



**The National VA
Parkinson's Disease
Consortium**

**Parkinson's Disease
Research, Education
and Clinical Center
(PADRECC)**

eCommuniqué

Welcome to this research bulletin of the National VA Parkinson's Disease Consortium. The eCommuniqué highlights information about Parkinson's disease (PD) and is provided as a service to members of the national Consortium, other colleagues, and community leaders interested in PD.

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In This Issue

Identifying Incident Cases of Parkinsonism Among Veterans
Subthalamic Nucleus Stimulation Modulates Afferent Inhibition in PD
New Animal Model for Parkinson's Levodopa Dyskinesias
A LRRK2 G2019S Mutation Test for Parkinson's Disease
Specialist Care in Parkinson's Disease
Neurologic Phenotypes Associated with Acanthocytosis
The Use of Zonisamide in the Treatment of Essential Tremor
Evidence-based Analysis of Physical Therapy in Parkinson's Disease
Resistance Training with Creatine Improves Upper-Body Strength in PD
FDA Withdraws Pergolide and Cabergoline from Market
A Capsule...of Information
Educational Opportunities
The National VA Parkinson's Disease Consortium

Identifying Incident Cases of Parkinsonism Among Veterans

A medical record review study at a tertiary referral VHA medical center identified 782 veterans with diagnostic codes for Parkinson's disease (PD) or secondary parkinsonism (SP) between 1998 and 2000. Based on structured medical record review, a movement disorder specialist confirmed diagnoses for incident parkinsonism cases. Among the 782, 191 incident parkinsonism cases were identified (100 PD, 75 SP, and 16 Parkinson's Plus). The incident cases were older at diagnosis (74.5 yr. vs. 70.4 yr; $p < 0.05$) and more likely to be white (81% vs. 62%; $p < 0.07$) than SP cases. Diagnostic codes were insufficient to distinguish between incident PD and SP (positive predictive value, 57% and 39% respectively). Since VA sources failed to identify 21% of confirmed deaths among the incident cohort by November 2004, limitations for identifying incident PD cases should be considered when developing future studies.

The senior author is Dr. Lai, Director of the Houston PADRECC, Michael E. DeBakey VAMC.

Authors Drs. White, Waring, Cook, and Ms. Moore were staff members of the Houston PADRECC when this research was conducted.

<http://www3.interscience.wiley.com/cgi-bin/abstract/114206723/ABSTRACT>

Subthalamic Nucleus Stimulation Modulates Afferent Inhibition in PD

This study examined the effects of deep brain stimulation (DBS) performed through the subthalamic nucleus (STN) on short latency afferent inhibition (SAI) and long latency affect inhibition (LAI) in seven patients with PD and age-matched controls. The patients were studied while off medication followed by a session while on medication. The stimulator was switched on or off in random order in each session. The findings suggest that the symptoms that respond to dopaminergic drugs are improved by STN stimulation. Those symptoms that do not respond to dopaminergic medications may also be improved by STN stimulation since the LAI appears to be partially normalized by STN stimulation in the medication-on condition. <http://www.neurology.org/cgi/content/abstract/68/5/356>

New Animal Model for Parkinson's Levodopa Dyskinesias

The neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydro-pyridine (MPTP) causes sustained Parkinson-like symptoms that can be reversed with levodopa but later result in levodopa-induced dyskinesia (LDID), which can be more debilitating than the PD symptoms themselves. An alternative animal model has been developed to study motor responses in mice that were given injections of MPTP followed by injections of levodopa plus carbidopa. In this study, only the previously MPTP-treated animals became hyperkinetic, as compared to levodopa-treated control animals that were not exposed to MPTP. The hyperactivity lasted 2 hours after each levodopa injection and the hyperkinesia increased with additional days of levodopa treatment even though the dose was the same. Results suggest that levodopa can cause reproducible hyperactivity in mice that were previously exposed to MPTP. Dr. Nicholas is the National VA Parkinson's Disease Consortium Center Director at the Birmingham VAMC.

<http://www3.interscience.wiley.com/cgi-bin/abstract/113489538/ABSTRACT>

A LRRK2 G2019S Mutation Test for Parkinson's Disease

This study assessed the performance characteristics of the G2019S mutation as a clinical test for PD. The sample included 1518 patients with PD and 1733 controls. All subjects were genotyped for the G2019S mutation using a TaqMan assay, and mutations were verified by direct sequencing. A total of 20/1518 patients and 1/1733 control subjects carried the mutation. Specificity was 99.9% (95% CI, 99.6-100%), sensitivity was 1.3% (0.8-2.1%), and the positive likelihood ratio was 22.8. A positive family history increased the likelihood ratio to 82.5. Information on gender, age at onset, or age at testing didn't improve the test performance. The gene test was shown to be most useful for those with a family history of PD in first-degree relatives. Sensitivity was low in all analyses probably because of the unknown multiple factors that cause PD. The ethical, legal, and social implications for this testing need to be further examined. Dr. Nutt, Director of the Northwest PADRECC in Portland and Dr. Samii from the Northwest PADRECC in Seattle are also authors of this study. <http://www.liebertonline.com/doi/pdf/10.1089/gte.2006.10.221>

