

Program

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

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

*To be held on Friday, 13 May 2011, in the Four Seasons Ballroom at the
Four Seasons Resort, Irving, Texas, 1:00 p.m. to 6:00 p.m.*

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

Movement Disorders: Beyond the classic model of the basal ganglia. This session is in honor of the late Clifford W. Shults, MD and hosted by the PSG Classic Motor Working Group.

1:00-1:10 PM

Introduction and acknowledgements by Robert Hauser, MD, Chair, PSG Classic Motor Working Group. The following presentations are 20 minutes followed by 10 minutes questions and answers by the audience.

1:10-1:40 PM

PRESENTATION: Regulation of motor behavior by optogenetic control of basal ganglia circuitry.

Alexxai V. Kravitz, PhD. *Postdoctoral Fellow. Gladstone Institute of Neurological Disease, San Francisco, CA, USA*

1:40-2:10 PM

PRESENTATION: Beyond dopamine: Non-dopaminergic treatment therapies of movement disorders.

Susan H. Fox, MD, PhD. *Associate Professor of Neurology, Movement Disorders Center, Toronto Western Hospital, UHN, University of Toronto, ON, Canada.*

2:10-2:40 PM

PRESENTATION: Outside the classic basal ganglia: Pedunculo-pontine Nucleus.

Elena Moro, MD, PhD. *Associate Professor of Neurology, Movement Disorders Center, Toronto Western Hospital, UHN, University of Toronto, ON, Canada.*

2:40-3:00 PM BREAK

3:00-3:30 PM

PRESENTATION: Outside basal ganglia systems: Dystonia.

H. A. (Buz) Jinnah, MD, PhD. *Professor of Neurology, Human Genetics and Pediatrics, Emory University School of Medicine, Atlanta, GA, USA.*

Presentations on Parkinson Disease and Other Movement Disorders. This session is hosted by the PSG Symposium Organizing Committee. This session consists of 5 platform presentations for 10 minutes with 5 minutes allotted time for questions and answers by the audience. The poster session follows with formal presentations by the authors.

3:30-3:45 PM

Patients with Impulsive Compulsive Behavior can adjust risk taking in response to negative consequences.

D. Claassen, G. F. Wooten, S. Wylie. *University of Virginia, Charlottesville, VA, USA.*

Objective: To determine if risk-taking in Parkinson Disease (PD) patients with Impulsive Compulsive Behaviors (ICB) are influenced by the prospect or occurrence of negative consequences.

Background: PD patients taking dopamine agonist (DAA) medication are at increased risk for developing ICB. It has been hypothesized that ICB may involve enhanced reward processing and reward seeking coupled with reduced processing of negative consequences. Empirical support for these hypotheses is limited. In the current study, we focus on how the processing of negative consequences may be important in explaining differences in behavior between patients who develop and do not develop ICB while taking dopamine agonists.

Methods: The Balloon Analogue Risk task (BART) simulates real world risk-taking behavior. Monetary reward increases with each inflation of a virtual balloon, and patients decide when to stop balloon inflations and cash the money. The risk of letting the balloon inflate is that it will pop and money will be lost. Adjustment to negative consequences was assessed in two ways: (1) varying the probability that a balloon pops with each inflation across separate blocks of trials, and (2) measuring risk-taking behavior after a negative consequence (i.e., popped balloon).

Results: We recruited 41 PD patients, both with (n=22) and without (n=19) active ICB symptoms. All patients reduced risk-taking when the probability of negative consequences associated with a risky decision increased. Similarly, all showed a similar reduction in risk-taking behavior after experiencing a negative consequence. Notably, these patterns did not depend on dopamine agonist state.

Conclusions: These data suggest that patients with and without ICD similarly process and adjust risk-taking behavior according to the prospect and occurrence of negative consequences. We conclude that the emergence of ICB does not reflect a global disregard for the negative outcomes associated with their pursuit of rewarding activities.

3:45-4:00 PM

The effects of subthalamic deep brain stimulation at individualized frequencies on parkinsonian motor signs and hand tapping speed.

E.W. Tsang^{1,4}, C. Hamani³, E. Moro², F. Mazzella¹, U. Saha¹, A.M. Lozano^{3,4}, M. Hodaie^{3,4}, R. Chuang², T. Steeves², S.Y. Lim⁵, B. Neagu¹, R. Chen^{1,2,4}. ¹Division of Brain Imaging & Behaviour Systems- Neuroscience, Toronto Western Research Institute, University Health Network; ²Division of Neurology, Department of Medicine, ³Division of Neurosurgery, Department of Surgery, University Health Network, ⁴Institute of Medical Science, University of Toronto, Canada; ⁵University of Malaya, Kuala Lumpur, Malaysia.

Objective: To investigate the effects of DBS at individualized STN frequencies on parkinsonian motor signs and tapping speed.

Background: Beta frequencies in the basal ganglia (BG) are considered antikinetic while gamma is prokinetic. We tested the hypothesis that DBS at individualized beta frequencies will worsen whereas at individualized gamma frequencies will improve motor signs and tapping speed on PD patients.

Methods: We studied 13 advanced PD patients. In both OFF and ON dopaminergic medication states, STN local field potential (LFP) was recorded while patients performed wrist movement 1-3days after DBS electrode implantation while the leads were externalized. Differences in LFP power spectra between the OFF and ON states (MED) and between rest and movement periods (MOVE) were obtained. Six individually established frequency peaks were extracted: greatest decreases in theta (4-10Hz), beta (11-30Hz) bands and greatest increase in gamma(31-100Hz) in MED and MOVE conditions. Stimulation studies were performed, in OFF and ON states, at least three months after DBS surgery. The six individually established frequencies, the frequency used for chronic stimulation (high frequency, HF), and no stimulation were applied in random order. After stimulation for 15min, the more affected body side was rated with mUPDRS and then patients performed hand tapping tests for 20s.

Results: rmANOVA showed significant main effects of medication states (lower mUPDRS scores and higher tapping rate in ON than OFF state) and stimulation frequencies. Post hoc paired t-tests showed that mUPDRS scores for DBS at individualized gamma frequencies (MED, mean=18.7; MOVE, mean=18.4) and HF (mean=17.9) were significantly lower than no stimulation (mean=21.3). The tapping rate for HF (mean=18) was significantly higher than those for the dopamine-dependent and movement-related theta (16.6, 16) and beta (16.2, 16.3) frequencies.

Conclusion: Short-term STN DBS at the individualized gamma frequencies was as effective as HF in reducing PD motor signs. Hand tapping test may be less sensitive in detecting subtle changes produced by individualized DBS frequencies.

4:00-4:15 PM

Circadian rhythm of melatonin secretion is altered in Parkinson's disease.

A. Videnovic, A. Marconi, C. Noble, K. Reid, T. Simuni, C. Zadikoff, T. Kuhta, P. Zee. *Parkinson's disease and Movement Disorders Center, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.*

Objective: To examine circadian melatonin secretion in PD.

Background: Circadian rhythms are physiological and behavioral cycles with a periodicity of approximately 24 hours. Clinical studies in PD report diurnal fluctuations of motor and non-motor symptoms,

suggesting modifications of circadian system in PD. Understanding the role of circadian rhythmicity in PD may provide new insight into the pathophysiology and provide a rationale for application of circadian-based therapies in PD.

