



THE TRANSMITTER

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Article Review

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Clinicopathological characteristics of freezing of gait in autopsy-confirmed Parkinson's disease

A quarter of PD patients experience freezing of gait with concomitant decreased quality of life. The investigators explored associated factors in 58 autopsy-proven PD patients who had substantia nigra Lewy bodies and a score of 1 or more on UPDRS item number 14. Progression was determined via serial scales and medical notes (average follow-up period= 9 years). Earlier onset gait freezing was associated with gait difficulty, dyskinesias, postural instability, memory impairments, hallucinations, and vivid dreaming. Early onset of hallucinations was associated with more rapid progression of gait freezing. Both progressive and more severe gait freezing were associated with higher Lewy body burden. The investigators concluded that early onset and rapid progression of gait freezing in the sample were associated with early cognitive issues and hallucinations that are potential markers of Lewy body development in the cortex.

Mov Disord., December 2015, Volume 30, Issue 14, pages 1874–1884

$\alpha 7$ nicotinic receptor agonists reduce levodopa-induced dyskinesias with severe nigrostriatal damage

Background

ABT-126 is a novel, safe and well-tolerated $\alpha 7$ nicotinic receptor agonist in a Phase 2 Alzheimer's disease study. This study tested the anti-dyskinetic effect of ABT-126 in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-treated squirrel monkeys with moderate and more severe nigrostriatal damage.

Methods

Monkeys (n = 21, set 1) were lesioned with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine 1-2 \times . When parkinsonian, they were gavaged with levodopa (10 mg/kg)/carbidopa (2.5 mg/kg) twice daily and dyskinesias rated. They were then given nicotine in drinking water (n = 5), or treated with vehicle (n = 6) or ABT-126 (n = 10) twice daily orally 30 min before levodopa. Set 1 was then re-lesioned 1 to 2 times for a total of 3 to 4 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine injections. The anti-dyskinetic effect of ABT-126, nicotine, and the $\beta 2^*$ nicotinic receptor agonist ABT-894 was re-assessed. Another group of monkeys (n = 23, set 2) were lesioned with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine only 1 to 2 times. They were treated with levodopa/carbidopa, administered the $\alpha 7$ agonist ABT-107 (n = 6), ABT-894 (n = 6), nicotine (n = 5), or vehicle (n = 6) and dyskinesias evaluated. All monkeys were euthanized and the dopamine transporter measured.

Results

With moderate nigrostriatal damage (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine 1 \times -2 \times), ABT-126 dose-dependently decreased dyskinesias (~60%), with similar results seen with ABT-894 (~60%) or nicotine (~60%). With more severe damage (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine 3-4 \times), ABT-126 and nicotine reduced dyskinesias, but ABT-894 did not. The dopamine transporter was 41% and 8.9% of control, with moderate and severe nigrostriatal damage, respectively. No drug modified parkinsonism.

Conclusion

The novel $\alpha 7$ nicotinic receptor drug ABT-126 reduced dyskinesias in monkeys with both moderate and severe nigrostriatal damage. ABT-126 may be useful to reduce dyskinesias in both early- and later-stage Parkinson's disease.

Mov. Disord., 2015 Vol 30: 1901–1911. doi: 10.1002/mds.26453

Cerebral autoregulation and white matter lesions in Parkinson's disease and multiple system atrophy

Cerebral autoregulation (CA) refer to the homeostatic process ensuring constant cerebral blood supply despite of systemic blood pressure (BP) fluctuations. CA regulates the diameter of cerebral vessels by promoting vasodilation or vasoconstriction in response to BP increase or decrease. This mechanism prevents vascular damage to the brain in case of disrupted BP control.

Parkinson's disease (PD) and multiple system atrophy (MSA) are neurodegenerative disorders. Both are characterized by intracellular aggregation of alpha-synuclein. Both has variety of non-motor symptoms, includes GI, urological and cardiovascular autonomic failure. The main CV autonomic failure is orthostatic hypotension (OH) which is defined as reduction of 20mmHg of systolic or 10 mmHg of diastolic BP within 3 min of standing. OH is very common symptom of MSA and about 30% of PD population. Recent studies showed that CV autonomic failure may be associated with increased cerebral white matter disease. A robust association between disruption of CA and cerebral white matter lesions has been demonstrated in chronic hypertension.

