins for tyrosine hydroxylase, dopamine transporter, dopamine receptors D1 and D2, and AMPA and NMDA glutamate receptors using western immunoblotting, immunohistochemistry, and in situ hybridization histochemistry. Electrophysiological analysis of dopamine release was determined using fast cyclic voltammetry on brain slices. Findings showed enhancement of both motor behavior recovery and rotarod learning in exercised mice. However, no change was noted in number of SNpc dopaminergic neurons and the striatal levels of dopamine. Molecular analysis showed down-regulation of DAT and TH, and significant changes in the pattern of expression of ionotropic glutamate receptors in the cortex and striatum. In addition, exercise increased dopamine release compared to MPTP-lesioned mice without exercise. These findings demonstrate that intensive exercise can induce dramatic neuroplasticity in an animal model of basal ganglia injury and provides a valuable framework for supporting exercise in patients with Parkinson's disease.

11:45-12:00 PM

LATE-BREAKING RESEARCH

Deep Brain Stimulation vs. Best Medical Therapy for Parkinson's Disease: Patient Outcomes from the VA CSP#468 Prospective, Randomized, Multi-Center Trial

The CSP #468 Study Group (Frances M. Weaver, presenter), VA Hospital, Hines, IL, USA.

Outcomes in 253 patients with Parkinson's disease (PD) were compared following six months of best medical therapy (BMT, N = 133) or bilateral deep brain stimulation (DBS, N = 120) in a prospective, randomized study. Patients were recruited from 7 VA and 6 affiliated university medical centers. Enrollment criteria included idiopathic PD, Hoehn & Yahr stage ≥ 2.0 off medications, and 3 hours or more/day in an "off" state and/or "on" state with troubling dyskinesias. The

BMT group received treatment by movement disorders neurologists, while the DBS group underwent DBS of either the GPi or STN (target randomly assigned). Subjects were assessed at baseline, 3 and 6 months using motor diaries, UPDRS motor subscale on and off medications, and quality of life (QoL) using the PDQ-39. The time spent in a good "on" state (without troubling dyskinesias) improved significantly following DBS (mean = 6.5 hours/day baseline to 11.7 hours/day at 6 months; $p < 0.001$), while only improving slightly in the BMT group (7.1 hours/day at baseline to 7.2 hours/day at 6 months). UPDRS motor scores assessed off medications by raters blinded to treatment showed significantly greater improvement for DBS than BMT patients at 6 months (35.2% vs. 4.6% respectively; $p < 0.001$). DBS subjects showed significant improvement in all subscales of the PDQ-39 except social support, while BMT subjects worsened slightly on the activities of daily living, social support, cognition, communication, and bodily discomfort subscales. DBS was superior to BMT, increasing average on time without troubling dyskinesias by 5.2 hours/day and improving motor function and quality of life.

12:00-1:30 PM

LUNCH

AFTERNOON SESSION: 1:30-4:45 PM

The afternoon session consists of a keynote speaker and 8 presentations by the following individuals with allotted time for questions and answers after each presenter.

1:30-2:15 PM

KEYNOTE ADDRESS: Ion Channel Dysfunction in the Dominant Spinocerebellar Ataxias

Stefan M. Pulst, MD. Cedars-Sinai Medical Center, Los Angeles, CA, USA.

2:15-2:30 PM

Predictors of Response to Tetrabenazine in Huntington's Disease

F.J. Marshall,¹ S. Eberly,¹ S. Frank,² D. Oakes,¹ and the Huntington Study Group/TETRA-HD Investigators.³ ¹University of Rochester School of Medicine and Dentistry, Rochester, NY; ²Boston University School of Medicine, Boston, MA, USA; ³Includes all authors listed in appendix to *Neurology* 2006;66:366-372.

Background: Tetrabenazine (TBZ) improved chorea in the TETRA-HD trial (*Neurology* 2006;66:366-372). **Objective:** To determine the baseline predictors of favorable and adverse responses to TBZ in TETRA-HD. **Methods:** TETRA-HD randomized 84 ambulatory patients with Huntington's disease (HD) to receive TBZ ($n = 54$) or placebo ($n = 30$) titrated to optimized dosages ≤ 100 mg/day in three divided doses for 7 weeks, followed by 5 weeks of maintenance therapy. Predictor variables studied included: demographics, Unified Huntington's Disease Rating Scale (UHDRS) components, and scores on the pilot Functional Impact Scale (FIS), Hamilton Depression, Epworth Sleepiness, and Barnes Akathisia scales. Outcome variables included: chorea responders (those completing 12 weeks and improving by ≥ 3.0 UHDRS units), TBZ dosage at 12 weeks, and adverse events (AE). Baseline scores were dichotomized at the median and analyses performed using Fisher's exact tests. **Results:** Among TBZ patients, high (poor) baseline FIS scores (46% vs 85%, $P = 0.005$) predicted favor-

able chorea response, as did low baseline Stroop color-naming scores (48% vs. 77%, $P = 0.043$). No baseline variables predicted TBZ dosage at week 12, somnolence, insomnia, or fatigue. High Stroop scores at baseline predicted anxiety and hyperkinesia (akathisia), while high verbal fluency scores predicted depressed mood. Older age and lower trinucleotide (CAG)_n repeats predicted falls. Among placebo patients, only longer duration of illness was associated with a higher rate of chorea responders. **Conclusion:** Patients with greater HD-related functional impairment at baseline seem to improve most with TBZ, but other clinical characteristics may also determine individual response.

2:30-2:45 PM

Onset Symptoms in Huntington's Disease: Association with Gender of Affected Parent

M.B. Harrison, C.A. Manning, L.J. Currie. University of Virginia, Charlottesville, VA, USA.

Objective: To determine if clinical phenotype in adult onset Huntington's disease is influenced by the gender of the affected parent. **Background:** Paternal inheritance affects age of onset and juvenile HD often has a rigid-dystonic phenotype. Whether onset or motor phenotype is influenced by the gender of the HD+ parent in adult onset HD is unknown. **Methods:** Data on family history, symptom onset and neurological evaluation (UHDRS) were obtained from 119 adult onset HD cases and analyzed by t-test and Chi square with logistic regression performed to assess relationship HD+ parent gender to onset symptom and motor phenotype. **Results:** There were 52 males (44%) and 67 females (56%), with onset age of 41 ± 10 (20-63), disease duration of 6 ± 5 years (1-20) and TFC score of 8.7 ± 4.1 (0-13). The father was affected in 62 cases (53%) and the mother in 55 cases (46%) with similar ages of onset (40 ± 11 father+; 42 ± 9 mother+; $P = 0.33$). Mean chorea score and mean score for bradykinesia, rigidity and dystonia did not differ. Motor onset did not differ by gender of HD+ parent ($n = 36$, 44% father+, 55% mother+; OR 1.6, CI 0.78-3.4, $P = 0.19$). Cognitive onset was strongly associated with paternal inheritance ($n = 12$, 83% father+, 17% mother+; OR 5.1, CI 1.1-24.4, $P = 0.04$), while psychiatric onset was associated with maternal inheritance ($n = 21$, 33% father+, 67% mother+; OR 0.37, CI 0.14-1.0, $P = 0.05$). **Conclusion:** Non-motor onset symptoms in HD may be influenced by maternal or paternal inheritance. Analysis of a larger sample will be needed to confirm these preliminary results.

2:45-3:00 PM

Brain Metabolism in Presymptomatic Huntington's Disease: A Longitudinal FDG PET Study

A. Feigin,¹ C. Tang,¹ Y. Ma,¹ M. Guttman,² J.S. Paulsen,³ D. Eidelberg.¹ ¹Feinstein Institute for Medical Research, North Shore-LIJ Health System, Manhasset, NY, USA; ²Division of Neurology, Department of Medicine, University of Toronto, Toronto, ON, Canada; ³Departments of Psychiatry and Neurology, University of Iowa College of Medicine, Iowa City, IA, USA.

Objective: To utilize FDG PET to follow regional changes in brain metabolism in presymptomatic Huntington's disease (pHD). **Background:** Biomarkers are needed for measuring progression in pHD. Brain metabolism is abnormal in pHD and may provide a means for following progression and for predicting disease onset. **Methods:** We performed FDG PET in 12

pHD subjects (age 46.8 ± 11.0 [mean \pm SD]; CAG repeat length 41.6 ± 1.7) at baseline and following 18 and 36 months. Baseline scans were compared to 11 age-matched controls utilizing SPM thresholded at $P < 0.001$. Regions with abnormal metabolism at baseline were assessed at the subsequent time points. UHDRS scores were used as a covariate in SPM as well. **Results:** Baseline UHDRS motor scores were 9.6 ± 11.8 , and these did not change over the course of the study (36 months 12.1 ± 14.3 , $P = 0.13$). In pHD we found hypometabolism in bilateral striatum and cingulate cortex, and hypermetabolism in bilateral mediodorsal thalamus. UHDRS correlated inversely with metabolism in striatum and thalamus ($P < 0.01$). Over the course of 36 months, metabolism declined in thalamus ($P < 0.005$), though it remained higher than in controls. In a subgroup of 4 subjects who were diagnosed with HD over the course of the study, thalamic metabolic rates declined to the normal range. Striatal and cingulate metabolism did not significantly change over time. **Conclusion:** Striatal hypometabolism precedes the onset of HD signs and symptoms and likely occurs in the setting of neuronal loss. Thalamic hypermetabolism likely represents a compensatory mechanism in pHD that ultimately fails as HD signs emerge.