Methods: Rest-activity cycles of PD participants (H&Y stage 2-4, on dopaminergic treatment) and age/gender matched controls were assessed by actigraphy and sleep diaries over 14 days. This was followed by blood sampling at 30-minute intervals for 24 hours, under constant routine conditions controlling light exposure, caloric intake and physical activity. Serum melatonin levels were measured by immunoassay. The area-under-the-curve (AUC) was calculated as a measure of the secreted amount of melatonin over 24-hour period. Circadian phase was assessed by melatonin midpoint (midpoint between melatonin onset and offset). Additional data included Epworth Sleepiness Scale (ESS) and the Pittsburg Sleep Quality Index (PSQI). Group differences were assessed using independent group *t* test.

Results: 20 PD participants (9M/11F), age 65±8.2 years, and 12 controls (1M/11F), age 63±6.3 years participated in this study. Total PSQI score was 6±3.3 in the PD group and 7.6±3.4 in the control group (p=0.19). ESS score was 12.7±5.9 in the PD group and 8.6±4.9 in the control group (p=0.05). 24-hour AUC of melatonin secretion was significantly diminished in PD participants compared to controls (p=0.01). Both daytime and nighttime AUC were significantly diminished in the PD group (p=0.03; p=0.01). Melatonin midpoint was significantly delayed in PD participants (circadian time 19.4) relative to the control group (circadian time 16.6) (p=0.02).

Conclusions: Circadian melatonin secretion is reduced, and phase of the melatonin rhythm delayed in PD. These results suggest that approaches aimed to improve circadian function have potential as complementary therapies for PD.

4:15-4:30 PM

A Multicenter Randomized Placebo- Controlled Clinical Trial of Pramipexole for Tourette's Syndrome.

R. Kurlan,¹ G. Crespi,² B. Coffey,³ K. Mueller-Vahl,⁴ S. Koval,² G. Wunderlich,⁵ On behalf of the "Pramipexole for TS Trial" Investigators. ¹Atlantic Neuroscience Institute, Overlook Hospital, 99 Beauvoir Ave., Summit, NJ; ²Boehringer Ingelheim Pharmaceuticals Inc.;³ Department of Child and Adolescent Psychiatry, New York University School of Medicine, New York, NY; ⁴Nathan Kline Institute for Psychiatric Research, Orangeburg, NY; ⁵Department of Psychiatry, Social Psychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany; ⁵Boehringer Ingelheim (Canada) Ltd.

Objective: Conduct a multicenter randomized controlled trial of the dopamine agonist pramipexole in patients with Tourette's syndrome (TS).

Background: DA agonists in low dose could theoretically normalize the suspected state of central DA hypersensitivity in TS by stimulating presynaptic autoreceptors to decrease synaptic DA and/or by desensitizing postsynaptic DA receptors. Preliminary clinical studies have reported tic suppressing effects of DA agonists in TS.

Methods: This was a multicenter randomized, placebo-controlled, double-blind, parallel groups flexible-dose clinical trial of the DA agonist pramipexole (0.0625 to 0.25 mg twice daily) given for 6 weeks in 63 children and adolescents (age 6-17 inclusive) with TS. The treatment effects on tic severity, obsessive-compulsive symptoms, symptoms of attention deficit hyperactivity disorder (ADHD), mood and anxiety were assessed.

Results: There were 63 patients randomized who received at least one dose of study medication. Two centers in Germany randomized a total of 8 patients and 14 centers in the U.S. randomized a total of 55 patients. There were no significant differences (p=0.996) in the adjusted mean change in the Total Tic Score of the Yale Global Tic Severity Scale (YGTSS) from baseline to the final visit for patients treated with pramipexole (-7.16) and placebo (-7.17). There were no significant treatment effects of pramipexole on the secondary measures of change from baseline in the Global Severity score of the

YGTS and parent- and investigator-scored Clinical Global Impression of Improvement. In patients with ADHD, there was evidence of improvement in DuPaul ADHD scale scores for patients receiving pramipexole compared with placebo. Overall, pramipexole was well tolerated.

Conclusion: There was no evidence that pramipexole has efficacy in suppressing tics among children and adolescents with TS. Our preliminary findings that pramipexole may decrease symptoms of ADHD in patients with TS may deserve further study. (This work was supported by Boehringer Ingelheim).

4:30-4:45 PM

LATE-BREAKING RESEARCH

Validity and reliability of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS).

D. Weintraub^{1,2,3,4}, E. Mamikonyan¹, K. Papay¹, J. Shea^{5,6}, S. Xie⁷, A. Siderow². ¹Department of Psychiatry, University of Pennsylvania, Philadelphia, PA; ²Department of Neurology, University of Pennsylvania, Philadelphia, PA; ³Parkinson's Disease Research, Education and Clinical Center (PADRECC), Philadelphia Veterans Affairs Medical Center; ⁴Mental Illness Research, Education and Clinical Center (MIRECC), Philadelphia Veterans Affairs Medical Center, Philadelphia, PA; ⁵Department of Medicine, University of Pennsylvania, Philadelphia, PA; ⁶Center for Health Equity Research and Promotion (CHERP), Philadelphia Veterans Affairs Medical Center, Philadelphia, PA; ⁷Department Biostatistics and Epidemiology, University of Pennsylvania School of Medicine Philadelphia, PA, USA.

Objective: We aim to analyze the validity and reliability of the newly-developed Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS), an instrument designed to measure the severity of impulse control disorders (ICDs) and related disorders in Parkinson's disease (PD) patients.

Background: ICDs, including compulsive gambling, buying, eating, and hypersexuality, occur in approximately 15% of PD patients. Many neuropsychiatric symptoms (NPS) are under-diagnosed and under-treated in clinical practice. The QUIP-RS was designed as a screening instrument for ICDs and related disorders in PD, but it does not measure the severity of symptoms. Thus, the QUIP-RS was designed to measure severity of ICDs and related symptoms to assist in clinical monitoring of PD patients.

Methods: The QUIP-RS uses a 5-point Likert scale, with scores ranging from 0-112 (higher score indicating greater severity of ICDs and related disorders). A mixture of a convenience sample of patients and participants in a treatment study for ICDs in PD completed the QUIP-RS and a semi-structured diagnostic interview for ICDs and related disorders to assess discriminant validity. A subset of patients completed the QUIP-RS at multiple time points in order to establish test-retest reliability, inter-rater reliability, and predictive validity.

Results: A total of 94 patients with idiopathic PD with (N=33) and without (N=61) an ICD diagnosis were assessed with the QUIP-RS and the semi-structured diagnostic interview for ICDs and related disorders. All 94 patients provided data for inter-rater reliability, 55 for test-retest reliability, and 23 for predictive validity. Data analyses are ongoing, and final results will be presented at the PSG symposium.

Conclusion: To be presented at the PSG symposium.

4:45-5:00 PM

AWARDS PRESENTATION and CLOSING REMARKS:

Presented by the PSG Symposia Committee.

5:00-6:00 PM

POSTER SESSION:

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

POSTER SESSION

POSTER 1

Serum urate and changes in the Unified Parkinson's Disease Rating Scale score in the CALM-PD trial.

