

 <p>The National VA Parkinson's Disease Consortium</p> <p>Parkinson's Disease Research, Education and Clinical Center (PADRECC)</p>	<p>eCommuniqué</p>
<p>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.</p>	

Vol. IV, Number 1 – January 2007

In This Issue

**Valvular Heart Disease and the Use of Dopamine Agonists in PD
Study Finds No Link Between Susceptibility Genes and PD Risk in General Population
Homocysteine Levels and PD
Improving Motor Functioning with Zonisamide
The Development of Motor Fluctuations and Dyskinesias in PD
Impulse Control Disorders and PD
The Association Between PD and Low Bone Density and Falls in Older Men
A Review of the Evidence for Premorbid Parkinsonian Personality
Driving Ability and PD
Professional Meetings
The National VA Parkinson's Disease Consortium**

Valvular Heart Disease and the Use of Dopamine Agonists in PD

155 patients taking dopamine agonists for PD and 90 control subjects were administered echocardiograms to determine the risk of valvular heart disease. Clinically important moderate to severe regurgitations (grade 3 to 4) were found with greater frequency in patients taking ergot-derived dopamine agonists (pergolide 23.4% or cabergoline 28.6%) than in patients taking non-ergot-derived dopamine agonists (0%) as compared with control subjects (5.6%). The relative risks for moderate to severe valve regurgitation in the ergot-derived agonist groups ranged from 4.2 -7.3 (p=0.01 and p=0.001). The mean mitral tenting area was significantly greater in ergot-treated patients and showed a linear relationship with the severity of mitral regurgitation. The authors conclude that these findings should be considered when evaluating the risk-benefit ratio of PD treatment with ergot derivatives.

<http://content.nejm.org/cgi/content/short/356/1/39>

Study Finds No Link Between Susceptibility Genes and PD Risk in General Population

A large-scale *validation* study (12,000 DNA samples) of PD risk, funded by The Michael J. Fox Foundation, has found no association between PD risk and 13 single-nucleotide polymorphisms (SNPs)-single-letter changes to the DNA code which were implicated in an earlier study. Although no single common variation in DNA explains PD risk in the general population, the results cannot conclusively deny that genetics plays no role since interactions may occur with other genetic and/or environmental factors. Results of an earlier study implicated 13 SNPs as possibly associated with an altered risk for idiopathic PD, although the overall contribution of any one SNP was low. Results from this study

provide a powerful tool with which to validate the initial results.

www.michaeljfox.org/news/article.php?id=269

Homocysteine Levels and PD

Increased homocysteine levels might accelerate dopaminergic cell death in PD through neurotoxic effects. Higher dietary intakes of folate, vitamin B12, and vitamin B6 (cofactors in homocysteine metabolism) might decrease the risk of PD through decreased plasma homocysteine. In a study of over 5,000 subjects without dementia or PD, the association between dietary intake of folate, vitamin B12 and vitamin were examined. After a mean follow-up of almost 10 years, 72 subjects were identified as having a diagnosis of PD. Stratified analysis showed that higher dietary intake of vitamin B6 was associated with a decreased risk of PD in smokers only. No association was observed for the presence of PD and dietary folate and vitamin B12.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16864826&query_hl=1&itool=pubmed_docsum

Improving Motor Functioning with Zonisamide

A multicenter, randomized, double-blind, placebo controlled trial was conducted in Japan to determine the efficacy and safety of zonisamide (ZNS) for patients with PD. Patients who showed insufficient response to levodopa were given a placebo for 2 weeks and then treated for 12 weeks with 25, 50, or 100 mg/day of ZNS or placebo. The primary endpoint was change from baseline in the total score of the Unified Parkinson's Disease Rating Scale (UPDRS) Part III and secondary endpoints included changes from baseline to total daily 'off' time; total scores of the UPDRS in Parts I, II, and IV, and the Modified and Yahr score. Findings revealed a significant improvement in the primary endpoint of the 25 and 50 mg. groups and the duration of 'off' time was reduced in the 50-100 mg groups. The incidence of adverse events was greatest in the 100 mg. group, but dyskinesias were not increased in any of the ZNS groups. The use of ZNS as an adjunctive treatment for PD is recommended by the findings of the study.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17200492&query_hl=4&itool=pubmed_docsum