3:00-3:15 PM

BREAK

3:15-3:30 PM

Chronic Pain in Machado-Joseph Disease

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Background: Machado-Joseph disease (MJD) is a neurodegenerative ataxia characterized by remarkable phenotypic heterogeneity. Although patients frequently report pain, systematic evaluation of its clinical features is lacking. **Objectives:** To compare the frequency of chronic pain among genetically-confirmed MJD patients, at-risk individuals and an age- and sex-matched control group. **Methods:** We included 70 MJD patients, 26 at-risk individuals and 70 controls from two centers. We assessed all individuals through a standardized pain questionnaire. We utilized a visual analog scale (VAS) to quantify pain intensity. **Results:** Thirty-three MJD patients (47%), 4 at-risk individuals (15%) and 6 controls (7%) reported chronic pain. Low back pain preceded ataxia in 6 patients. Twenty nine patients had daily pain, which was continuous in 23. Mean VAS score was 6.1 in MJD. Pain was muscle-skeletal in 26, dystonic in 2, neuropathic in 2 and mixed in 3 cases. Typically pain was lumbar (17) or at the lower limbs (15). Three out of the four at-risk individuals with pain presented low-back pain. We did not find significant differences regarding duration of disease, sex or severity of ataxia among MJD patients with and without chronic pain. Expanded (CAG)_n were larger in MJD patients with pain. **Conclusion:** In our series, pain was significantly more frequent in MJD patients than in at-risk or controls. Low back pain was the most frequently reported location both in MJD and in at-risk individuals. Chronic pain was a frequent and disabling complaint among our MJD patients in spite of being systematically underreported in the literature.

3:30-3:45 PM

Medication Effects on Psychosis and Motor Function in Dementia with Lewy Bodies (DLB)

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Objective: To assess effects of dopaminergic, neuroleptic, and cognitive-enhancing medications on psychosis and motor function in DLB. **Background:** Pharmacological treatment in DLB requires balancing risks of worsened psychosis, neuroleptic sensitivity, and limited motor benefit. **Methods:** Probable/possible DLB (McKeith criteria) subjects were assessed before and after changes in dopaminergic, neuroleptic, and cognitive-enhancing medications with standard clinical measures: Thought Disorder (TD) scores from UPDRS part I, total motor scores-UPDRS part III, and Hoehn-Yahr (HY) staging. Wilcoxon signed rank tests compared baseline with follow-up. Statistical significance was $P < 0.1$. **Results:** We identified 32 subjects, mean age 74 years (SD 5.1), baseline mean UPDRS motor score 37.6 (10.5), MMSE 20.7 (6.4), Hoehn-Yahr 3.6 (range 2-5), and baseline mean levodopa dose 332.2 mg/day (220.7) with additional parkinsonian medications in 8/32. Follow-up assessment of increased (21) or decreased dopaminergics (12), initiation of neuroleptics (14) or cognitive-enhancers (12) occurred at a mean of 3.6 months (SD 2.5). Thought disorder (TD), UPDRS motor, and HY score changes were not significant with any medication intervention. However, TD scores worsened with dopaminergic increases (4/20) and improved with dopaminergic decreases (2/11); cognitive-enhancers improved TD scores (3/11), but neuroleptics worsened them (4/13) and improved none. **Conclusion:** Medications for parkinsonism, psychosis, or cognition did not significantly affect psychosis or motor function in DLB. Dopaminergic agents had limited motoric benefit but did not clearly worsen psychosis. Risk of neuroleptic sensitivity and absence of improvement with neuroleptics suggests a less useful strategy than cognitive-enhancers.

3:45-4:00 PM

Quantitative Tremor Analysis in Welders: Comparison with Idiopathic Parkinson's Disease (IPD) and Essential Tremor (ET)

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Workers chronically exposed to manganese in welding fumes may develop an extra-pyramidal syndrome with postural and action tremors. The goal of the study was to compare the tremor in welders to the tremors exhibited by IPD and ET patients. **Method:** Twenty cases each of IPD and ET and 37 welders with tremor were selected for the study from a retrospective chart review. IPD and ET cases had undergone tremor recordings at a University-based PD/Movement Disorders Clinic. Welders were included in the present analysis if they had tremor recordings as part of a screening for movement disorders organized by the Welders Union. Rest and postural tremors were recorded with a bi-axial accelerometer built into a hand-held pen (Catsys System, Danish Production Development, Ltd). Fast Fourier transform (FFT) analysis was used to

determine the normalized power distribution of the tremor across a range of frequencies (0.9-15.0 Hz). Tremor parameters calculated included tremor intensity (Ti), tremor center frequency (Cf) and harmonic index (HI) for each hand at rest and with arms extended. *Results:* Cohorts of IPD, ET and welders with atypical parkinsonism were distinguishable on the basis of quantitative tremor parameters and clinical features. Both welders and ET exhibited significantly greater postural tremor intensity and higher Cfs than did the IPD group. In addition, welders exhibited greater tremor intensity and higher Cf at rest than the ET group. In summary, quantitative tremor analysis in the context of an appropriate exposure history and neurological examination can contribute significant information to facilitate the diagnosis of manganese-related extra-pyramidal manifestations. *Acknowledgment:* D.R., P.A.N., and J.S.-R. have received consulting fees from the Welding Rod Plaintiff's Consortium (WRPC). P.A.N. and J.S.-R. have also served as expert witnesses for the WRPC.

4:00-4:15 PM

Embouchure Dystonia (ED) and Focal Task-specific Dystonia of the Hand (FTSDh) in Musicians: Susceptibility Factors or Peripheral Modifiers?

S.J. Frucht. *Columbia University Medical Center, New York, NY, USA.*

Aim: To characterize the clinical phenotype of musicians' dystonia in order to investigate possible susceptibility factors or peripheral modifiers. *Methods:* Database and video recording of 128 musicians with dystonia prospectively evaluated from 1998-2006. *Results:* Of 82 musicians with ED and 46 with FTSDh, age at symptom onset was 36.7 (SD 10.9) and 36.9 (SD 13.4) years respectively; 80% were male. 6% of all patients had a clear precipitant (trauma or infection) and 2% had a family history of dystonia. Dystonia spread to other tasks in 15%, and sensory tricks that improved dystonic movements were present in 9%. ED symptoms affected a specific register (69%) or technique (49%), and pain was uncommon (16%). 6% of ED patients had coincident writer's cramp. Of the 44 patients with ED of the task-specific tremor or lip-pulling phenotype, 61% played high register instruments (French horn or trumpet), while all 13 patients with lip-locking ED played low register instruments (trombone or tuba). 74% of 19 patients with jaw or tongue ED played woodwind instruments, and in 58% dystonia spread to speech or eating. 15% of patients with FTSDh had bilateral dystonia (all woodwind or keyboard performers). *Conclusions:* These observations of male predominance, coincident writer's cramp in ED, family history of dystonia, and bilateral FTSDh suggest that some musicians may possess a genetic susceptibility to develop dystonia. Peripheral modifiers may influence the dystonic phenotype, particularly in low brass and woodwind instrumentalists. Given the risk of spread to speech or eating, patients with jaw or tongue ED should abandon playing.

4:15-4:30 PM

Abnormal Affective Startle Modulation in Psychogenic Movement Disorders

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Objective: To test the hypothesis that there is a physiological change in emotional processing in patients with psychogenic movement disorders (PMD). *Background:* Despite the prominent role attributed to emotional difficulties in the etiology of PMD, no studies thus far have examined physiological reactivity to emotional stimuli in this population. *Methods:* Startle eyeblink reflexes were measured in subjects with psychogenic movement disorders (diagnosed by a fellowship-trained movement disorders physician). Emotional reactions to affective pictures were also recorded. Twelve subjects with PMD and twelve control participants viewed positive, neutral and negative pictures while eyeblink responses to white noise bursts were simultaneously recorded. *Results:* Control participants revealed the expected pattern of startle modulation, with potentiation by negative stimuli and inhibition by positive stimuli, linear trend $F(1, 11) = 10.48$ ($P < 0.05$). In contrast, participants with PMD had startle potentiation by both negative and positive stimuli, quadratic trend $F(1, 11) = 8.32$ ($P < 0.01$). The results could not be explained by co-morbid depression symptomatology, or by self-reports of emotional reaction to the pictures used in the paradigm. *Conclusion:* The data suggest that subjects with PMD experience negative physiological activation in response to arousing stimuli, regardless of valence. Future studies will be required to examine the interplay between emotional reactivity and the generation of psychogenic movements.

POSTER SESSION

Posters will be staffed from Noon to 1:30 PM in the Grand Ballroom E & F.