D.A. Lieberman,¹ S. Eberly,² K. Biglan,² I. Shoulson,² D. Oakes,² A. Ascherio,^{1,3} M.A. Schwarzschild^{1,4}. ¹Harvard Medical School, Boston, MA; ²University of Rochester, Rochester, NY; ³Harvard School of Public Health, Boston, MA; ⁴Massachusetts General Hospital, Boston, MA, USA.

Background: Higher serum urate levels in patients with newly diagnosed Parkinson's Disease (PD) have been linked to slower PD progression as measured by time to the need for dopaminergic therapy and by rate of change in Unified Parkinson's Disease Rating Scale (UPDRS) score prior to that need. It is not known whether urate levels are associated with PD progression in more advanced PD populations.

Subjects: 301 subjects with idiopathic PD requiring dopaminergic anti-parkinsonian therapy were enrolled in a four-year randomized clinical trial of levodopa versus pramipexole as initial treatment of PD (CALM-PD).

Methods/Analysis: UPDRS score determinations after 26 weeks of dopaminergic therapy were used for repeated measures analyses (to reduce confounding from symptomatic improvements due to initiation of therapy). The analyses were conducted by fitting a linear mixed model with random intercept and slope and fixed effects for treatment, age, sex, urate concentration, and the interaction between urate concentration and time.

Results: Repeated measures analysis using urate as a continuous variable showed no significant association between serum urate concentrations and rate of UPDRS change (p=0.10). Analysis using urate quartiles suggested a U-shaped association between serum urate and UPDRS progression; compared to individuals in the lowest quartile, Q1 (<4.2 mg/dL), the annualized rate of UPDRS progression was 0.7 points lower in Q2 (4.2 to 5.0 mg/dL; p=0.03); 0.6 points lower in Q3 (5.1 to 5.8 mg/dL; p = 0.08); and 0.7 points higher in Q4 (>5.8 mg/dL; p = 0.05).

Conclusions: Among individuals with PD initially treated with dopaminergic drugs, serum urate did not significantly predict rate of UPDRS change. The results may reflect a lack of strong association with disease progression at later disease stages or limitations of UPDRS change as an index of progression in treated PD. Future studies examining whether lower urate levels predict more functional outcomes of long-term disability such as falls would be informative.

POSTER 2

Urate as a Predictor of the Rate of Cognitive Decline in the DATATOP Trial.

D. Gunzler,² S. Eberly,² D. Oakes,² A. Ascherio,^{1,3} M.A. Schwarzschild^{1,4}. ¹Harvard Medical School, Boston, MA; ²University of Rochester, Rochester, NY; ³Harvard School of Public Health, Boston, MA; ⁴Massachusetts General Hospital, Boston, MA, USA.

Objective: To investigate whether serum urate measured at baseline is associated with a slower rate of cognitive loss in Parkinson disease (PD).

Background: In PD patients slower clinical progression has been linked to higher concentration of urate, a major antioxidant.

Subjects: Eight hundred subjects with early PD enrolled in the Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP) trial. Pretreatment serum urate concentration was measured for 775 subjects.

Methods: The relationship between baseline urate and annualized rate of change in the UPDRS mental score was assessed using linear regression, adjusting for age, sex, and treatment group (deprenyl,

α -tocopherol). A secondary analysis of the UPDRS mental score was conducted by fitting a repeated measures model.

Results: Urate was not, overall, a significant predictor of the annual rate of change in UPDRS mental score ($P=.14$). Among subjects not treated with α -tocopherol ($n=394$), however, the annual rate of worsening in the mental score significantly slowed ($P=0.025$) as the level of urate increased, while analysis of those treated with α -tocopherol ($n=381$) did not show a significant trend (P for α -tocopherol and urate interaction = 0.078). Consistent with results from the primary analyses, the repeated measures analysis of UPDRS mental score confirmed the interaction between urate and treatment with α -tocopherol ($P=.039$). Higher urate levels were associated with a slower rate of decline among subjects not treated with α -tocopherol ($P=.022$) but not in subjects treated with α -tocopherol ($P=.32$).

Conclusions: Baseline serum urate was not significantly associated with a slower rate of cognitive loss among all PD subjects in this study. However, among subjects not on α -tocopherol, higher serum urate concentrations at baseline were associated with a slower rate of worsening in UPDRS mental score, consistent with previous analyses of urate and changes in total UPDRS.

POSTER 3

A Randomized, Multi-Center, Double Blind Study to Assess Rasagiline as a Disease Modifying Therapy in Rapid-Eye-Movement Behavior Disorder Subjects at Risk of Developing Parkinson's Disease or Related Disorders (REM-PD): Rationale and Design.

S. Chen, R. Hoque, R. Zweig. *Department of Neurology, Louisiana State University in Shreveport, Shreveport, LA, USA.*

Disease modification is an important medical need in Parkinson's disease and the related alpha synucleinopathies, i.e., dementia with Lewy Bodies and multiple system atrophy (PD/PD+). Evidence that the monoamine oxidase B inhibitor rasagiline is disease-modifying has been confounded by symptomatic benefits. No clinical trials have tested whether a therapy can delay the clinical onset of PD/PD+ or slow disease progression in high risk subjects, such as those with rapid-eye-movement behavior disorder (RBD) and evidence of dopamine deficiency on imaging studies. In one study (Iranzo 2010), 40% of 43 subjects with RBD without PD/PD+ had abnormal 123I-FP-CIT SPECT imaging, and 35% of these patients developed PD/PD+ within 2.5 years. We propose a study enrolling subjects meeting research criteria for RBD. Subjects with history or clinical signs of PD/PD+ will be excluded. Subjects will have imaging with 123I-FP-CIT SPECT or a related compound. Those with scans meeting qualitative criteria for striatal dopamine deficiency will have baseline assessments including vital signs, UPDRS, MoCA, PDQ39, and Schwab and England scores before 1:1 randomization to rasagiline 1mg daily or placebo. These assessments will be repeated every 4 months for 5 years. Subjects will be switched to open-label rasagiline 1mg daily when criteria for a clinical diagnosis of PD/PD+ are met (primary endpoint 1). At visits following switch to open-label rasagiline, the need for levodopa or dopamine agonist therapy will be assessed (primary endpoint 2). Motor UPDRS scores (>12 hours off PD medication) will be the third primary endpoint. If rasagiline delays onset of clinical PD/PD+, this may be due to a symptomatic/masking effect. But a delay in need for levodopa /dopamine agonist, or lower motor UPDRS scores in the early-start rasagiline versus placebo groups, when all subjects are switched to open label rasagiline at symptom onset, would indicate disease modification.

POSTER 4

Evidence of increased intestinal permeability in Parkinson Disease patients: a step towards the validation of Braak's dual-hit hypothesis?

Movement Disorders, Vol. 26, No. 5, 2011

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Objective: We evaluated whether gastrointestinal permeability is increased in Parkinson's Disease patients, in order to test some of the implications of the dual-hit theory.

Background: It has been claimed that gastrointestinal involvement, a frequent and early event in the course of Parkinson Disease, may have a prominent role in the early pathophysiology of the disease, but this assumption has not been corroborated in a clinical setting.