Specialist Care in Parkinson's Disease

Medical records of 401 veterans with PD were examined to determine whether care met key indicators of PD care quality. Specialty care was defined as care provided by a movement disorder specialist or a general neurologist. Overall, the care provided by movement disorder specialists involved a greater adherence to 10 indicators of PD quality of care than did general neurologists ($p=0.006$) and nonneurologists ($p<0.001$). The difference in quality of care between movement disorder specialists and nonneurologists included four indicators: treatment of wearing-off, assessments of falls, depression, and hallucinations. Room for improvement is needed for the care of patients who are not able to access specialist care. Dr. Cheng, first author, and Dr. Vickrey, senior author, are from the West LA PADRECC. Dr. Siderow is from the Philadelphia PADRECC and Dr. Swarztrauber was formerly with the Northwest PADRECC.

<http://www3.interscience.wiley.com/cgi-bin/abstract/114098640/ABSTRACT>

Neurologic Phenotypes Associated with Acanthocytosis

The term "neuroacanthocytosis" is normally used to refer to autosomal recessive chorea-acanthocytosis and X-linked McLeod syndrome, but there are other movement disorders in which erythrocyte acanthocytosis may also be seen, such as Huntington disease-like 2 and pantothenate kinase-associated neurodegeneration. Disorders of serum lipoproteins such as Bassen-Kornzweig disease form a distinct group of neuroacanthocytosis syndromes in which ataxia is observed, but movement disorders are not seen. Genetic testing has provided the ability to distinguish between these disorders, even when there are considerable similarities between phenotypes. Improved detection is important for accurate genetic counseling, for monitoring of complications, and for implementing causal treatments, once these become available. As in other neurodegenerative conditions, animal models are a promising strategy for the development of such therapies. The first author, Dr. Walker, is the National VA Parkinson's Disease Consortium Center Director, James J. Peters VAMC, Bronx, NY.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17210889&query_hl=2&itool=pubmed_docsum

The Use of Zonisamide in the Treatment of Essential Tremor

An antiepileptic agent, zonisamide (ZNS), was used in a placebo-controlled randomized trial to evaluate its effectiveness in treating patients with essential tremor (ET). Twenty patients were randomized to receive either ZNS (escalating doses of 100-200 mg.) or a placebo. Measures used to assess improvement were accelerometry, the Fahn-Tolosa-Marin (FTM) rating scale, and the Clinical Global Impression (CGI-C scale). At endpoint, subjects assigned to ZNS were taking a mean dosage of 160 mg/day. There were no significant improvements in the FTM scales and the CGI-C scores did not significantly improve. Three patients in the treatment group discontinued the study due to side effects of fatigue, headache, and paresthesias. The major finding was that tremor amplitude as assessed by accelerometry significantly

improved in the ZNS group as compared with the controls. The first author of this article, Dr. Zesiewicz, is the Director of the National VA Parkinson's Disease Consortium Center in Tampa, Florida.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17149715&query_hl=4&itool=pubmed_docsum

Evidence-based Analysis of Physical Therapy in Parkinson's Disease

Practice recommendations for the uniformity and efficacy of physical therapy intervention in patients with PD were developed following an evidence-based literature review of 29 articles that was supplemented by clinical expertise. Six specific core areas were identified: transfers, posture, reaching and grasping, balance, gait, and physical capacity. Four specific treatment recommendations were based on evidence from more than two controlled trials: cueing strategies to improve gait, cognitive movement strategies to improve transfers; exercises to improve balance, and training of joint mobility and muscle power to improve physical capacity. These practice recommendations provide a basis for current clinical practice for physical therapists working with patient with PD, and for future research in this field.

<http://www3.interscience.wiley.com/cgi-bin/abstract/113490162/ABSTRACT>

Resistance Training with Creatine Improves Upper-Body Strength in PD

This study evaluated the therapeutic effects of resistance training with and without creatine supplementation in patients with mild to moderate PD. Twenty patients were randomized in a double-blind study to receive either creatine monohydrate plus resistance training or placebo (lactose monohydrate) plus resistance training. Both groups participated in progressive resistance training twice a week for 12 weeks and were evaluated for muscle endurance and functional performance (3 consecutive chair rises). Both groups improved their upper-body muscular endurance but those treated with creatine showed a significantly greater gain. The functional performance also improved more with the creatine group than with the placebo group. The authors conclude that resistance training is an effective countermeasure to the sarcopenia and strength loss associated with PD. Resistance training exercises may lead to an improved quality of life for those with PD, and safe doses of creatine may be a promising supplement when monitored for side effects.

