



# THE TRANSMITTER

September 2017

## Article Reviews

Prepared by: George R. Jackson, M. D., PhD. ~ Houston PADRECC

### **Association between poor cognitive functioning and risk of incident parkinsonism: The Rotterdam study.**

Prodromal symptoms of Parkinson disease (PD) are thought to precede motor symptoms by years; these include autonomic dysfunction, REM sleep behavior disorder, and changes in mood and sense of smell. Darweesh and colleagues used the population-based, prospective Rotterdam Study to probe the connection between cognitive impairment and parkinsonism. The cognitive testing panel administered consisted of the following: the Stroop color word test, letter-digit substitution, semantic fluency (e.g., animals named per minute), and verbal learning. More than 7,000 subjects aged 45 years and older were enrolled and followed for 8 years on average. Over the course of the study, one percent of the participants were diagnosed with parkinsonism (more than two thirds of these with probable PD). Cognitive impairment at enrollment was a risk factor for development of parkinsonism and PD (hazard ratios 1.79 and 1.52, respectively; 95% CI for each). These findings suggest that cognitive impairment should be considered a component of prodromal PD.

*JAMA Neurol.* 2017. Epub ahead of print Sept. 25.

### **β2-Adrenoreceptor is a regulator of the α-synuclein gene driving risk of Parkinson's disease.**

In this study, Scherzer and colleagues at Brigham and Women's screened libraries of compounds for their ability to decrease expression of endogenous alpha-synuclein in a human neuroblastoma cell line. Two interesting compounds that were discovered were studied: clenbuterol and salbuterol. These drugs act as beta 2 adrenergic receptor (B2AR) agonists. B2AR agonists also were found to reduce alpha synuclein expression in the mouse. Antagonism of B2AR using propranolol (a drug commonly used to treat essential tremor) increased alpha-synuclein. B2AR agonist use in a parallel epidemiologic study of Norwegians decreased the risk of developing PD, whereas propranolol increased PD risk. These data highlight the potential importance of adrenergic signalling in PD pathogenesis.

*Science* 2017 Sep 357(6354):891. <https://www.ncbi.nlm.nih.gov/pubmed/28860381>

### **Dopamine oxidation mediates mitochondrial and lysosomal dysfunction in Parkinson's disease.**

Abnormal function of mitochondria and lysosomes have both been described in PD, but how these abnormal subcellular organelles are linked remains unclear. Krainc and colleagues at Northwestern derived induced pluripotent stem cells (iPSCs) from fibroblasts of patients with homozygous mutations of the familial PD gene DJ-1, as well as patients with sporadic PD and normal controls. These iPSCs were then induced to differentiate into dopaminergic neurons. Mitochondrial oxidative stress began to occur in sporadic and inherited PD-derived neurons. Neuromelanin and oxidized dopamine began to accumulate. Mutations in glucocerebrosidase, a lysosomal enzyme, are a risk factor for PD. Activity of this enzyme began to diminish in inherited PD-derived neurons; a more delayed decrease was observed over time in culture for sporadic PD-derived neurons. Many mouse models of PD fail to develop pathology in the substantia nigra, so the authors compared human and mouse neurons. DJ-1 knockout mice failed to accumulate oxidized dopamine; nor was diminution of glucocerebrosidase activity observed. However, mice with both DJ-1 knockout and overexpressed alpha-synuclein did accumulate oxidized dopamine and showed attenuated glucocerebrosidase activity. The differences between human and mouse neurons appeared to depend upon variations in calcium homeostasis and dopamine metabolism. This paper establishes a framework for understanding the linkage between mitochondrial

and lysosomal pathways in PD pathogenesis, and it emphasizes the utility of studies in cell culture using patient-derived neurons.