Methods: The intestinal permeability of non-selected "probable PD" patients was studied using a validated, non-invasive test, and these results were compared to predefined age-adjusted reference values.

Results: We present the first seven patients included in the study (inclusion is ongoing, and we expect to study at least five more patients). The study group is composed of early to mildly-advanced PD patients without prominent gastrointestinal symptoms followed in our Clinic. In total, 3 patients (43% of our sample) had evidence of abnormal gastrointestinal permeability; 2 of them had both an abnormal lactulose/mannitol ratio and an abnormal sucrose concentration, and 1 patient had an isolated abnormal lactulose/mannitol ratio.

Conclusion: Intestinal permeability is increased in a significant proportion of unselected PD patients with minimal gastrointestinal symptoms. The significance of this finding, however, needs to be further evaluated.

POSTER 5

Innovative Web-based matching service, Fox Trial Finder, as a means to improve clinical trial recruitment.

L.M. Dalle Pазze, S. Chowdhury, J.L. Eberling, C.C. Meunier, D.W. Brooks. *The Michael J. Fox Foundation, New York, NY, United States, 10004.*

Objective: (1) To provide Parkinson's disease (PD) patients and potential control subjects with a mechanism for identifying and pursuing clinical trial opportunities on an ongoing basis. (2) To provide trial coordinators with an efficient way to connect with potential subjects.

Background: Two significant obstacles prevent timely trial recruitment: 1) patient access to information about trials for which they may be eligible and 2) coordinator connections to networks of motivated volunteers. A 2003 National Institutes of Health survey found that 85% of trials finish late due to low patient accrual, while a 2005 Harris Survey found that only 9% of Parkinson's patients had participated in a trial. The two existing PD clinical trial Web resources serve mainly as information and trials aggregators and offer no mechanism to match volunteers and trials on an ongoing basis. Fox Trial Finder (FTF) is poised to leverage improvements in Web technology to address this need.

Methods: FTF will provide an efficient, user-friendly mechanism for connecting volunteers with trials. A PD-specific match algorithm identifies trial leads based on data provided by PD users, including current and past medication use, location, and Hoehn and Yahr stage. A PD patient or healthy individual creates a profile with these match-points and other demographics to "match" to a relevant subset of all recruiting trials. Simultaneously, "matching" users are identified as qualified candidates for coordinators assigned to trials. FTF enables trial volunteers and coordinators to connect through a secure messaging interface. A sophisticated alert system supports continued engagement through a built-in feature to alert all users of new matches.

Results: To date, MJFF has convened a task force to advise on key features of the tool, engaged a technology design firm to build the tool and begun the formal spec and creative build process. FTF is

ABSTRACT

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currently under development and will complete user testing in spring 2011. FTF is expected to launch in summer 2011.

Conclusions: FTF seeks to help speed trial recruitment by bridging the gap between volunteers and recruiting clinical trials.

POSTER 6

Prognostic Value of Milestones of Disease Progression in Parkinson Disease.

S.A. Parashos, C.L. Wielinski. *Struthers Parkinson's Center, Golden Valley, Minnesota, USA.*

Objective: To assess PD prognosis as a function of events occurring during the natural progression of the disease.

Background: We hypothesize that certain disease-related events (milestones) predict poor disease outcomes.

Methods: The presence of the following milestones was ascertained in a cross-sectional cohort of 203 consecutive PD patients: motor complications; use of a gait assistive device; cognitive impairment without dementia; dementia; history of fall resulting in serious injury; and, permanent residence in a nursing home. Subjects were followed for 5 years for the following outcomes: death and permanent nursing home placement. Patient demographics, HY stage, and disease duration were also recorded. Survival analyses were used to assess the impact of each milestone separately, and Cox-regression analyses were used to generate multivariable models for the 2 outcomes.

Results: 58.6% were men; at baseline age was 72.4 ± 10.1 , and disease duration 8.1 ± 6.0 years; 26% had Hoehn and Yahr stage greater than 3; 59.1% had motor complications, 38.9% used a gait assistive device, 19.7% had cognitive impairment without dementia, 15.3% had dementia, 10.3% had history of fall resulting in a serious injury, and 8.9% were permanently in a nursing facility. 5.9% were lost to follow up. Among remaining subjects, 35.6% died by the end of the follow up period. Among subjects living independently at baseline (N=173) 12.7% were permanently placed in a nursing home during follow up. Univariate analyses showed significant effects on both survival and time to permanent nursing home placement for all milestones examined. Cox regression analyses indicated the following significant predictors for survival: dementia ($p=0.001$), nursing home residence ($p=0.002$), cognitive impairment ($p=0.004$), and gait assistive device ($p=0.04$); and, for time to nursing home placement: cognitive impairment ($p<0.001$) and dementia ($p=0.002$).

Conclusions: Among indicators of PD progression, dementia and cognitive impairment predict shorter survival, and earlier need for nursing home care.

POSTER 7

Excessive Sleepiness and Chronotype in Parkinson's Disease.

A. Sarwar,^{1,2} M. Hirshkowitz,^{1,2} R. Varghese,¹ E.C. Lai.^{1,2} *¹Parkinson's Disease Research Education and Clinical Center, Michael E. DeBakey VA Medical Center; ²Baylor College of Medicine, Houston, TX, USA.*

Objective: A study to determine the prevalence of Excessive Daytime Sleepiness (EDS) in Veterans with Parkinson's disease (PD); and its association with periodicity of the underlying circadian rhythm of sleep.

Background: EDS is common in PD. While its etiology is presumed to be multifactorial, periodicity of underlying biological rhythm with respect to sleep (or sleep- chronotype) may be a contributing factor.

Methods: 100 consecutive PD patients were questioned using the Home and Ostberg's Morningness and Eveningness scale. Subjective sleepiness, motor and cognitive impairment was assessed using Epworth Sleepiness Scale (ESS), Hoehn and Yahr (H&Y) scale, and Unified Parkinson's Disease Rating Scale (UPDRS) respectively.

Results: 55 subjects (96.4% men, 89% W, mean age 72.7, mean H&Y 2.85) had ESS > 10 (mean 14.69, 95% CI 13.79-15.59) and

were termed "Sleepy". The "Non-sleepy" 45 subjects (97.8% men, 82% W, mean age 72.1, mean H&Y 2.58) had ESS ≤ 10 (mean 6.98, 95% CI 6.18-7.77) Chronotype distribution - Sleepy group - **Morning** type: Definitive- M+ [7.2% (4/55)], Moderate -M [43% (24/55)], **Neither-N** [49% (27/55)], **Evening** -E [0% (0/55)] Non-sleepy group- M+ [18% (8/45)], M [56% (25/45)], N [24% (11/45)], E [2% (1/45)] ESS score was > 15 in 8%, 14.6% and 23% of subjects in M+, M, and N groups respectively.

Conclusion: More than half of the Veterans with PD suffer from excessive daytime sleepiness (EDS). EDS is significantly more common and more intense in the "Neither" (N) chronotype. This phenomenon requires further exploration.

POSTER 8

Social Support as a Predictor of Perceived Treatment in a Double-Blind Placebo Surgery Trial.