Poster 1 (PD)

Racial and Socioeconomic Disparities in Elderly Patients with Parkinsonism

L.M. Shulman,¹ M. Baumgarten,² A.L. Gruber-Baldini,² K.E. Anderson,^{1,3} M. Shardell,² P.S. Fishman,¹ S.G. Reich,¹ and W.J. Weiner.¹ ¹*University of Maryland School of Medicine, Dept of Neurology, Baltimore, MD;* ²*University of Maryland School of Medicine, Dept of Epidemiology and Preventive Medicine, Baltimore, MD;* ³*University of Maryland School of Medicine, Dept of Psychiatry, Baltimore, MD, USA.*

Objective: To investigate whether there are racial and socioeconomic differences in severity of parkinsonism and disability in elderly patients initially presenting to a movement disorders center. *Background:* Little is known about disparities in access to care for parkinsonism. *Methods:* Patients age 65 and over with Parkinson's disease ($n = 205$) and non-PD parkinsonism ($n = 81$) were examined with the UPDRS motor subscale at initial presentation to the Maryland Parkinson's Disease and Movement Disorders Center. Information on race, income, education, activities of daily living and instrumental activities of daily living (Older Americans Resource and Services ADL and IADL Subscale) was obtained by self-report. *Results:* Greater ADL disability and disease severity were observed in Black ($n = 18$) vs. White ($n = 265$) patients on initial presentation (ADL 14.3 vs. 10.4, respectively, $P = 0.018$; UPDRS motor 40.9 vs. 30.6, respectively, $P = 0.003$). Greater disease

severity was associated with lower income ($P = 0.018$). Greater ADL and IADL disability and disease severity were associated with lower educational attainment (ADL $P = 0.019$, IADL $P = 0.007$, UPDRS motor $P = 0.006$). **Conclusions:** Black patients with parkinsonism on initial evaluation to our movement disorders center were more disabled and had more advanced parkinsonism than White patients. Greater disability and disease severity were also seen among persons with lower income and lower educational attainment. These results are consistent with the hypothesis that racial and socioeconomic disparities in access to care result in Blacks and persons of low socioeconomic status receiving specialized tertiary care at a later point in the progression of their disease.

Poster 2 (PD)

Cognitive and Affective Symptoms of Hispanic Patients Diagnosed with Idiopathic Parkinson's Disease: A Case Series

L. San Miguel-Montes, I. Pita, C. Serrano, M. Margarida, O. Cardona. *Neurology Section, University of Puerto Rico School of Medicine, Medical Sciences Campus, San Juan, Puerto Rico.*

Cognitive and psychiatric symptoms frequently appear in Parkinson's disease (PD) and yet these have not been frequently studied in Hispanic patients. This study aims to describe and explore associations on functions of verbal memory, verbal fluency and executive functions of Hispanic PD patients. The IRB-approved case series studied 12 volunteers both male (7) and female (5), mean age 65 (SD = 7.41), with moderate PD (Hoehn & Yahr m = 2.5), mean education 13 years (SD = 2.26), at the Movement Disorders Clinics-University of Puerto Rico. After informed consent, CES-D, Dementia Rating Scale-II (DRS-II), Boston Naming Test (BNT) and Wisconsin Card Sorting Test Computer Version (WCST) were administered by trained Neurology staff. Statistical analyses used SPSS. Scores yielded mild depressive symptoms on CES-D (mean = 18 [SD = 11.8]), mild to moderate memory impairment on DRS-II (mean = 8 [SD = 3.8]), moderate naming deficits on the BNT (mean = 44 [SD = 5.9]) and moderate to severe executive difficulties on tasks of planning, categorizing and shifting on WCST (mean = 2 categories [SD = 1.5]). Correlation analyses suggest a significant relationship among executive and motor functions (-0.76 , $P = 0.05$), memory and executive functions (-0.92 , $P = 0.007$), depressive symptoms and memory (-0.76 , $P = 0.05$) and depressive symptoms and memory (0.78 , $P = 0.01$). Conclusively, results suggest that Hispanic patients with moderate PD experience depressive symptoms and deficits in memory, verbal retrieval and executive functions. Executive functions were more related to motor indexes and memory functions than depressive symptoms. Findings are consistent with the frontal sub-cortical circuits affected in PD and suggest that executive functions are associated with various cognitive deficits. Larger studies of PD with Hispanics should be conducted.

Poster 3 (PD)

8,12-iso-IPF_{2 α} -VI Isoprostanes as a Possible Biomarker for Dementia in Parkinson's Disease

A. Siderowf, J. Connolly, D. Mu and D. Pratico. *University of Pennsylvania, Philadelphia, PA, USA.*

Objective: To determine the utility of serum and urine 8,12-iso-IPF_{2 α} -VI as a biomarker for dementia in Parkinson's disease. **Background:** 8,12-iso-IPF_{2 α} -VI is a subtype of F₂-iso-

prostane that has been shown to be an accurate biomarker for Alzheimer's disease (AD). Among AD patients, 8,12-iso-IPF_{2 α} -VI levels are elevated in the brain, serum and urine. Other dementias, such as frontotemporal dementia (FTD), do not show increased levels. Small studies suggest that 8,12-iso-IPF_{2 α} -VI levels may be normal in Parkinson's disease (PD), however levels in PDD have not been specifically assessed. **Design/Methods:** Assessments of cognitive functioning including MMSE, HVLIT, GDS, DRS were performed on PD patients with (n = 18) and without (n = 19) dementia. Serum and urine samples were collected and 8,12-iso-IPF_{2 α} -VI levels were analyzed. Serum and urine 8,12-iso-IPF_{2 α} -VI levels in demented subjects were compared to those from non-demented subjects. **Results:** We found no differences between serum or urine 8,12-iso-IPF_{2 α} -VI levels in demented compared to non-demented subjects ($P > 0.5$ for all comparisons). For both demented and non-demented subjects, 8,12-iso-IPF_{2 α} -VI levels were not significantly different from normal controls. We did find a strong correlation between serum and urine isoprostane levels ($R = 0.89$) indicating the integrity of the assays. **Conclusions:** 8,12-iso-IPF_{2 α} -VI levels in serum and urine appear to be substantially lower in PD patients than values previously reported in AD patients, and are not associated with severity of dementia. Our results support existing data showing that serum and urine 8,12-iso-IPF_{2 α} -VI levels are a specific biomarker for dementia due to Alzheimer's disease.

Poster 4 (PD)

Associated Risk Factors for Compulsive Behaviors in Parkinson's Disease

J.S. Hui,¹ G. Murdock,¹ J. Moon,² D. Fly,² M. Gomez,¹ M. Langille,¹ S. Christensen,¹ M.D. Welsh.¹ ¹University of Southern California, Los Angeles, CA; ²Fuller Theological Seminary School of Psychology, Pasadena, CA, USA.

Objective: To determine the association between expression of compulsive behaviors (CBs) in Parkinson's disease and medication use, personality traits, and other demographic factors. **Background:** Compulsive behaviors, including pathological gambling, hypersexuality, and binge eating, have been increasingly described in PD. Although dopaminergic medication has been implicated in the expression of CBs, other risk factors such as personality traits, may be associated with an increased susceptibility towards the development of CBs. **Methods:** 48 consecutive PD patients were interviewed by a clinical psychologist, screening for impulse-control disorders and obsessive-compulsive traits. Subjects also completed the Tridimensional Personality Questionnaire (TPQ-R), Beck Depression Inventory II (BDI-II), and Epworth Sleepiness Scale (ESS). CBs were determined using pre-determined clinical criteria. Differences between subjects with and without CBs were assessed using Wilcoxon rank sum and chi-square tests. **Results:** 13/48 (27%) of subjects expressed CBs. The median age of subjects with CBs (62 yrs) was significantly younger than those without CBs (73 yrs) ($P = 0.0003$). Subjects with CBs also had a longer median duration of disease (7 yrs vs. 3 yrs) ($P = 0.007$), and scored higher on the BDI-II ($P = 0.01$). Personality assessments demonstrated a higher Novelty Seeking dimension in subjects with CBs compared to those without ($P = 0.009$). CBs were not related to gender, use of dopamine agonists, or daytime sleepiness. **Conclusions:** Compulsive behaviors in PD are common, and may be associated with factors other than medication class. Differences in personality traits,

age, and duration of disease indicate that certain individuals may have an underlying susceptibility to the development of CBs, independent from exposure to dopaminergic medication.

Poster 5 (PD)

Is Pathological Gambling Associated with Pramipexole Therapy in Parkinson's Disease?

A. Imamura, J. Slowinski, L. Brown, R.J. Uitti, Z.K. Wszolek, Y.E. Geda. *Department of Neurology, Mayo Clinic Jacksonville, Jacksonville, FL, USA.*

Introduction: Recent case series studies indicated that anti-parkinsonian medications might 'cause' pathological gambling (PG). There is a need to conduct a case-control or cohort study to examine if indeed dopamine agonists are associated with pathological gambling in patients with Parkinson's disease. **Materials and methods:** We searched the medical database system of Mayo Clinic Jacksonville from 1996 to 2006. Eleven patients with PD with no past history of gambling, and who have developed a PG were found. They were matched by age (61-65 years) and sex to the control group of 36 PD patients without PG (1:4). One of us (AI) kept blind as to case-control status, measured exposure i.e. anti-parkinsonian medications, by reviewing medical charts. **Results:** Treatment with pramipexole was associated with increased risk of PG in PD (OR = 3.6; 95% CI = 0.9-14.9). The mean dose of pramipexole in patients with gambling was higher than in controls ($P < 0.001$); however, the mean levodopa equivalent dose was smaller in patients with PG than in control group. The combined therapy with pramipexole and levodopa did not increase risk of PG (OR = 0.15 and 95% CI = 0.01-1.26), compared to monotherapy with pramipexole. The disease duration and age at onset did not differ between study groups. **Conclusions:** Pramipexole is a possible risk factor for PG in PD.