*Science* 2017. Sep 357(6357):1255. epub ahead of print Sep 7.  
<https://www.ncbi.nlm.nih.gov/pubmed/28882997>

## Committee Activities

### Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Southwest PADRECC leads the committee for August/September. The committee meets via conference call the first Tuesday of the month at 12pm (EST)
- **Standardize and Optimize Clinical Care:** The committee continues to discuss latest research on PD, new treatment strategies and a variety of clinical issues to improve patient care and outcomes. It also serves 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 discussions on:
  1. Discussion of the new medications deutetrabenazine and valbenazine for Huntington's chorea and tardive dyskinesia.
  2. The management of orthostatic hypotension including the role of the newly FDA-approved agent droxidopa (Northera).
  3. Continued discussion focused on clinical experience sharing among the group regarding 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
  4. The prevalence of vitamin D deficiency in Parkinson's disease and the need to monitor and adequately replete levels for bone and cognitive health.
  5. Practical aspects regarding the use of DAT scans; applications and pitfalls, including the issue of drug interference
  6. Continued discussion on the use of Pimavaserin (Nuplazid) in the treatment of psychosis associated with PD, compared to quetiapine and clozaril.
  7. Continued discussion of Rytary and conversion and titration dosing strategies. Consensus that often more than a three times/day dosing is needed.
  8. Discussion of the possible role for levodopa-induced hyperhomocystinemia in Parkinson's disease and the strategies to monitor and manage this problem
  9. Discussion of the role of exercise in the treatment of PD and the practical aspects of "prescribing" exercise to patients.

### Education Committee

- **PADRECC/EES Movement Disorder Series:** The final audioconference for FY 17 was held on **September 14, 2017** "*Cognition and Exercise*" by Dr. Megan Gomez, PhD, Long Beach VAMC, West LA PADRECC. The audioconferences are archived on the National website [www.parkinsons.va.gov](http://www.parkinsons.va.gov) under the Movement Disorder Series tab. Please see the **Dates to Remember** section below for a listing of upcoming FY 17 audioconferences and mark your calendars.
- **PD at Home:** Monthly PD telephone education/support group conference available nationwide on the 2<sup>nd</sup> Tuesday of each month: 10am PT, 11am MT, 12p CT, 1pm ET. Developed and led by West LA

PADRECC. Monthly flyers will be emailed to all Consortium Members, please advertise to your PD patients.

- **National Newsletter:** The newsletter was completed and emailed to all Consortium Members and is available for viewing on the National website [www.parkinsons.va.gov](http://www.parkinsons.va.gov) under the For Professionals tab.
- **Suggested Education Essentials Handout:** This hand-out has been updated and provides useful links to PD resources in the following areas: Overview of PD, Exercise, Medications, Nutrition, and PD Organizations. The handout can be found on the National Website, please share with your patients: <https://www.parkinsons.va.gov/resources/EducationEssentialsNewlyDx.6.2017.pdf>
- **Patient Education Brochures:** In response to the 2016 National VA PD Consortium Education Needs Assessment, the PADRECC Patient Education Brochures have been updated and are now available for download on the National Website. Please share with your patients: <https://www.parkinsons.va.gov/patients.asp>
- **National Website Maintenance:** The committee performs monthly maintenance checks of the National Website to ensure information is current and up-to-date.
- **PADRECC Transmitter:** This committee continues to assemble and distribute this e-newsletter every other month.

## Dates to Remember

**November 9, 2017**

*EES/PADRECC Movement Disorders Series*

Topic: Initial Therapeutic Paradigms in PD

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

**January 11, 2018**

*EES/PADRECC Movement Disorders Series*

Topic: The Role of Kinesiotherapy in the Treatment of PD and Movement Disorders

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

**March 8, 2018**

*EES/PADRECC Movement Disorders Series*

Topic: TBD

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

**April 21-27, 2018**

*American Academy of Neurology~ Annual Meeting*

Los Angeles, CA

<https://www.aan.com/conferences/annual-meeting/>

**May 10, 2018**

*EES/PADRECC Movement Disorders Series*

Topic: Psychiatric Issues in Parkinson's Disease

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

**September 13, 2018**

*EES/PADRECC Movement Disorders Series*

Topic: TBD

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

**October 5-9, 2018**

*International Parkinson and Movement Disorder Society (MDS)~International Congress*

Hong Kong

<http://www.mdscongress.org/Congress-2018.htm>

## **Houston PADRECC Updates**

### **Houston PADRECC**

Director: Dr. Aliya I. Sarwar, M.D.