Parkinsonism and related disorders: Vol 21; Number 12; December 2015; P-1393-1397

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Richmond PADRECC leads the committee for January/February. Committee meets via conference call the first Tuesday of the month at 12pm (EST)
- **Standardize and Optimize Clinical Care:** The committee continues to discuss a variety of clinical issues to improve patient care and outcomes. The focus is to provide clinical support to the consortium network by focusing on measures to standardize clinical care across the PADRECC network. Recent agenda items have included discussion on:
 1. New treatment options for Parkinson's Disease including DUOPA™ (carbidopa and levodopa) enteral suspension delivered directly into the small intestine for the treatment of motor fluctuations for people with advanced Parkinson's disease and Rytary (carbidopa/levodopa IR/Sa combination oral medication). Discussion focused on development of standardized protocol for this therapy across the PADRECC network, logistical issues, education and support aspects.
 2. Current practice regarding the use of various Neurotoxins across the PADRECC network with the objective to improve this specialized clinical practice and develop neurotoxin selection criteria for various conditions in the Veteran population.
 3. Practical aspects regarding the use of DAT scans; Applications and pitfalls, including the issue of drug interference
 4. Palliative Care: Review of palliative care resources and practices in the PADRECCs
 5. Veteran's Choice Program, optimization of care across the PADRECC network.
- **PADRECC Transmitter:** PADRECC clinicians provide reviews of recent movement disorder publications that are included in the PADRECC Transmitter

Education Committee

- **PADRECC/EES Movement Disorder Series:** The 2nd audioconference for FY 2016 was held on **January 14, 2016-"Nutrition and PD: What Your Patients Need to Know"** by Dr. John Duda, Director

Philadelphia PADRECC. The audioconferences are archived on the National website www.parkinsons.va.gov under the Movement Disorder Series tab. Please see the **Dates to Remember** section below for a listing of upcoming FY 16 audio conferences.

- **National Newsletter:** Currently accepting articles for the **2016 VA Parkinson Report**. Topics for consideration: education, telemedicine, speech, DBS, support groups, activities, and research by the PADRECC's and their consortium members. If you are interested in submitting an article for the newsletter please email Glennys Asselin-Cavey (Glennys.Asselin@va.gov). Articles are due by **April 29, 2016**.
- **“Mood Disorders in PD: What’s New”:** This enduring material project was done in collaboration with EES and is an on-line TMS self-study program that offers CME credit for a 3 year period. This program provides VHA healthcare professionals with a broadened medical awareness of Mood Disorders in PD. The program is **NOW** available on TMS:

https://www.tms.va.gov/learning/user/deeplink_redirect.jsp?linkId=ITEM_DETAILS&componentID=14771&componentTypeID=VA&revisionDate=1343926380000

- **National Website Maintenance:** The committee performs monthly maintenance checks of the National Website to ensure information is current and up-to-date.
- **PADRECC Transmitter:** The committee continues to assemble and distribute this e-newsletter every other month.

Richmond PADRECC Service Area Update

Richmond/Southeast PADRECC News

- A research proposal by Mark Baron, MD, Paul Wetzel, PhD, and George Gitchel, PhD has been awarded a \$1 million grant by the Michael J Fox Foundation to study eye movements in movement disorders using a tracking device as a diagnostic tool. The original study site is the Richmond PADRECC with over 3000 subjects. The grant will provide for expansion of the study to Virginia Commonwealth University, Emory University and the University of Iowa with the aim to validate eye tracking as a rapid, non-invasive, highly accurate clinical biomarker for prodromal and symptomatic Parkinson's disease.
- In 2015, Dr. Jessica Lehosit was named Interim Director, Nurse Practitioner Debbie Dellinger, MSN, ACNP-BC joined the clinical team, and Research Health Science Specialist, George Gitchel completed his doctoral thesis on “Development of an accurate differential diagnostic tool for neurological movement disorders utilizing eye movements” earning a PhD in biomedical engineering. Miriam Hirsch, RN, DBS team, advanced her nursing practice earning a BSN. The PADRECC Administrative Officer position remains vacant due to VACO hiring freeze.
- Each month, a SCAN-ECHO session focuses on a Movement Disorder topic presented by Richmond PADRECC team members. SCAN-ECHO is held on the first Friday from 12-1pm. Contact PADRECC Teleheath RN, Jackie Johnson at Jackie.johnson2@va.gov to get on the email distribution list and learn connectivity options for SCAN-ECHO.
- An initiative began in late 2015 to emphasize the Parkinson's disease quality measures. Each month one quality measure is highlighted by the providers during clinic visits with supporting educational materials on the clinic bulletin board, and at support groups. Topics addressed so far have included: motor fluctuations and keeping motor diaries, psychiatric symptom and cognition impairment assessment, and medications to avoid when on dopaminergic agents.

Southeast Consortium Center News

Gainesville, FL - Christopher Hess, MD will be speaking at the Michael J. Fox Partners in Parkinson's Disease Event in Tampa, FL on February 6th.