Poster 6 (PD)

Safety and Tolerability of Transdermal Rotigotine in Early-Stage Parkinson's Disease

M. Tagliati,¹ R.L. Watts,² J. Patton,³ W. Poewe,⁴ B. Boroojerdi.⁵ ¹Mount Sinai School of Medicine, New York, NY, USA; ²University of Alabama at Birmingham, Birmingham, AL, USA; ³Asheville Neurology Specialists, P.A., Asheville, NC, USA; ⁴Medical University Innsbruck, Innsbruck, Austria; ⁵SCHWARZ PHARMA AG, Monheim, Germany.

Objectives: Rotigotine, a transdermal D₃/D₂/D₁ dopamine receptor agonist, is approved for Parkinson's disease monotherapy in the EU. To further evaluate its safety/tolerability, adverse event (AE) data from three double-blind, placebo-controlled early-stage PD trials were pooled. **Methods:** Subjects received rotigotine 6.0 mg/24 h or 8.0 mg/24 h and were maintained for 6 months (two trials) or up to 8.0 mg/24 h for 7 weeks (one trial). Data were collected for titration and maintenance phases; a descriptive by-age analysis was also performed. **Results:** The pooled data consisted of 938 patients: 289 placebo, 649 rotigotine. Overall AE incidences were 74% rotigotine versus 64% placebo and 62% rotigotine versus 64% placebo in Titration and Maintenance phases, respectively. AE-related discontinuations occurred in 13% of rotigotine-treated patients versus 6% of placebo-treated patients. Although the older cohort in the by-age analysis was small (n = 79), this analysis revealed some differences for common dopaminergic AEs. For example, older patients (≥75 years) experienced less nausea and vomiting compared to younger patients

regardless of treatment and numerically higher rates of dizziness, particularly for placebo. Rotigotine-treated patients had a similar rate of somnolence regardless of age; somnolence was notably higher for older placebo-treated patients. Hallucination was higher for placebo in older patients; no hallucinations were reported for rotigotine-treated patients ≥ 75 years. Application site reactions occurred most frequently with rotigotine, regardless of age. **Conclusions:** Transdermal rotigotine was generally safe and well tolerated in this pooled population of early PD patients. Among notable age effects on dopaminergic-related AEs in rotigotine-treated patients was the decrease in vomiting and hallucination in the older subgroup.

Poster 7 (PD)

Long-term Safety and Efficacy of the Rotigotine Transdermal Patch in Early-Stage Parkinson's Disease

R.L. Watts,¹ R.Pahwa,² K.E. Lyons,² B.Boroojerdi.³ ¹University of Alabama at Birmingham, Birmingham, AL, USA; ²University of Kansas Medical Center, Kansas City, MO, USA; ³SCHWARZ PHARMA AG, Monheim, Germany.

Objective: To assess the long-term efficacy, safety and tolerability of rotigotine in the treatment of early-stage, idiopathic Parkinson's disease (PD). Rotigotine, a new dopamine agonist is approved for monotherapy of PD in the EU. A previously conducted, multi-center, double-blind, placebo-controlled trial demonstrated that PD patients treated with the rotigotine patch showed significant improvement in the UPDRS score. Interim results of an ongoing, open-label extension to this double-blind phase are reported. Early-stage PD patients completing 6 months of double-blind treatment were titrated over 4 weeks before entering a maintenance phase using rotigotine patches (2 mg/24 h to 6 mg/24 h), with dose escalations up to 16 mg/24 h permitted after one year. Patients were evaluated every 3 months using the UPDRS (II + III). Scores were compared with the scores collected in the double-blind trial at baseline. Adverse events (AEs) were also assessed. At the initiation of the open-label phase 216 patients comprised the safety population. The most common AEs included somnolence, application site reactions (ASRs), nausea and dizziness. The majority of ASRs were rated as mild in severity, transient, and accounted for 6/24 AE-related discontinuations. On the UPDRS (II + III), patients showed improvement during the titration phase when rotigotine was reintroduced. Of 208 patients entering the open-label extension with efficacy data, 168 (81%) had 85 weeks of exposure in the open-label study. On average, the UPDRS (II + III) score remained below the double-blind baseline score indicating patients maintained benefit throughout the duration of the study. Rotigotine was well tolerated and patients showed sustained improvement after 85 weeks of treatment in this long-term study.

Poster 8 (PD)

Ropinirole 24-Hour Prolonged Release Reduces "Off" Time and Improves Mood when Used as Adjunctive Therapy in Patients with Parkinson's Disease Not Optimally Controlled with L-Dopa

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Introduction: Ropinirole improves the clinical manifestations of Parkinson's disease (PD). A 24-hour, prolonged-release formulation offers a simple, once-daily treatment option. This study evaluates ropinirole 24-hour prolonged release in reducing "off" time and improving mood in patients with PD. **Methods:** In this pivotal study (EASE-PD Adjunct), patients with PD not optimally controlled with L-dopa and ≥ 3 hours "off" time per day were randomized to adjunctive ropinirole 24-hour prolonged release ($n = 202$) or placebo ($n = 191$), once daily for 24 weeks. Initial dose was 2.0 mg/day, titrated to a maximum of 24.0 mg/day. At 8.0 mg/day, and with each subsequent increase, L-dopa dose reduction was required. Primary endpoint was mean change from baseline in awake time "off" at Week 24 last observation carried forward (LOCF). Also assessed was the mean change in Beck Depression Inventory II (BDI-II) total score. **Results:** At baseline, mean "off" time and BDI-II total scores were similar between treatment groups. At Week 24 LOCF, reduction in adjusted mean awake time "off" was significantly greater in the ropinirole group compared with placebo (adjusted mean treatment difference [AMTD]: -1.7 hours; $P < 0.0001$). Ropinirole treatment also led to statistically significant improvements in BDI-II total score at Week 24 LOCF: adjusted mean change from baseline -2.1 versus -0.5 in the placebo group (AMTD: -1.6 ; $P = 0.0130$). At Week 24, mean dose of ropinirole was 18.8 mg/day. **Conclusions:** Ropinirole 24-hour prolonged release as adjunctive therapy significantly reduces "off" time and significantly improves mood, compared with placebo, in patients with PD not optimally controlled by L-dopa. Study supported by GlaxoSmithKline and SkyePharma.

Poster 9 (PD)

Low-Frequency Repetitive Transcranial Magnetic Stimulation for Treatment of Levodopa-Induced Dyskinesias: An Open-Labelled Study with Blinded Assessments

A. Wagle-Shukla, M. Angel, C. Zadikoff, M. Enjati, C. Gunraj, A.E. Lang, R. Chen. *Division of Neurology, Krembil Neuroscience Centre, Toronto Western Research Institute, University Health Network, University of Toronto, Toronto, ON, Canada.*

Levodopa-induced dyskinesia (LID) in Parkinson's disease (PD) may be associated with increased activity of the Primary Motor Cortex. Low frequency repetitive transcranial magnetic stimulation (rTMS) decreases excitability of Primary Motor Cortex, and may therefore represent a potential therapy for levodopa-induced dyskinesias. We evaluated the efficacy of low frequency rTMS for the treatment of LID. Six PD patients with moderate LID participated in an open-labeled study. The treatment protocol was 1-Hz rTMS at 90% resting motor threshold intensity for 15 minutes per day for 10 days excluding weekends (days 1-14). Dyskinesias were assessed during levodopa challenge 1 day before (day 0), 1 day after (day 15) and 2 weeks after (day 28) rTMS. The primary outcome measure was video rating of CAPSIT dyskinesia scores performed by two blinded raters. The total dyskinesia scores calculated as average of dyskinesia scores during early "on," peak "on" and late "on" periods were significantly lower for day 15 (2.5 ± 0.7) compared to day 0 (3.3 ± 1.4), but there was no significant difference between days 0 and 28 (3.3 ± 1.8). The peak dyskinesia score (the "on" period with maximal levodopa benefit and lowest UPDRS III rating) was also significantly lower for day 15 (3.5 ± 1.6) compared to day 0 (6.1 ± 2.8), but there was no significant difference between days 0 and 28 ($5.3 \pm$

2.6). A two-week course of low frequency rTMS to Primary Motor Cortex may produce a short-term improvement in LID.