- **New Consortium Center:**  
VA St. Louis HCS John Cochran Division
- **New Consortium Members added in FY 17 include:**  
Zachary P. Macinski, MD, Topeka, Kansas City VAMC  
Farhat Husain, MD, Oklahoma City VAMC  
Robert White, MD, VA St. Louis HCS, MO

- **Current Consortium Activities:**

Monthly Consortium call: Discussions include practical support for DBS programming and management strategies to optimize care for complicated PD and other MD patients.

Our Consortium Network Directors and their staff receive special orientation, materials, and other support for participation in the Houston Consortium Network.

Enduring educational material related to PD management and safety developed in collaboration with other PADRECCs, continued to be distributed and used at our various consortium sites as an educational resource for the patients, their care providers and healthcare professionals.

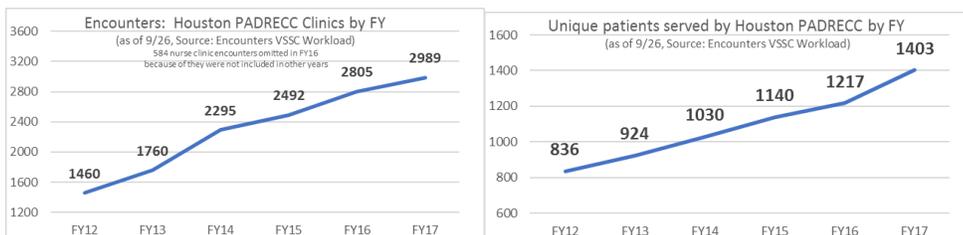
- **Future Projects:**

A collaborative research initiative with all consortium directors is being planned for FY18. Mini-educational/clinical fellowship and case conference using AV technology is being planned with consortium sites

- **Clinical Update:**

Service area: Southcentral and Midwestern United States.

### Growth in Clinical Encounters



Continue to experience increases in clinic encounters and unique patients seen, despite having to re-schedule August/September patients due to Hurricane Harvey flooding in Houston and surrounding areas

**Face-to-face clinics:** DBS- 3 clinics/week, Movement Disorders- 14 clinics/week, Neurotoxin- 8 clinics/month

**Telemedicine:** 3 clinics/week

- **Deep Brain Stimulator Implantations**

For FY17, we performed 8 DBS surgeries and 10 battery replacements. We continued our collaboration with Neurosurgery and other Texas Medical Center investigators to analyze human electrophysiological data collected during deep brain stimulator or pulse generator (IPG, battery) implantation on PD or ET patients to individualize and optimize surgical outcome.

- **PADRECC Telehealth Expansion**

PADRECC telehealth clinic appointments are now available with 4 of our community clinics (CBOC) within the Greater Houston Area, (Katy, Richmond, Lufkin, and Conroe).

- **Education Update:**

5 Patient Education programs (Support groups, Educational Conferences, Clinic Education, Community Educational Conferences, Educational Newsletters)

9 Provider Education programs (Live lectures, Audio Lectures, Journal Club, Clinic based Education, Mandatory BCM PGY4 monthly elective, Pharmacy residency elective, Community lectures, Case Conferences, Educational Teleconference)

Additional Projects:

- EES Movement Disorder Series: *Creativity and Parkinson's Disease*, by Michele York, PhD, ABPP-CN, May 11, 2017
- Houston updated the *Agent Orange and Toxic Exposures* brochure.
- 4 Quarterly educational conferences were held in auditorium: "Patient and Family Forums" Topics included: Advances in PD, Is PD Genetic, PD and the Stomach, and Impaired Balance & Falls in Veterans with PD.
- Collaborated with Houston Area Parkinson's Society (HAPS) in their annual Caregiver Symposium (11/19/2016) and Education Symposium (8/5/2017).

- **Research Update:**

Ongoing projects: 7

Collaborations in development: 2

Abstracts: 9

Papers: (published, in-press, submitted) 9