Tampa, FL - Theresa A. Zesiewicz, MD, FAAN reports the AMVETS will be sponsoring a "Shakes, Rattles, Rides and Rods" fundraiser in Tampa on January 23, 2016 to benefit Parkinson's disease research at University of South Florida (USF). Dr. Sanchez-Ramos has officially retired from the VA, but is still practicing at USF. Some recent research publications:

- **A Randomized Controlled Exploratory Pilot Study to Evaluate the Effect of Rotigotine Transdermal Patch on Parkinson's Disease-Associated Chronic Pain.** Rascol O, Zesiewicz T, Chaudhuri KR, Asgharnejad M, Surmann E, Dohin E, Nilius S, Bauer L. *J Clin Pharmacol.* 2015 Dec 2. doi: 10.1002/jcph.678.
- **Occupational Characteristics and Patterns as Risk Factors for Parkinson's Disease: A Case Control Study.** Sullivan KL, Mortimer JA, Wang W, Zesiewicz TA, Brownlee HJ, Borenstein AR. *J Parkinsons Dis.* 2015 Sep 23;5(4):813-20. doi: 10.3233/JPD-150635.

Lexington, KY - John T. Slevin, MD, MBA shares these recent publications:

- **Long-term safety and maintenance of efficacy of levodopa-carbidopa intestinal gel: An open-label extension of the double-blind pivotal study in advanced Parkinson's disease patients Slevin, J.T., Fernandez H.H., Zadikoff C., Hall C., Eaton S., Dubow J., Chatamra K. and Benesh J..** *J Parkinson's Dis* 5:165-174, 2015. doi: 10.3233/JPD-140456, PMID: 25588353
- **Initiation and dose optimization for levodopa-carbidopa intestinal gel: Insights from phase 3 clinical trials.** Lew M.F., Slevin J.T., Krüger R., Martínez Castrillo J.C., Chatamra K., Dubow J.S., Robieson W.Z., Benesh J.A., and Fung V.S.C. *Parkinsonism & Related Disorders* 21(7):742-8, 2015. doi:10.1016/j.parkreldis.2015.04.022, PMID: 25962554
- **Physician perspectives on non-oral medication approaches for the management of clinically important unresolved issues in Parkinson's disease: results from an international survey and discussion program.** Odin P., Chaudhuri R.K., Slevin, J.T., Volkman J., Dietrichs E., Martinez-Martin P., Krauss J.K., Henriksen T., Katzenschlager R., Antonini A., Rascol O., and Poewe W. *Parkinsonism & Related Disorders* 21(10):1133-44, 2015. doi: 10.1016/j.parkreldis.2015.07.020, PMID: 26233582
- **Dopaminergic modulation of medial prefrontal cortex deactivation in Parkinson depression.** Andersen A.H., Smith C.D., Slevin, J.T., Kryscio R.J., Martin C.A., Schmitt F.A. and Blonder L.X. *Parkinson's Disease*, 2015. doi.org/10.1155/2015/513452
- **Long-term Integrated Safety of Levodopa-Carbidopa Intestinal Gel from Prospective Clinical Trials.** Lang A.E., Rodriguez R.L., Boyd J.T., Chouinard S., Zadikoff C., Espay A.J., Slevin, J.T., Fernandez H.H., Lew M.F., Stein D.A., Odin P., Fung V.S.C., Klostermann F., Fasano A., Draganov P., Schmulewitz N., Robieson W.Z., Eaton S., Chatamra K., Benesh J.A., Dubow J. *Movement Disorders*, in press. doi: 10.1002/mds.26485/abstract. PMID: 26695437

Dates to Remember

February 20-March 2, 2016

2016 PAN Forum

Washington, DC

<http://parkinsonsaction.org/events/forum/>

March 10th, 2016

EES/PADRECC Movement Disorders Series

Topic: Duopa

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

April 15-21, 2016

2016 American Academy of Neurology (AAN) Meeting

Vancouver, Canada

www.ann.com

May 12th, 2016

EES/PADRECC Movement Disorders Series

Topic: Complementary and Alternative Medicine

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

June 19-23, 2016

2016 Movement Disorder Society International Congress

Berlin, Germany

www.mdsccongress2016.org

September 8th, 2016

EES/PADRECC Movement Disorders Series

Topic: Palliative Care and PD

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

September 19th, 2016 (*tentative*)

National VA PD Consortium Conference

Portland, Oregon

Additional information to follow

September 20-23, 2016

4th World Parkinson Congress

Portland, Oregon

<http://www.wpc2016.org/>