Poster 10 (PD)

Deep Brain Stimulation Decreases the Risk for Parkinsonism-Hyperpyrexia Syndrome and Suppresses Levodopa-Induced Dyskinesias: A Case Report

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Objective: To prevent recurrence of Parkinsonism-Hyperpyrexia Syndrome (PHS) in a patient with advanced Parkinson's disease (PD). **Background:** PHS is an infrequent life threatening complication of PD clinically similar to neuroleptic malignant syndrome. **Case report:** A 52-year-old woman with an 18-year history of PD, wearing off and dyskinesias, had been having episodes of severe tremor, rigidity, diaphoresis and hot feelings lasting 1-2 hrs every evening for 5 years despite regular medication intake. She then developed a severe PHS with fever of 40.5°C , rhabdomyolysis (CPK = 16380 U/L) and multiple complications. Tremor and rigidity would instantly change to dyskinesias. On hourly doses of levodopa and dopamine agonists she became mainly dyskinetic. The daily episodes of milder PHS persisted. Bilateral subthalamic deep brain stimulation (B-STN DBS) was performed in the "on" medication, dyskinetic state due to concerns of triggering severe PHS. **Results:** Intra-operative DBS suppressed her dyskinesias immediately. The dyskinesias restarted as soon as DBS was turned off. Continuous DBS was initiated the same day. The total dose of medications was decreased by 75%; the interval was prolonged to every 4 hrs. During the next 4 months there was no recurrence of PHS. The patient gained 13 kg of weight and became independent in activities of daily life (ADL). **Conclusions:** B-STN DBS prevented daily episodes of PHS, improved motor disability and ADL, decreased dyskinesias and fluctuations. It was superior to optimal medical treatment for PHS and should be considered in patients at risk. B-STN DBS immediately suppressed levodopa induced dyskinesias.

Poster 11 (PD)

Unilateral vs. Bilateral Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease

A. Samii,¹ V.E. Kelly,² J.C. Slimp,² A. Shumway-Cook,² R. Goodkin.³ ¹Department of Neurology, University of Washington, Seattle Parkinson Disease Research Education and Clinical Center (PADRECC), VA Puget Sound Health Care System, Seattle, WA; ²Department of Rehabilitation Medicine, University of Washington, Seattle, WA; ³Department of Neurological Surgery, University of Washington, Seattle, WA, USA.

We report on the comparative effects of unilateral and bilateral subthalamic nucleus (STN) stimulation in Parkinson's disease (PD) after staged electrode implantations. In 15 consecutive PD patients, bilateral STN stimulators were implanted during staged surgeries separated by 3-6 months. We performed the Unified Parkinson's Disease Rating Scale (UPDRS) and the Goetz Dyskinesia Scale (Mov Disord 1994;9:390-394) off and on medications: 1) prior to any surgery; 2) after the first surgery, with unilateral stimulation turned off and on; and 3) after the second surgery with bilateral stimulation turned off and on. Off-medication and on-medication activities of daily living (ADL) scores improved after unilateral stimulation with no further improvement after bilateral stimulation. Off-medi-

ication motor UPDRS scores improved from 53.7 (± 17.0) to 41.3 (± 13.0) after unilateral stimulation and to 31.1 (± 10.0) after bilateral stimulation. On-medication motor UPDRS scores improved only after bilateral stimulation. Dyskinesia scores improved from 8.7 (± 6.2) to 2.7 (± 3.3) after unilateral stimulation with no further improvement after bilateral stimulation. Complications of therapy scores improved from 11.8 (± 3.0) to 7.6 (± 2.3) after unilateral stimulation and further improved to 5.9 (± 3.2) after bilateral stimulation. Medication doses were reduced after each surgery, but more so after unilateral stimulation. In summary, most improvements in off- and on-medication ADL scores, dyskinesia scores, and medication dose reduction occurred after unilateral surgery. The second surgery led to further improvements in off- and on-medication motor UPDRS scores, complications of therapy scores, and further modest medication dose reduction.

Poster 12 (PD)

The Florida Surgical Questionnaire for Parkinson's Disease (FLASQ-PD): A Potential Triage Tool for Cognitive Dysfunction in DBS Candidates

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Background: Cognitive dysfunction in PD patients is not always readily appreciated. Embedded in the FLASQ-PD are several cognitive and non-cognitive items that may be relevant to identifying and excluding patients with dementia. **Objective:** To pilot the effectiveness of using certain items on the FLASQ-PD for screening cognitive status in PD patients. **Design/Methods:** Subjects with idiopathic PD at the UF MDC underwent formal neuropsychological and independent FLASQ-PD testing. Certain characteristics of PD patients, as assessed through FLASQ-PD sections B ("red flags") and D (questions on memory and dementia), were investigated for correlations with MDRS and MMSE. Additionally, we compared our screening items to cognitive profiles determined by standard neuropsychological tests. **Results:** 114 subjects (68% male, mean age 65.6 years, mean UPDRS 25.7, SD = 10.9) were assessed. In the "red flags" section, the presence of primitive reflexes ($ry1 = -0.35, P < 0.001$; $ry1 = -0.36, P = 0.001$), ideomotor apraxia ($ry1 = -0.50, P < 0.001$; $ry1 = -0.46, P < 0.001$), and severe psychosis ($ry1 = -0.82, P < 0.001$; $ry1 = -0.84, P < 0.001$) were associated with lower Mattis Dementia Rating Scale (MDRS) and MMSE scores. Additionally, frequency of hallucinations correlated with lower MDRS scores (mean difference vs. no hallucinations = 9.8 points for "occasional"; 26.8 points for "frequent"). Two FLASQ-PD cognitive items were associated with MDRS and MMSE: physician global impression of "more than mild dementia" ($ry1 = -0.59, P < 0.001$; $ry1 = -0.58, P < 0.001$), and endorsement of "memory difficulties or frontal deficits," ($ry1 = 0.30, P = 0.003$; $ry1 = 0.37, P < 0.001$), respectively. A subanalysis revealed that the endorsement of memory and dementia items was significantly associated with multiple overlapping portions of the formal neuropsychological evaluation

(especially in domains of verbal memory and language). Details of the correlations will be presented. **Conclusions/Relevance:** Items on the FLASQ-PD questionnaire may be useful in triaging and screening patients for DBS surgery, and identifying subjects who will require in-depth neuropsychological testing.

Poster 13 (PD)

Milestones of Disease Progression and Disability in Parkinson's Disease

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Objective: To assess PD progression and disability as a function of specific events occurring during the natural evolution of the disease. **Background:** We postulate that it is possible to describe the natural history of PD by using disease-related events as markers, or "milestones" of disease progression. **Methods:** The presence of the following milestones was ascertained in a cross-sectional cohort of 209 consecutive PD patients: symptomatic treatment; motor complications; use of a gait assisting device; cognitive impairment without dementia; dementia; and, permanent need for 24-hour nursing care. Results were correlated with patient demographics, HY stage, and disease duration. **Results:** The majority of patients had reached the first two milestones within the first 8 years (100% for symptomatic treatment and 62% for motor complications). About half of the patients reached the milestones of gait assisting device (55%), and cognitive impairment (51%) within the first 12 years. Among patients with disease duration greater than 20 years, 44% had reached the milestone of dementia and 22% needed permanent nursing care. The total number of milestones reached correlated well with disease duration ($R = 0.535, P < 0.01$). In a multivariate model analysis, gait assisting device, cognitive dysfunction, dementia, and need for nursing care correlated well with HY stage, while symptomatic treatment and motor complications did not. **Conclusions:** The concept of "milestones of disease progression" can be reliably used as a descriptor of disease progression, and as a surrogate measure of disability in PD. Additional milestones may be identified and utilized to cover non-motor aspects of the disease, and describe associated disability.

Poster 14 (PD)

Nonsteroidal Anti-Inflammatory Drug Use and the Risk of Parkinson's Disease

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Inflammation may contribute to the pathogenesis of Parkinson's disease (PD). We explored the relationship between using nonsteroidal anti-inflammatory drugs (NSAIDs) and the risk of developing PD through a retrospective cohort study using the British Columbia Linked Health Databases (BCLHD). The BCLHD contain linkable, individual, anonymized health data for four million residents of British Columbia. BCLHD include comprehensive data on prescription drug use, hospitalizations, physician visits, and vital statistics. We created a cohort of

individuals who received at least one prescription from 1997-2003. The date of the first prescription was the date of cohort entry. Cohort members were followed to the first diagnosis of PD, termination of the study period, date of emigration from the province, or death. PD was defined as having had a physician visit (ICD-9 code 332), and at least two PD medication prescriptions (all forms of levodopa, bromocriptine, pergolide, selegiline, amantadine, pramipexole, ropinirole) within 6 months of the physician visit. A time-dependent Cox model was created and exposure to NSAIDs every month from cohort entry to index date (date of first PD diagnosis) was assessed. Exposure to NSAIDs was taken as a time-dependent variable. In the regression model, we adjusted for age, sex, co-morbidity (measured as the total number of prescriptions prior to index) and use of antipsychotic medications. A total of 697,078 subjects were included in the initial cohort. The hazard ratio at any time for NSAID use was 0.84 (0.81-1.09). Our study did not show a statistically significant protective effect against PD with NSAID use.