The Development of Motor Fluctuations and Dyskinesias in PD

A retrospective analysis involving 301 patients with early PD were followed for 48 to 58 months and evaluated at 3 month intervals for the presence of motor fluctuations and dyskinesias. Main outcome measures of motor fluctuations and dyskinesias were the order of appearance and the time to the first occurrence. 189 subjects (62.8%) developed motor complications, and of these, 37.6% developed fluctuations, but not dyskinesias, 12.2% developed dyskinesias but not fluctuations, 25.4% developed fluctuations before dyskinesias, 17.5% developed dyskinesias before fluctuations, and 7.4% developed both at the same time. Higher cumulative levodopa dose or levodopa equivalent dose were associated with the earlier occurrence of motor complications. Motor fluctuations and dyskinesias appear to be interrelated because the presence of one is associated with the earlier development of the other

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17172616&query_hl=7&itool=pubmed_docsum

Impulse Control Disorders and PD

Impulse control disorders (ICD) such as hypersexuality, pathologic gambling, and excessive shopping can be devastating complications of antiparkinsonian treatment. 100 subjects (66 men and 34 women) with idiopathic PD (65 years and under) were recruited to participate in a longitudinal study of PD work- and social-related disability. All subjects had no evidence of dementia, a current substance abuse, a psychiatric disorder, or a neurosurgical procedure for PD. Findings revealed a 9% (n=9) prevalence for the 3 types of ICDs with more severe symptoms of depression, irritability, disinhibition, and appetite changes in this group. There were no significant group differences in PD-related or demographic variables. All patients with ICDs were taking dopamine agonists and at the time of ICD onset, used

combined agonist/L-dopa therapy while 38% of the non-ICD group received L-dopa and agonist therapy concurrently. While the prevalence of comorbid psychiatric diagnoses was higher in the ICD group, the difference was not significant. This study was unique because ICDs were regarded as a spectrum of behaviors not individual behaviors, and subjects received an interaction of antiparkinsonian medications and dopamine agonists. www.neurology.org/cgi/content/full/67/7/1258

The Association Between PD and Low Bone Density and Falls in Older Men

A large cross-sectional and prospective cohort study (5995 community subjects) was conducted to examine the association between PD and bone mineral density (BMD) and the risk of falls. PD was determined from self-report. BMD was measured at the hip and spine and incident falls were determined for 1 year using mail surveys. 52 participants (0.9%) reported a history of PD and these patients reported nearly three times greater age-adjusted risk of fall that was statistically significant. In multivariate models, PD was associated with significantly lower bone marrow density at the spine and total hip. The researchers suggested that clinicians should screen older men with PD for osteoporosis. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16137287&itool=pubmed_AbstractPlus

A Review of the Evidence for Premorbid Parkinsonian Personality

Studies as early as 1913 noted a personality type associated with PD characterized by rigidity, depression, introversion, and cautiousness. This study examined the literature from 1989-2004 using standard databases and search terms related to personality, depression, anxiety, and PD. Only studies that evaluated personality characteristics using standardized methods and that met all inclusion and exclusion criteria were reviewed. Four studies met the majority of criteria and all were retrospective case-control studies. None measured personality before the onset of PD. The authors conclude that the term 'premorbid' is inappropriate for studies that assessed current personality traits and that the existence of a premorbid personality in patients with PD is inconclusive. Future research should involve correlating personality characteristics to specific activities or regions of the brain and determining whether personality is a risk factor or an early indicator of the disease. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16755553&query_hl=11&itool=pubmed_docsum

Driving Ability and PD

The driving ability of 154 individuals with PD was evaluated at a driving assessment center where clinical tests, reaction times, and an in-car driving test were administered. The majority of subjects (104, 66%) were able to continue driving although 46 required automatic transmission and 10 others needed car modifications. Ability to drive was predicted by disease severity (Hoehn & Yahr stage 3), duration of illness, age, comorbid conditions such as dementia, brake reaction time, and scores on a driving test (all $p < 0.0001$). This was the largest study of consecutive patients seen at a driving assessment center in the UK, and the first to devise a scoring system for on-road driving assessment. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16718266&query_hl=13&itool=pubmed_docsum

Professional Meetings

American Academy of Neurology – Annual Meeting: April 28-May 5, 2007, Boston, MA.

American Neurological Association - 132nd Annual Meeting: October 7-10, 2007. Marriott Wardman Park Hotel, Washington, D.C.

Movement Disorder Society - 11th International Congress of Parkinson's Disease and Movement Disorders. June 3-7, 2007. Istanbul, Turkey.

National Parkinson Foundation - Young Onset Conference. July 5-7, 2007. Chicago, IL.

Parkinson's Disease Foundation – 50th Anniversary Educational Symposium. Oct. 11-12, 2007. New York City, NY.

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

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/Naomi Nelson, PhD (Education Committee Co-Chairs)

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

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](mailto:naomi.nelson@med.va.gov)