C. McRae¹, E. Fazio¹, D. Russell², H. Ellgring³, P. Greene⁴, S. Fahn⁴. *¹University of Denver, Denver, CO; ²Iowa State University, Ames, IA; ³University of Wuerzburg, Wuerzburg, Germany; ⁴Institute of Neurology, Columbia University, New York, NY, USA.*

Objective: Links between social support and health have been found in various patient populations, but little is known about the specific types of support that may be important determinants of outcomes. Social support was found to be a predictor of perceived treatment at 8 and 12 months in a double-blind placebo surgery trial for the treatment of Parkinson's disease (PD). The present study was undertaken to better understand which *types* of social support were related to perceived treatment at these time points.

Methods: Forty participants were randomly assigned to receive either neural implantation or sham surgery; 30 patients participated in the related Quality of Life study upon which this investigation was based. The double-blind was maintained for 12 months. The Social Provisions Scale, which assesses six types of social support, was used to measure perceived support. Data were analyzed based on "actual" as well as "perceived" treatment groups, or type of surgery patients *thought* they received.

Results: Previous results indicated there were no differences at any time between the implant and sham surgery groups in terms of social support. Patients who *thought* they received the implant reported higher levels of social support than those who *thought* they received sham surgery at 8 and 12 months (both $p < .05$). Results of two analyses of variance indicated differences between the two groups on subscales of Social Integration and Attachment at both times ($p < .05$).

Conclusions: The significant subscales represent a sense of belonging to a social network and receiving emotional support. Patients who *thought* they received the implant reported more social integration and emotional support than patients who *thought* they received sham surgery. Although directionality cannot be determined, these results underscore the value of these types of social support in this study.

POSTER 9

Effects of Video Review of Baseline Performance on Global Ratings at 12 Months in a Double-blind Placebo Surgery Trial.

C. McRae¹, J. Caspari¹, D. Russell², H. Ellgring³, E. VandeRiet¹, D. Northart¹, A. Teves¹, P. Greene⁴, S. Fahn⁴. *¹University of Denver, Denver, CO; ²Iowa State University, Ames, IA; ³University of Wuerzburg, Wuerzburg, Germany; ⁴Institute of Neurology, Columbia University, New York, NY, USA.*

Objective: A double-blind sham surgery-controlled trial was conducted to determine the effectiveness of implantation of human embryonic dopamine neurons into the putamen of patients with advanced Parkinson's disease (PD). Forty participants were randomly assigned to receive either neural implantation or sham surgery. A

video of each participant performing UPDRS Motor activities off medications was made at baseline and archived for review at the 12 month assessment before the blind was lifted. The primary outcome variable was a 1 item Global Rating Scale (GRS) ranging from -3 (much worse since surgery) to +3 (much improved since surgery). At 12 months patients rated themselves on the GRS before and after viewing the archived video. This investigation determined whether patient scores on the GRS changed as a result of the video. Because of the strong placebo effect in this study, differences in scores between both "actual" and "perceived" treatment groups were examined.

Methods: Mean age of participants was 57.8; mean disease duration was 15.7 years; 19 women and 21 men participated. When patients entered the hospital for the 12 month evaluation, they immediately rated themselves on the GRS, watched the video recorded prior to surgery, and rated themselves again.

Results: Scores on the GRS improved for the total sample after viewing the video ($p < .001$). There were no differences in ratings between the "actual" implant and sham groups before or after the video. Ratings of the perceived implant group were higher than the perceived sham group at both times ($p < .001$). Examination of changes in the 4 subgroups based on actual/perceived treatment provided information related to the placebo effect.

Conclusions: Results supported previous findings about the strong placebo effect in this study, suggested the value of investigating subgroups in double-blind studies and examining ways to optimize the use of video review in future research.

POSTER 10

Baseline Psychological Distress and Psychological Outcome Following STN or GPI DBS.

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Objective: To investigate the psychological outcome of subthalamic nucleus (STN) and globus pallidus internus (GPI) deep brain stimulation (DBS) versus best medical treatment (BMT) for Parkinson's disease (PD) patients who do not endorse elevated levels of baseline psychological distress.

Background: DBS is an effective treatment for PD motor symptoms; however, psychological side effects have been reported inconsistently and a consensus has not been reached. Additionally, research suggests that DBS mood declines are possible given the target's connectivity to the neighboring limbic system.

Methods: We evaluated 39 STN-DBS, 21 GPI-DBS and 18 BMT PD patients at baseline and 6 months on the Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI). These groups were further divided on their baseline BDI and STAI scores as elevated (Psych) or not elevated (NPpsych) for psychological distress (elevation: BDI > 12 and/or STAI > 74thile). The groups were matched on baseline age, gender and Hoehn and Yahr stage.

Results: For the NPpsych groups at the 6 month follow-up, the STN-DBS patients endorsed greater depressive and trait anxiety scores while the GPI patients reported only higher trait anxiety scores compared to the BMT group. Furthermore, the STN-DBS patients endorsed higher levels of state anxiety symptoms compared to the GPI-DBS group. For the Psych groups, no significant differences between the surgical and non-surgical groups were found, with the exception of the STN-DBS patients endorsing more symptoms of state anxiety compared to the GPI-DBS patients.

Conclusions: PD patients who did not endorse emotional dysfunction at baseline reported higher levels of psychological distress 6 months following STN and GPI-DBS as compared to a medically managed group. In contrast, the psychological profile of PD patients who endorsed baseline psychological distress did not change significantly

after surgery, with the exception that the STN-DBS patients compared to their GPI-DBS counterparts endorsed higher levels of state anxiety.

POSTER 11

Retinal thickness changes over time in Parkinson Disease patients.

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Objective: Quantify change in retinal thickness in PD in a one year span.

Background: Previous postmortem studies and in-vivo electrophysiological studies have pointed to the retina as one major site for visual impairment in PD. Recently Optical Coherence Tomography (OCT) an in-vivo imaging technique came into use to quantify retinal thickness of the retina. OCT is a widely available, inexpensive and objective brief test of retinal thickness. These advantages raise the possibility that OCT may be useful as a biomarker in PD. There are however caveats. Previous studies agree on OCT changes in PD (albeit not in complete histological agreement), but there has been no longitudinal studies.

Methods: We studied foveal thickness (Hajee et al 2008) in each eye of 60 PD patients. We repeated in 15 patients the same test after a year and quantified thickness of the foveal region in small steps. We established the sensitivity and specificity (SS) of the measures against a data base of neurologically and ophthalmologically completely screened controls using receiver operating characteristics (ROC) in each eye of each patient at each sampled distance from the foveola. Each patient had complete neurological examination at each time, including the UPDRS evaluation by the same investigator. Correlating the UPDRS score change and OCT thickness change was hampered by our currently small sample of retested patients.

Results: The most sensitive distance from the fovea is not uniform and ranges between 0.75 and 1.5 mm. The minimum change we could detect is 8 microns in the inner retina.

Conclusions: By zooming in on select retinal structures OCT may not be insensitive to progression of PD.

POSTER 12

Screening Accuracy of Comorbid Anxiety and Depression in Parkinson's Disease.