Poster 15 (PD)

Drug-Induced Parkinsonism: Still Common, Under-Recognized, and Treatable

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Background: Drug-induced parkinsonism (DIP) is classically associated with typical neuroleptics. The recent use of atypical antipsychotics (AA) suggests that DIP may occur less frequently, but may also be less recognized. **Objective:** To examine the frequency, causative agents, and diagnostic accuracy of DIP patients seen in a movement disorders clinic, 2004-2005. **Methods:** Retrospective database and record review. **Results:** Of 304 consecutive new parkinsonian patients seen, 8% had DIP. Symptom onset to clinic presentation averaged 1.6 years. Average age of onset was 71 years and 73% were female. 50% had concomitant tardive dyskinesia and 83% had tremor. 82% were not diagnosed with DIP at presentation, and of those cases, 80% were previously evaluated by a neurologist. 46% were diagnosed with Parkinson's disease and started on dopaminergic medication. 55% were due to AA including risperidone, olanzapine, ziprasidone, and aripiprazole; other causative agents were metoclopramide and typical neuroleptics. Of 13 patients followed, 11 improved or remitted 3 months after withdrawal of medication. **Conclusion:** DIP remains a common, often under-recognized cause of parkinsonism, even by neurologists. A high index of suspicion, including risks related to AA, is warranted. Cessation of the offending agent results in improvement of symptoms.

Poster 16 (OMD)

A Rater-Blinded, Exploratory, Tolerability and Efficacy Study of Sodium Oxybate (Xyrem) in Patients with Treatment-Refractory Hyperkinetic Movement Disorders

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Background: In a prior study of 20 patients, we showed that sodium oxybate improved essential tremor and myoclonus in selected patients (Neurology 2005;65:1967-1969). **Methods:** We treated 22 new patients with medication-refractory hyperkinetic movement disorders in an IRB-approved, open-label,

dose-titration, add-on trial. Patients were videotaped using the WHIGET scale (ET) or a disease-specific validated rating scale, and an observer blinded to dose and trial order rated the videos. Accelerometry and computerized spiral analysis pre- and post-treatment were performed in three patients with ET. **Results:** 12 patients with ET (7 men, average age 65.2 yrs), three with task-specific tremor, two with cerebellar tremor, and one each with secondary dystonia, ethanol-responsive torticollis, myoclonus-dystonia, posthypoxic myoclonus and tremor-predominant PD enrolled. In ET patients we observed improvements in mean sustention tremor scores (3.7 [SD 1.8] to 1.7 [SD 1], $P = 0.002$), and mean action tremor scores (19.4 [SD 3.8] to 13.0 [SD 5], $P < 0.001$). Physiologic studies confirmed reduction in tremor amplitude without change in frequency. Blinded ratings of task-specific tremor improved by 30%, and severity of dystonic neck tremor by 55%. Ratings of other patients did not change. Three patients (2 ET, 1 posthypoxic) did not tolerate the drug, and one significant adverse event occurred (depression exacerbation). Sedation was common (10 patients) and dose dependent. Nine patients chose to continue treatment after completion of the trial, at average daily dose 5.5 gm. **Conclusion:** Sodium oxybate may be useful in patients with treatment-refractory ET, myoclonus, task-specific tremor and ethanol-responsive torticollis. Double-blind, placebo-controlled studies are warranted.

Poster 17 (OMD)

Tolerability and Efficacy of Ropinirole in Patients with Intermittent Restless Legs Syndrome (RLS): Open-Label Results

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Ropinirole (0.25-4.0 mg/day, flexibly titrated, taken once-daily, 1-3 hrs before bedtime) is the only FDA-approved treatment for moderate-to-severe primary RLS. Many patients have symptoms frequent enough to require daily treatment; however, those experiencing symptoms less frequently may benefit from taking ropinirole as needed (PRN). Fixed-dose ropinirole, 0.5 mg PRN, was evaluated in patients with intermittent RLS symptoms. A multicenter study was conducted to assess the tolerability and efficacy of ropinirole PRN in adults with primary RLS. The initial 3-week open-label phase of the study is presented. Patients experiencing symptoms 1-3 nights/week, severe enough to require treatment and causing sleep disturbance, were eligible for inclusion. Patients took the first dose in clinic and met tolerability criteria 3hrs post-dose to continue. Primary endpoint: proportion of nights patients had "successfully treated" RLS symptoms (rated "very much"/"much" improved the morning following dosing, or a night during which symptoms were mild at time of dosing, rated "no change" or "minimally improved," and were not associated with sleep disturbance). 163 patients were enrolled in the 3-week open-label phase. Mean (SD) number of nights patients treated symptoms during the open-label phase was 5.0 (2.3) (range 1-12). Most patients (98%) met the tolerability criteria; 33% reported on-treatment AEs. The most commonly reported AEs were nausea (10%), somnolence (7%) and dizziness (6%). Few patients withdrew from the open-label phase due to AEs (3%). During the 3 weeks 73% of symptomatic nights were treated successfully. Ropinirole, 0.5mg PRN, was generally well tolerated and effective for intermittent RLS symptoms. Supported by GlaxoSmithKline R&D.

*Poster 18 (OMD)***Open-Label Flexible Dosing 8-Week Trial of Aripiprazole in Tourette Syndrome**

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Objective: To investigate the effects of aripiprazole on tics, behavior, cognition and mood in children and adults with Tourette syndrome (TS). **Method:** 15 TS patients, 12 male, mean age 15 years (range 9-25) were placed on aripiprazole 2.5 mg q.d. and eventually increased to a maximum of 15 mg q.d. (mean 7.5 mg/day) with IRB-approved informed consent. Initially, concomitant medications were continued, 9 on SSRI, 3 on atypical neuroleptics, and 5 on psychostimulants. Personal evaluation was at baseline, weeks 4 and 8, and weekly by telephone. Comparisons are baseline versus week 8. **Evaluation instruments:** Tics-Yale Tic Rating Scale (YTRS); Behavior-DSM-IV Rating Scale (DSM-IV), Achenbach Child Behavior Checklist (CBCL); Cognition-Test of Variables of Attention (TOVA), 3-Letter Cancellation Test (LCT), Digit Span (DS); Mood-Children's Depression Inventory (CDI), CBCL, Hamilton Depression Rating Scale (Ham-D). **Results:** > 50% reduction or normalized-Tics: Simple motor: 12/15 (YTRS scores: mean 58 [range 14-161] versus mean 28 [range 0-126]), Complex motor: 11/13 (mean 33 [range 0-105] versus mean 16 [range 0-97]), Simple phonic: 10/11 (mean 54 [range 0-147] versus mean 24 [range 0-115]), Complex phonic: 9/10 (mean 35 [range 0-112] versus mean 11 [range 0-105]). Behavior: DSM-IV 10/12 attention, 4/6 hyperactivity, 4/7 impulsivity; CBCL 8/12 attention. Mood: CDI 4/4, CBCL obsessive 2/2, Ham-D 1/2. Cognition: LCT 3/6, DS 4/7, TOVA 2/4. Adverse effects: laboratory 0/15, nausea 4, > 5 percentile weight increase 4, > 5 percentile weight decrease 1, akathisia 4. **Conclusion:** Short term use of aripiprazole is a safe, effective treatment for TS tics and may benefit cognitive, behavioral and mood symptoms.

*Poster 19 (OMD)***Postural Anomalies in Tourette Syndrome**

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Gilles-de-la-Tourette syndrome (TS) is often associated with motor excitability but little is known of the effects of TS on postural instability. This study examined the presence of postural control problems in children and adolescents with TS. Center of pressure (COP) displacements were recorded in children aged 6 to 16 yrs with and without TS in three conditions: 1) Eyes-Open, 2) Eyes-Closed, 3) One-Leg standing with eyes open. Results showed that the COP range and velocity were higher in children with TS than in unaffected siblings in all conditions especially in younger children. These differences could not be attributed to tics, comorbidities (hyperactivity, compulsions, anxiety) or medication. We propose that impaired closed-loop postural control is affected in TS, resulting in fast and large corrections of the COP. This appears to be an unrecognized feature of the TS phenotype. This sub-clinical symptom suggests that interactions between striatum and brainstem should be further examined in TS.

*Poster 20 (OMD)***Safety and Tolerability of Tetrabenazine Use with Concomitant Medications in Huntington's Chorea**

M. S. Jog, N. Khandekar, A. Attar. *University of Western Ontario, London, ON, Canada.*

This project was a retrospective chart review of patients from a large academic Huntington's disease (HD) clinic. The objective of the study was to understand the patient profile that required the use of tetrabenazine and the necessity and safety of concomitant medications. **Methods:** Ninety charts were reviewed and 87 entered into the database. A multi-question survey was designed to extract already existing data from the charts. No patients were contacted during the study. The data was then entered into an Excel spreadsheet for further analysis. Each survey was then re-conducted for every chart for consistency. Three charts, found to have insufficient follow-up records were excluded. **Results:** The single, common reason for beginning treatment with tetrabenazine was symptomatic chorea. Tetrabenazine (30%) was the most commonly prescribed medication followed by benzodiazepines (25%) and risperidone (15%). 29% stayed on tetrabenazine for longer than 3 months. 15% of patients discontinued tetrabenazine (average time to discontinuation 7.7 months) and the remaining patients continued for 29 months. Most common reasons for discontinuation were sedation and anxiety. 92% of the patients remaining on tetrabenazine were on concomitant medications. Clonazepam, risperidone, olanzapine, and Paxil made up 80% of the concomitant medications. **Discussion:** It is likely that many patients that had substantial chorea simply did not want treatment. Patients with HD tolerate tetrabenazine well, are able to continue on it along with concomitant medications and withdrawal rates were low and unrelated with concomitant medications. Tetrabenazine is safe and well tolerated along with benzodiazepines, SSRIs and atypical antipsychotics. There were no dropouts due to worsening depression. No patients required an increase in their anti-depressants.