<http://nnr.sagepub.com/cgi/content/abstract/21/2/107>

FDA Withdraws Pergolide and Cabergoline from Market

Pergolide (Permax) and its generic forms have been taken off the market after a pair of studies implicated the dopamine agonist in causing serious heart valve damage. The nested case-control analysis, within the cohort of 40-80 years, found significantly increased cardiac-valve regurgitation among those who were taking pergolide and another dopamine agonist, cabergoline. The evidence pointed to the activation of the serotonergic receptor 5-hydroxytryptamine 2B that caused a distinct form of fibrotic valvulopathy. <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01596.html>

A Capsule...of Information

* On May 9, 2007, The U.S. Food and Drug Administration (FDA) announced the approval of rotigotine transdermal system (Neupro), a skin patch designed to treat symptoms of early PD. Rotigotine, a member of the dopamine agonist class of drugs, activates the dopamine receptors and mimics dopamine. The patch is replaced every 24 hours.

<http://www.fda.gov/bbs/topics/NEWS/2007/NEW01631.html>

* The projected number of people with PD in Western Europe's 5 most populous countries and the world's 10 most populous nations, 2005 through 2030, is estimated between 4.1 and 4.6 million in 2005 with these figures predicted to double between 8.7 and 9.3 million in 2030.

Dr. Siderowf from the Philadelphia PADECC is one of the authors. <http://www.neurology.org/cgi/content/full/68/5/384>

* A form of Holmes tremor of the lower extremity was observed in a patient who developed tremor in three body parts following a hemorrhage of the posterior brain stem. Further details of this brief report are found at

<http://www3.interscience.wiley.com/cgi-bin/abstract/113508068/ABSTRACT?CRETRY=1&SRETRY=0>. Dr. Samii from the Northwest PADRECC in Seattle is the senior author of this case report.

* Statistics obtained from the Centers for Disease Control and Prevention:

- By 2030, the number of Americans aged 65 and older will more than double to 71 million, roughly 20% of the U.S. population.
- The State of Aging and Health in America 2007 report includes calls to action on reducing injuries associated with falls.

- The cost of providing health care for an older American is 3-5 times greater than the cost for someone younger than 65.
- Influenza vaccination saved \$117 per person vaccinated.
- Among adults at high risk for heart attack, daily aspirin regimen saved 80,000 lives annually.
- For every dollar spent on arthritis self-help programs, \$3.42 was saved in physician hospital costs.

Educational Opportunities

- * The Movement Disorder Society's 11th International Congress will be held June 3-7th, 2007 in Istanbul, Turkey. <http://www.movementdisorders.org/>
- * The American Neurological Association Annual Meeting will be held Oct. 7-10th, 2007 in Washington, DC. <http://www.aneuroa.org/>
- * The Parkinson's Disease Foundation presents its 50th Anniversary Educational Symposium "Frontiers of Science and Clinical Advances in Quality of Life" on Oct. 11-12, 2007 at the South Street Seaport area in NYC. www.pdf.org/50th .
- * The American Academy of Neurology Annual Meeting will be held April 12-19th, 2008 in Chicago, IL. <http://www.aan.com/>
- * A 266-page text/DVD package of Practical Neurology (Lippincott, \$99) consists of 102 cases classified in 19 sections, covering adult subspecialties of neuromuscular disorders, epilepsy, neuro-ophthamology, sleep medicine, and others. A review section consists of 260 multiple choice questions. <http://www.neurology.org/cgi/content/full/68/11/E13>

The National VA Parkinson's Disease Consortium

Mission statement: ...to support the provision of optimal care and education for veteran patients diagnosed with Parkinson's disease and related movement disorders through advocacy, scientific inquiry and enhanced clinical expertise.

Coordinating Center:

Philadelphia VA Medical Center ATTN: Rebecca Martine, APRN, CS, BC (Phone: 215-823-5934) Email:

Rebecca.Martine@med.va.gov

PADRECC Website: <http://www.parkinsons.va.gov>

National Consortium Leadership:

Rebecca Martine, APRN, CS, BC (Chairperson)

Jeff Bronstein, MD, PhD (Co-Chairperson)

Dawn McHale (National Consortium Coordinator and National PADRECC Co-Coordinator)

Lori Anzaldo (National PADRECC Co-Coordinator)

Mark Baron, MD (Research Committee Chairperson)

Eric Cheng, MD (Communications Committee Chairperson)

Gretchen Glenn, LSW (Education Committee Co-Chair)

Editors:

Naomi D. Nelson, PhD, Co-Associate Director of Education, Houston PADRECC

Eugene C. Lai, MD, PhD, Director, Houston PADRECC

To unsubscribe: contact.naomi.nelson@med.va.gov