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Objective/Background: In patients with Parkinson's disease (PD), the frequent occurrence of anxiety, either alone or concurrently with depression, can confound diagnosis and treatment. Depression screens are recommended in all medical clinics to increase its recognition; it is not known how co-occurring anxiety and depression impact health-related quality of life in PD or the ability of screening tools to identify patients needing psychiatric treatment.

Method: Persons (N = 250) with idiopathic PD completed a psychiatric diagnostic interview (Structured Clinical Interview for Diagnoses of DSM-IV) and measures of activities of daily living [United Parkinson's Disease Rating Scale (UPDRS-II)], and depression [Patient Health Questionnaire -9 (PHQ-9); Geriatric Depression Scale (GDS); and Beck Depression Inventory - II (BDI-II); Hamilton Depression Scale - 17 (HAM-17)]. One-way between-groups analysis of variance examined differences in measures by diagnosis. Receiver

operating characteristic curves evaluated the prediction of anxiety and depression diagnoses stratified by anxiety diagnosis.

Results: Patients with comorbid anxiety and depressive disorders ($n = 42$) had more impaired scores on the UPDRS-II OFF than either patients with anxiety disorders ($n = 62$) or major depression ($n = 45$) alone (both $p < .001$). In general, depression scores were more severe when patients had comorbid anxiety and depression. Although the scales did not adequately predict an anxiety diagnosis ($AUCs < .7$), their predictive ability for depression was not significantly different compared to a comorbid anxiety disorder ($AUCs = .81 - .83$).

Conclusions: Presence of anxiety and depression indicates more severe symptoms and impairments than either alone. While comorbid anxiety and depression do not impact predictive validity of measures to identify depression, anxiety alone may remain undetected. Given the impact of anxiety and depression in PD, independent screening for each is needed to provide the best treatments available.

POSTER 13

Identifying Persistent Depression in Parkinson's Disease.

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Objective/Background: Several self-report depression rating scales are recommended as screening tools to identify Major Depressive Disorder (MDD) in patients with Parkinson's disease (PD). It is unclear whether the same screening tools and cut-off scores used at baseline can detect persistent or residual symptoms that may warrant adjustments in antidepressant therapy.

Method: Patients with PD ($N=78$) participating in the Methods of Optimal Depression Detection in PD study and diagnosed with MDD at baseline were re-evaluated 3-months later using a structured diagnostic interview and self-report [Beck Depression Inventory-II (BDI-2), Center for Epidemiologic Studies of Depression Rating Scale-Revised (CESD-R), Geriatric Depression Scale (GDS-30), Inventory of Depressive Symptoms-Patient (IDS-SR), Patient Health Questionnaire-9 (PHQ-9)] and clinician-rated scales [17-item Hamilton Depression Rating Scale (HAM-D-17), Inventory of Depressive Symptoms-Clinician (IDS-C), Montgomery-Asberg Depression Rating Scale (MADRS)]. Group differences in scale scores for remitted MDD (rMDD) versus unremitted MDD (uMDD) were examined using nonparametric tests. Fishers exact test was used to examine relationships between MDD (rMDD or uMDD) and positive 'screens' for uMDD at follow-up using cut-off scores from psychometric analyses of baseline scale data.

Results: Nearly 90% of subjects had uMDD at follow-up. Compared to uMDD ($n=70$), rMDD ($n=8$) had lower IDS-SR, MADRS, HAM-D-17, and IDS-C scores (all $ps < .05$). Among uMDD at follow-up, 23 to 39% had scale scores that were lower than screening cut-off scores. Subjects with follow-up scores that exceeded screening cut-offs on the BDI2, PHQ-9, IDS-SR, HAM-D-17, MADRS, and IDS-C were more likely to be diagnosed with uMDD, relative to when scores were below the screening cut-off (all $ps < .05$).

Conclusions: Once MDD is diagnosed, monitoring response to treatment is important. Any of these scales are adequate for monitoring. Lower cut-off scores than those derived for initial screening may be needed to identify persistent, unremitted major depressive episodes.

POSTER 14

Phone-based Cognitive Behavior Therapy for Depression in Parkinson's disease.

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Objective: The purpose of this study was to examine the feasibility and effectiveness of phone-based Cognitive Behavior Therapy (CBT) for depression in Parkinson's disease (PD).

Background: Limited access (due to physical disability and geographic restriction) to movement disorder specialists, geriatric psychiatrists, and evidence-based psychotherapy, such as CBT, may be one factor implicated in the sub-optimal management of depression in Parkinson's disease (dPD). Telemedicine may represent a potential approach for overcoming barriers to effective mental healthcare utilization in this medical population.

Methods: Twenty-one depressed (DSM-IV criteria) PD patients participated in an NIH-sponsored uncontrolled pilot trial of phone-based CBT in an academic medical center from October 2009 to January 2011. The Hamilton Depression Rating Scale (HAM-D 17) was the primary outcome. Several secondary outcomes were also explored [i.e., treatment response (much improved or very much improved on the Clinical Global Impression-Improvement Scale or $\geq 50\%$ reduction in the baseline HAM-D 17 score), Hamilton Anxiety Rating Scale (HAM-A), Beck Depression Inventory (BDI)]. Individual CBT was provided to PD patients for 10 weeks, modified for delivery over the phone, and supplemented with 4 separate phone-based caregiver educational sessions. Assessments were completed at baseline and 5 (midpoint), 10 (end of treatment), and 14 weeks (follow-up) post-enrollment by independent evaluators. Data was analyzed using Repeated Measures ANOVA with an intent-to-treat approach.

Results: Twenty (95%) patients completed the study treatment; 19 (90%) completed all study evaluations. Phone-based CBT was associated with significant reductions in depression (HAM-D 17: $F(2,19)=16.66$, $P<.0001$; BDI: $F(3,18)=16.88$, $P<.0001$) and anxiety (HAM-A; $F(3,18)=11.77$, $P<.0001$). Improvements were noted by week 5 and maintained throughout follow-up. 62% of the sample met criteria for treatment response at week 10, with 57% classified as responders at week 14.

Conclusions: Phone-based CBT may be a feasible and helpful approach for treating depression in Parkinson's disease and warrants further exploration in randomized-controlled trials. Response rates were comparable to those observed in the few in-person CBT studies for dPD conducted to date.

This project was funded by 3 K23 NS052155-03S1, awarded to Dr. Dobkin from the National Institute of Health/National Institute of Neurological Disorders and Stroke (NIH/NIH/NINDS).

POSTER 15

LATE-BREAKING RESEARCH

Caregiver Involvement Predicts Treatment Response to Cognitive Behavior Therapy for Depression in Parkinson's disease.

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Objective: The purpose of this study was to examine predictors of treatment response to Cognitive Behavior Therapy (CBT) for depression in Parkinson's disease (PD).

Background: In a randomized controlled trial, we have recently demonstrated that CBT was associated with notable improvements in PD depression over a 14-week period. Identifying predictors of treatment response may help to delineate future treatment recommendations for this population, as a paucity of research to guide clinical care currently exists.