*Poster 21 (OMD)***Willingness to Consent for Future Use of DNA Collected in the Prospective Huntington At Risk Observational Study (PHAROS)**

Huntington Study Group PHAROS Investigators (M. Aileen Shinaman, presenter), *University of Rochester, Rochester, NY, USA.*

Objective: To determine the willingness of individuals at risk for Huntington's disease (HD) to consent for future research use of DNA collected during an observational study. **Background/Methods:** Between 1999 and 2004, 1001 research participants were enrolled in PHAROS to determine the earliest signs of HD. Participants were asked if they would consent to retention of their DNA for future unspecified HD research. Following a protocol change (addition of survey instruments), 525 participants were given the opportunity to change their consent instructions. **Results:** As of May 2006, samples and consent instructions were available for 997 participants. 940 (94.3%) agreed to have their DNA saved, while 57 (5.7%) instructed that it be destroyed. There were 2.7 ± 1.2 years between the initial and second consents for the participants who consented twice. In the initial consent, 495 participants gave permission for their DNA to be saved, and 30 instructed the sample be destroyed. In the revised consent, 510 (97.1%)

permitted their sample to be saved, and 15 (2.9%) instructed it be destroyed. Of the 525 participants, only 25 (4.7%) changed their instructions: 5 from "Save" to "Destroy," and 20 from "Destroy" to "Save." **Conclusions:** Research participants at risk for HD are overwhelmingly willing to consent and reaffirm consent for future unspecified HD research using their DNA. A small proportion of participants changed their instructions, largely to retain samples they initially instructed be destroyed.

Poster 22 (OMD)

Essential Tremor Phenotyping and Molecular Genetics: ET Database Cases and a New Large Pedigree

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Essential tremor (ET) is a disabling, common disorder. There are at least two separate genetic loci linked to autosomal dominant ET. We hypothesize that ET comprises a family of neurodegenerative disorders that result from mutations in genes with interrelated functions. Several inherent ET features complicate genetic studies: high prevalence, variable age of onset, poor tremor self-reporting, and the uncertain range of clinical features. Although the classic ET definition does not include Parkinson's disease (PD) signs, ET is associated with parkinsonism in some kindreds. It remains unclear whether ET/parkinsonism and classic ET are overlapping or separate entities. The goal of this study was to generate a database including unbiased prospective clinical assessments for accurate correlation between phenotypes, pathology, and genetics. Using detailed questionnaires and exams, we enrolled subjects and identified families. Small ET families were characterized to determine the degree of phenotypic and potentially genetic overlap. Large families were enrolled for individual genotyping studies. We screened 52 ET cases, 134 sporadic PD cases, 86 PD cases with family history, and 221 controls for the ET-associated polymorphism, an 828C → G HS1-BP3 gene variant. We found no GG genotypes, 90% CC and 10% GC in all groups. The G variant did not associate with ET in families. Finally, we fully enrolled one large pedigree with classic ET and ET/parkinsonism, highly variable severity and onset, and low symptom self-reporting accuracy. We continue with genotyping for PD-related mutations and linkage analyses for ETM1 and ETM2. Overall, clear detailed phenotyping data leads to informative molecular genetics.

Poster 23 (OMD)

Lower Limb Holmes Tremor with Hypertrophic Olivary Degeneration

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Holmes tremor is an arrhythmic 2- to 5-Hz rest, postural, and kinetic tremor of an upper limb, with a delay between pathology and onset of tremor. We present a patient who after a brainstem hemorrhage developed tremor in three body parts which evolved over one year in association with hypertrophic olivary degeneration (HOD). A 43-year-old man suffered an acute right brainstem hemorrhage which initially resulted in left

hemiparesis, right lower motor neuron facial paralysis, left hypesthesia, and severe dysarthria. Early MRI revealed hemorrhage extending from the right dorsal midbrain to the brachium pontis. Five months after the hemorrhage, he developed a high amplitude postural and intention tremor of the left upper extremity and dystonic head tremor with a hypertrophied right sternocleidomastoid muscle. MRI performed four months post-hemorrhage revealed T2/Flair hyperintensities in the right inferior olivary nucleus suggestive of early HOD. At ten months, MRI showed hypertrophy of the right inferior olivary nucleus and residual hemosiderin in the area of hemorrhage. Almost one year post-hemorrhage, he developed an irregular low frequency (2-3 Hz) high amplitude left lower extremity tremor at the hip and knee, present at rest, exacerbated with movement, suggestive of a Holmes tremor. His left upper limb Holmes tremor was now less severe than his left lower limb Holmes tremor. Palatal tremor and palatal myoclonus were never features of his clinical course. To our knowledge, this combination of tremors, including a severe lower limb Holmes tremor has not been previously reported in association with brainstem injury and HOD.

Poster 24 (OMD)

Mozart's Movements

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Wolfgang Amadeus Mozart was a musical prodigy who died pre-maturely at age 35 (born 1756; died 1791). After his death, a number of personal biographies were published. In 1938 Mozart's letters were translated into English by Emily Anderson. All of the previously suppressed, unexpurgated letters were made available. Mozart's frequent use of scatological language in his letters suggested to medical sleuths that he may have suffered from Tourette syndrome (TS). Other peculiarities in Mozart's letters included word games, word scrambling, repetitions of words just heard or written by someone else (echolalia) and repetitions of his own words (palilalia). But did Mozart have the co-morbid disorders that often accompany TS? Review of his biographies and of his medical history suggests that Mozart suffered from several episodes of high fever, swollen glands and erythema nodosum as a child. Biographers who recounted stories from individuals close to Mozart have described his hyperactivity, motor tics and obsessive compulsive behaviors. It is possible that Mozart's involuntary movements were a result of post-streptococcal complications (Sydenham's chorea-SC), an interesting perspective in light of the controversial PANDAS hypothesis (Pediatric Autoimmune Neuropsychiatric Disorders) that suggests TS may be a form fruste of SC.

Poster 25 (OMD)

Paraneoplastic Neurologic Autoimmunity with DLB-like Presentation

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Background: Dementia in the setting of parkinsonism, REM sleep behavior disorder (RBD) and visual hallucination is suggestive of dementia with Lewy bodies (DLB). Iranzo et al. (*Ann Neurol* 2006;59:178-182) reported 5 men

who had concurrent RBD and voltage-gated potassium channel (VGKC) antibody (Ab)-associated limbic encephalitis. Here we report 4 patients with neurologic autoimmunity and a presentation resembling DLB. *Methods:* We reviewed longitudinally clinical, laboratory, imaging, and electrophysiological profiles of all patients. *Results:* Two men (73 and 77) and two women (58 and 49) presented with cognitive decline (forgetfulness, language and/or executive dysfunction; subacute in 3) with parkinsonism. Three had history of dream enactment or RBD with visual hallucination before or with cognitive decline; one developed visual hallucination and RBD after the initial cognitive decline. N-type and/or P/Q-type voltage-gated calcium channel (VGCC) Abs were identified in three (coexisting with ANNA-1 in one); none had detectable VGKC-Ab. Three had elevated spinal fluid protein levels; MRI and EEG abnormalities were non-specific in all. Lung carcinoma was found in the ANNA-1(+) man; the other had multiple squamous carcinomas of skin 3 years after onset. Breast carcinoma was found in the older woman, and no Ab or cancer was found in the younger woman to date (12 mos) who improved repeatedly with IVMP therapy. *Conclusion:* Detailed CNS histopathology is required to determine whether a DLB-like syndrome associated with paraneoplastic Abs (and cancer) represents neurodegeneration unmasked by intercurrent paraneoplastic autoimmunity, or associated with but not etiologically-related to autoimmunity, or a primary paraneoplastic disorder.

Poster 26 (OMD)

Pain in Cervical Dystonia is Associated with Female Gender and Greater Disability

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Objective: To identify factors associated with pain in cervical dystonia (CD) before and following botulinum toxin (BoNT) treatment. *Background:* Pain is a frequent and disabling feature in patients with CD. *Methods:* Subjects with CD were included. Before BoNT and at week 4, subjects completed a pain interview subscale of the Toronto Western Spasmodic Torticollis Rating scale (TWSTRS) with ratings from 0 (no pain) to 20 (severe and constant). Statistical analysis included Spearman correlations, Wilcoxon rank sums and signed rank tests. *Results:* There were 94 women and 44 men included, with mean age of 57 years (SD 11). At baseline before BoNT, there were 131 subjects (95%) with pain at a mean severity of 9.7 (SD 4.6). Pain at baseline was more frequent in women than men ($P = 0.0012$ Wilcoxon rank sums) and was not associated with current age, duration of CD, motor severity of CD measured using TWSTRS or predominant head posture. Following BoNT, pain was improved by a mean of 3.6 (SD 4.5) ($P < 0.0001$). The improvement in pain following BoNT correlated with improvement in disability ($r = 0.40$, $P < 0.0001$) but did not correlate with change in head posture or dose of BoNT. *Conclusions:* Pain is a common feature in CD and is more frequent in women than men. Pain is associated with disability due to CD and improvement in pain following BoNT treatment is associated with improvement in disability independent of improvement in head posture.