Methods: Eighty depressed (DSM-IV criteria) PD patients participated in an NIH-sponsored randomized controlled trial of CBT vs. clinical monitoring (with no new treatment) in an academic medical center from April 2007 to July 2010. Treatment response was defined as much improved or very much improved on the Clinical Global Impression-Improvement Scale or $\geq 50\%$ reduction in the baseline

HAM-D 17 score. Individually-administered CBT was provided to PD patients for 10 weeks and supplemented with up to 4 separate caregiver educational sessions. It was hypothesized (a priori) that number of caregiver sessions attended (caregiver), executive functioning (Trails B-A), number of comorbid Axis I diagnoses (comorbidity), and baseline UPDRS motor scores (motor functioning) would be significant predictors of response at end-of-treatment (week 10) and follow-up (week 14). Data was analyzed with logistic regression, controlling for treatment group.

Results: The a priori model fit the data at weeks 10 ($\chi^2=11.85$, $df=4$, $p=.02$, 34% of variance) and 14 ($\chi^2=13.99$, $df=4$, $p=.007$, 38% of variance). The relative contribution of each individual predictor was as follows: week 10-caregiver (Wald=6.25, $p=.01$), Trails (Wald=3.36, $p=.07$), motor functioning (Wald=.762, $p=.38$), comorbidity (Wald=.49, $p=.48$); week 14- caregiver (Wald=7.02, $p=.008$), Trails (Wald=4.7, $p=.03$), motor functioning (Wald=.228, $p=.63$), comorbidity (Wald=.208, $p=.65$). Several exploratory models will also be presented.

Conclusions: Caregiver participation may enhance response to psychosocial interventions for depression in PD. Interpretation is limited by sample size and results warrant replication.

This project was funded by 3 K23 NS052155-03S1, awarded to Dr. Dobkin from the National Institute of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS).

POSTER 16

LATE-BREAKING RESEARCH

Clinical-pathological disagreement in Parkinson disease and multiple system atrophy (MSA).

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Objective: Our aim is to further define the clinical boundaries between Parkinson disease (PD) and multiple system atrophy (MSA) by highlighting three unusual cases.

Background: PD and MSA are commonly considered diagnoses in patients presenting with parkinsonism, however, diagnosis can be challenging in some cases, partly due to the lack of an in vivo marker of each disease. Shared symptomatology and increasing reports of levodopa response in some patients with MSA further complicate the clinical diagnosis and management of patients with parkinsonian disorders.

Methods: We report the clinical history, videotaped examinations, ancillary testing, and autopsy results on three cases of parkinsonism followed at a major teaching hospital with the neuropathologic diagnoses of PD or MSA, but with clinical presentations suggesting the other.

Results: Case 1 was a 48 year old woman at symptom onset meeting UK Brain Bank Criteria for PD with good levodopa-responsiveness, who at 10 years had an autopsy demonstrating MSA. Case 2 was a 47 year old woman at symptom onset meeting UK Brain Bank Criteria for PD with good levodopa-responsiveness and dyskinesias, who underwent deep-brain stimulation (DBS), and at 8 years had an autopsy demonstrating MSA. Case 3 was a 68 year old man at symptom onset with an akinetic-rigid syndrome and imbalance, with non-sustained levodopa response and progression to generalized rigidity and dystonia, and at 10 years had an autopsy demonstrating PD.

Conclusions: A spectrum of levodopa-responsiveness and levodopa-induced dyskinesias may exist between PD and MSA, that is not as clearly defined as once thought. Recent reports highlight an increasing awareness of some degree of levodopa responsiveness in atypical parkinsonian disorders as well as a small fraction of PD patients who lack sustained response. This contributes to diagnostic uncertainty with implications for patient enrollment into research trials, therapeutic measures such as DBS, and prognosis. There is a need for bio-

markers and other methods to confirm diagnoses in patients with parkinsonian disorders.

POSTER 17

LATE-BREAKING RESEARCH

Comparison of Dyskinesia Rating Scales: Use in the IV Levodopa Paradigm.

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Objective: To evaluate the clinimetric properties of commonly used dyskinesia rating scales in the i.v. Levodopa paradigm for use in phase IIa studies in PD.

Background: Translation of novel drugs for dyskinesia into clinical use requires an objective assessment of efficacy in phase IIa studies. Such studies usually involve an acute i.v. Levodopa infusion with a cross-over design in a small number of subjects. Several dyskinesia rating scales exist for measuring severity and disability of dyskinesia. At present, it is unclear which scale is the most reliable and valid in the setting of the i.v. Levodopa infusion paradigm.

Methods: Advanced PD subjects on stable medication and bothersome dyskinesia (MDS-UPDRS IV pt 4.2 > 2) were recruited from the Movement Disorder Centre. Each subject had 2 standard i.v. Levodopa infusions, separated by 1 - 4 weeks. Subjects were evaluated using a designed video protocol incorporating elements of 4 dyskinesia scales, motor MDS-UPDRS and timed tapping tests, in the practically defined-off state and at 30 min intervals during the i.v. Levodopa infusion over 2h and for 2h post-infusion. The primary outcome measures were modified AIMS scale, Rush Dyskinesia Disability scale, CAPSIT scale, UDysRS (part III) scores evaluated by two blinded raters using a post-hoc video analysis. Secondary outcomes were timed tapping, motor MDS-UPDRS and AEs. Test-retest reliability for each scale was assessed by non-parametric correlation coefficient.

Results: Preliminary data from five participants are presented. Male and female subjects, median age 69y (range: 63-76), with 15 (9-21) years of disease; baseline MDS-UPDRS-III 21 (10-24), H&Y staging was 2 (2-3) and UDysR part III was 11 (4-23). Primary outcome measure: a strong test-retest reliability for maximum intensity of dyskinesia was obtained with CAPSIT ($r=1.0$, $p=0.05$); in the remaining scales results were non-significant: AIMS ($r=0.18$, $p=0.72$), Rush Dyskinesia Disability scale ($r=0.71$, $p=0.18$) and UDysR ($r=0.67$, $p=0.17$). For the total amount of dyskinesia, a strong correlation was obtained for UDysR ($r=1.0$, $p=0.05$) but not the remaining scales AIMS ($r=0.33$, $p=0.5$), Rush Dyskinesia Disability Scale ($r=0.33$, $p=0.5$) and CAPSIT ($r=0.33$, $p=0.5$). Secondary outcomes: maximum change in MDS-UPDRS III ($r=-0.67$, $p=0.17$) and timed tapping ($r=0.0$, $p=0.5$).

Conclusion: The results of this study confirm that the i.v. Levodopa paradigm is a stable method of evaluating Levodopa-induced dyskinesia in PD patients. The preliminary findings suggest that the CAPSIT and UDysR scales may be the best scales for evaluating dyskinesia in the i.v. Levodopa paradigm. Further studies are ongoing.

POSTER 18

Gluten Ataxia – Pathological Results of a Case of Rapidly Progressive Ataxia with Positive Anti-gliadin antibodies.

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Objective: To describe the pathological findings of a case of rapidly progressive ataxia with anti-gliadin antibodies.

Background: Gliadin ataxia is a controversial entity. Hadjivassiliou has documented many cases; describing a generally mildly progressive ataxia often associated with a peripheral neuropathy and cerebellar atrophy. Others suggest that gluten antibodies (AGAb's) do not play a pathological role, asserting just association. In support of association not causation is the observation that 60% of SCA2 patients have positive AGAb's.