Poster 27 (OMD)

Validation of a Computerized Neuropsychological Assessment (Mindstreams[®]) in Movement Disorders: Interim Analysis

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Background: Movement disorders are often accompanied by multi-domain cognitive impairment. Cognitive assessment of such individuals can be expensive, lengthy, and limited to centers with neuropsychologists. *Objective:* To evaluate the construct validity of a novel computerized comprehensive neuropsychological battery that is inexpensive, brief, and not requiring administration by a neuropsychologist. *Methods:* Consecutive movement disorders patients seen at the University of Florida were asked to undergo a full paper-based neuropsychological testing followed by a Mindstreams[®] (NeuroTrax, NY) computerized battery (testing time: 45-60 minutes). Construct validity was assessed by Pearson correlations between computerized and paper-based measures assessing similar domains. *Results:* Thus far, 37 patients (age: 60.3 ± 13.4 years; education: 13.6 ± 2.4 years; 10 female; MMSE: 28.3 ± 2.3) with a primary movement disorder diagnosis (18 PD; 15 ET; 4 primary dystonia) were recruited. See table on next page.

Conclusions: Based on our interim analysis, Mindstreams[®] showed good correspondence with traditional neuropsychological tests measuring similar cognitive domains in a cohort of movement disorders patients.

Poster 28 (PD) Late-Breaking Research

Unmasking Differences Between Normal and Pathological Neural Circuits: Functional Brain Mapping in a Rat Model of Nigrostriatal Damage During Locomotor Challenge

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Investigation on dynamic brain activation, in human Parkinson's disease (PD) has shown promise for unmasking underlying differences between normal and pathological neural circuits that are not apparent while the subject is in the resting state. We report the first study of brain activation in a PD animal model during a treadmill challenge. Rats with unilateral striatal 6-hydroxydopamine lesions (16 micrograms) or sham-lesions received intravenous injection of the perfusion tracer [¹⁴C]-iodoantipyrine, either while resting or walking on a rotarod. Cerebral blood flow (CBF) was measured from autoradiographs by region-of-interest analysis and statistical parametric mapping. Sham-lesioned and lesioned rats showed significant activation in response to treadmill walking in primary and secondary motor cortex. This response was attenuated bilaterally in lesioned compared to sham-lesioned rats, but more so ipsilaterally than contralaterally to the lesion. Dramatic increases in CBF in response to the locomotor challenge were noted in the midline cerebellum in both sham-lesioned and lesioned rats, a response that was exaggerated in lesioned animals. Lesioned rats uniquely demonstrated an asymmetric increase in CBF in the contralateral substantia nigra and subthalamic nucleus, but only during the motor challenge. Our

Cognitive Domain	Mindstreams® Test	Paper-based Test	Correlation, <i>P</i> -value
MEMORY	Verbal Memory	Hopkins Verbal Learning	$r = 0.72, P = 0.001$
	Non-Verbal Memory	Brief Visuospatial Memory Test-Revised	$r = 0.66, P = 0.003$
EXECUTIVE FUNCTION	Go-NoGo	Brief Visuospatial Memory Test-Revised	$r = 0.84, P < 0.001$
		Hopkins Verbal Learning	$r = 0.71, P < 0.001$
	Stroop Interference	Wechsler Memory Scale III (WAIS-3)	$r = 0.64, P < 0.001$
	Catch Game	Trails B	$r = 0.63, P < 0.001$
		WAIS-3 Digit Symbol	$r = 0.63, P < 0.001$
VISUAL SPATIAL	Visual Spatial	WAIS-3 Digit Symbol	$r = 0.63, P < 0.001$
	Verbal Function: Naming	Trails B	$r = 0.70, P < 0.001$
VERBAL FUNCTION	Verbal Function: Rhyming	WAIS-3 Digit Symbol	$r = 0.65, P < 0.001$
		Judgment of Line Orientation	$r = 0.70, P < 0.001$
ATTENTION	Go-NoGo (RT ¹ variability)	Boston Naming test	$r = 0.66, P = 0.002$
	Catch Game (RT ¹ variability)	Hopkins Verbal Learning	$r = 0.69, P = 0.001$
MOTOR SKILLS	Finger Tapping (inter-tap interval)	Brief Visuospatial Memory Test-Revised	$r = 0.77, P < 0.001$
		Hopkins Verbal Learning	$r = 0.76, P < 0.001$
INFORMATION PROCESSING SPEED	Information Processing: Medium Speed, High Load	Brief Visuospatial Memory Test-Revised	$r = 0.67, P = 0.002$
		Trails B	$r = 0.74, P < 0.001$
		Trails B	$r = 0.65, P < 0.001$
INFORMATION PROCESSING SPEED	Information Processing: Fast Speed, Low Load	Trails A	$r = 0.60, P < 0.001$
		Trails B	$r = 0.60, P < 0.001$
		Hopkins Verbal Learning	$r = 0.71, P < 0.001$
INFORMATION PROCESSING SPEED	Information Processing: Fast Speed, Medium Load	WAIS-3 Digit Symbol	$r = 0.70, P < 0.001$
		Trails B	$r = 0.65, P < 0.001$

¹RT: response time

results show that following unilateral damage of the nigrostriatal system, intact cells in motor circuits of both hemispheres are able to increase their functional response to a motor challenge. Furthermore, activated brain states may serve to accentuate differences that only manifest partially while a subject is at rest. Supported by the NIBIB (1R01 NS050171).

Poster 29 (PD) Late-Breaking Research

Clinical and Economic Determinants of Caregiver Burden in Parkinson's Disease

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Background: Caregiver burden in Parkinson's disease (PD) has been associated with disease severity and the physical and mental condition of the caregiver. Little is known about the impact of economic factors on caregiver burden. **Objective:** To examine factors associated with caregiver burden and identify factors that may reduce burden. **Design/Methods:** In this cross-sectional study, 70 PD patients/caregiver pairs were evaluated for caregiver burden (Zarit Burden Interview score [ZBI]), disease severity (H&Y stage, UPDRS, MMSE), health-related quality of life (SF-12, PDQ-8), and health-economic factors (household income, medical insurance, ancillary medical therapies, durable medical equipment). **Results:** Thirty-four percent of PD caregivers experience at least mild-to-moderate burden (ZBI > 20). In univariate analyses, caregiver burden is correlated with H & Y stage, UPDRS, disease duration, and measures of patient quality of life ($p < 0.001$). Caregiver burden is

correlated with duration of caregiving and caregiver mental-health-related quality of life ($p < 0.001$). Caregiver burden is not impacted by household income, medical insurance type, and use of ancillary therapy (physical, occupational, speech, etc.). But, with utilization of at least 4 types of medical equipment (cane, walker, commode, etc.), there is a favorable trend towards lessened caregiver burden ($p < 0.08$). This benefit was greatest among patients with moderate-to-severe disease (H&Y > 3), with a 52% reduction in burden as ZBI decreases from 26.4 to 12.7 at this level of equipment usage. **Conclusion:** Caregiver burden appears to be independent of a number of economic factors. However, the utilization of medical equipment may reduce caregiver burden in PD, particularly as disease progresses.

Poster 30 (OMD) Late-Breaking Research

Longitudinal Investigation of At-Risk Members of the PPNF Family: 8 Year Follow-up

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Pallido-ponto-nigral degeneration (PPND) is an autosomal dominant condition that is one of the FTDP-17 disorders. PPND has the N279K mutation on the tau gene of chromosome 17. Extensive neuropsychological evaluation of 10 at-risk family members was completed in 1998. Of those individuals, 1 developed the disease; 1 was gene-negative; 7 other family members were recently reassessed. It was hypothesized that over the intervening 8 years, results of evaluations would show significant decline in some areas for those individuals who are gene-positive. Current age of participants ranged from 29 to 52. Tests assessing three neurocognitive domains of (a) learning

and memory, (b) visuospatial sequencing, and (c) executive function were administered at both times. Test results for most people did not change more than 1 standard deviation (SD). The most consistent declines were in the domain of learning and memory where scores for 4 individuals declined more than 1 SD on a list-learning task and scores for 2 individuals (1 in both groups) declined on a logical memory task. Two persons exhibited impaired letter fluency at both time periods. Results

appear to be inconclusive in terms of predicting clearly which individuals may develop PPND. It is possible that we did not choose instruments that were sensitive enough to detect changes at this stage, or that it is too early in the course of disease to register decline or deficits in functioning. It is also possible that these results do distinguish gene-positive individuals, but in ways that will only become obvious with future testing.