Methods: Case report of patient with apparent gliadin ataxia.

Results: The patient was a previously healthy 64 year old man, who developed a rapidly progressive ataxia. In less than 18 months the patient progressed from slight trouble with his golf swing to the inability to stand without assistance. An extensive work-up was notable for positive serum AG IgA Ab's on multiple occasions with titers as high as 392. There was significant cerebellar atrophy on MRI. He did not have improvement or slowing of progression with a strict gluten free diet for well over a month. He entered hospice and died of inanition 23 months after the initial signs of ataxia. Brain autopsy was performed and neuropathologic findings were notable for atrophy, neuronal loss, myelin pallor and gliosis of the cerebellar dentate nucleus and Purkinje cell layer, and the medullary inferior olivary nucleus. Inflammatory infiltrates were sparse and localized predominantly around small vessels. Characteristic inclusions associated with multiple systems atrophy or other neurodegenerative diseases were not identified. The morphologic features were compatible with those described in instances of immune-mediated ataxia.

Conclusion: The pathological findings are consistent with those in the limited pathological case reports available for gliadin ataxia. These pathological findings are more commonly seen in paraneoplastic diseases, but serum studies, CSF findings, or the lack of a known cancer do not support this diagnosis.

POSTER 19

Bilateral Masseter and Temporalis Hypertrophy: Case Report and Review of Literature.

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Objective: To report two cases of bilateral masseter and temporalis hypertrophy that responded well to botulinum toxin type A.

Background: Hypertrophy of the masseter and temporalis muscles, bilateral or unilateral was first described by J.W. Legg in 1880. It is not gender-specific and occurs usually between the ages of 20 and 40 years. The underlying etiology may be chronic bruxism, masseteric hyperfunction, and parafunctional jaw habits. Treatment approach was by occlusal splints and muscle relaxants. Surgery involved partial resection of the masseter and bony prominence in the mandibular angle. In a few cases, injection of botulinum toxin type A was tried.

Design/Methods: A retrospective chart review revealed two cases of patients with bilateral masseter and temporalis hypertrophy.

Case 1: A 39-year-old female presented with complaints of headache and heaviness on both sides of her face. She was diagnosed with bilateral masseter and temporalis hypertrophy. During her two pregnancies, she had spontaneous resolution of symptoms. When seen she was very uncomfortable with a sense of facial heaviness, facial pain and headache. She was treated with onabotulinum toxin A (BOTOX[®]) with 165 units spread over bilateral masseter and temporalis muscles. On 4 week follow-up, hypertrophy of masseter and temporalis muscles had improved and facial discomfort and headache had subsided.

Case 2: A 36-year old male presented with a history of lifelong bruxism and headache, who noticed progressive hypertrophy of the right temporalis and bilateral masseter muscles. He had a sensation of constant heaviness and excruciating pain mainly on the right side

of his face, causing significant distress. He was treated with abobotulinum toxin A (Dysport[®]) with 100 units used in each masseter muscle and 25 units in each temporalis muscle. At 4 week follow-up, hypertrophy of masseter and temporalis muscles had subsided and he experienced significant pain relief. His chronic bruxism persisted however.

Conclusions/Relevance: Bilateral masseter and temporalis hypertrophy is a relatively rare entity that may occur spontaneously or secondary to jaw bruxism. Local injections of botulinum toxin type A provide a useful treatment option.

POSTER 20

Using judgment of line orientation to assess visuospatial functioning in Huntington's disease.

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Objective: To examine the usefulness of the Judgment of Line Orientation Test in Huntington's disease (HD).

Background: The Benton's Judgment of Line Orientation Test (JLO) is commonly used to assess visuospatial functioning and requires minimal motor demands. Previous studies have shown visuospatial deficits in subcortical dementias, such as Parkinson's disease (PD) and HD. The JLO has demonstrated sensitivity to visuospatial deficits in PD; however, no study has examined the JLO in HD.

Methods: A global cognitive measure, the Mattis Dementia Rating Scale (DRS), was used to determine degree of HD cognitive severity. Thirty-one (M=20, F=11) mild HD subjects (DRS \geq 128) and 30 (M=20, F=11) moderate to severe HD subjects (DRS<128) were administered the JLO test Form H.

Results: Mild HD subjects (mean DRS=132.9) had a mean age of 46.2 (SE=2.5) years, mean education of 14.1 (SE=0.6) years, mean CAG repeat lengths of 46.0 (SE=0.8), and mean duration of disease of 6.2 (SE=0.5) years. Moderate to severe HD subjects (mean DRS=116.7) had a mean age of 49.5 (SE=1.9) years, mean education of 13.4 (SE=0.3) years, mean CAG repeat lengths of 44.8 (SE=0.6), and mean duration of disease of 6.0 (SE=0.7) years. One-Sample T-Tests revealed that both mild (p=0.02) and moderate to severe (p<0.01) HD subjects scored significantly lower on the JLO compared to normative data for healthy, community-dwelling adults, obtained from Woodard et al. (1998).

Conclusion: The JLO may be a useful measure for detecting visuospatial impairment in manifest HD. Further studies will be needed to confirm and extend these findings.

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POSTER 21

Cranio-cervical dystonia following chemical modulation of parvocellular red nucleus.

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Objective: To study the behavioral and motor responses following chemical modulation of parvocellular red nucleus in primates.

Background: Cranio-cervical dystonias are the most common forms of adult-onset focal dystonia. Blepharospasm, oromandibular, lingual, laryngeal and cervical dystonia are the various form of cranio-cervical dystonia. Meige syndrome is characterized by blepharospasm, cervical dystonia, and facial oromandibular dystonia. There is a growing interest in the use of deep brain stimulation (DBS) in medically re-

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ABSTRACT

factory forms of dystonia but the optimal target for Meige syndrome remains unclear.

Methods: Experiments were performed using Cynomaglous monkey (*Macaca Fascicularis*). Monkey was trained to perform a self initiated behavioral task of reaching out and grabbing presented food reward for 6 weeks. After behavioral training implant surgery was performed. Neural activity within parvocellular red nucleus was identified and mapped using tungsten microelectrodes (10-30 μ m tip exposure length). Micropipettes (10 μ m tip opening diameter) were used to record neural activity and to perform activation of parvocellular red nucleus by injecting Bicuculline(100nl), Kainic Acid(200nl,0.25 Mmol) and Gabazine (250 nl,0.2 Mmol). To avoid any residual effects injections were made at weekly intervals. Ten minutes after the injection, micropipette was removed and monkey was observed

for any behavioral change and moved to the cage for observation. Digital video recordings were obtained.

Results: Following Bicuculline injection dystonic tremors were noticed in the contralateral distal hindlimb. Contralateral focal dystonia of the neck and oro-facial dystonia including jaw deviation was noted with Gabazine injection. Kainic acid stimulation caused hyper-vigilence and contralateral focal dystonia of neck along with circling motion to side contralateral to injection. These motor responses were short lasting and reversible. Topography of stimulation site was correlated with histology after completion of experiments.

Conclusions: Chemical neuromodulation of parvocellular red nucleus causes cervical and oromandibular dystonia. Further studies are needed to verify these changes and evaluate the target as potential site for neuromodulation of medically refractory Meige syndrome.