



# THE TRANSMITTER

September 2018

## Article Reviews

Prepared by: Fariha Jamal, M.D. & George R. Jackson, M.D., Ph.D. ~ Houston PADRECC

**Immunosuppressants and risk of Parkinson disease.** Numerous studies have been conducted to identify the prodromal phase of Parkinson disease (PD). There is an emerging hypothesis that use of neuroprotective medications during this phase may slow down disease progression. Racette et al. developed a PD predictive model that uses administrative data from the Medicare program to identify PD patients during the prodromal phase. They conducted an analysis in this population to examine the risk of PD in relation to use of immunosuppressants. 48,295 PD cases and 52,324 controls were identified from comprehensive Part A and B Medicare claims data for 2004-2009. Use of immunosuppressants prior to the diagnosis of PD was explored. The following drug classes were identified: calcineurin inhibitors, Inosine monophosphate dehydrogenase inhibitors (IMDH), dihydrofolate reductase inhibitors, biologics, corticosteroids, and miscellaneous. Logistic regression models were constructed with PD as the outcome and immunosuppressants as the independent variables. Relative risk was calculated by using odds ratios (ORs) and 95% confidence intervals (Cis) from these models. The authors found that two categories of immunosuppressants, corticosteroids (RR = 0.80; 95% CI 0.77-0.83) and IMDH inhibitors (RR = 0.64; 95% CI 0.51-0.79), were associated with a lower risk of PD. The other classes of immunosuppressants were not clearly inversely associated with PD risk. This study provides additional evidence for a role of the immune system in PD risk and a promising potential drug class for PD neuroprotection.

*Ann. Clin. Transl. Neurol.* 2018. July 5(7): 870.

**Anti-tumor necrosis factor therapy and incidence of Parkinson disease among patients with inflammatory bowel disease.** Inflammation is a hallmark of both Parkinson disease (PD) and inflammatory bowel disease (IBD). Despite genetic and pathophysiologic connections between the two disorders, clinical data on co-morbid PD and IBD is lacking. Peter et al. designed this retrospective cohort study to determine the incidence of PD in IBD patients and effects of early exposure to anti-tumor necrosis factor (TNF) therapy on PD risk. Data were collected from the Truven Health Marketscan administrative claims database and the Medicare Supplemental Database between January 1, 2000 and March 31, 2016. 657,637 patients who had at least 2 IBD claims were identified. Of them, 144,018 were at least 18 years old, had 6 months follow up and had no prior PD on or before index date. They were matched with 720,090 unaffected controls. 13,083 patients with IBD were treated with anti-TNF therapy. 1796 patients were identified as having PD among the 864,108 patients included in the study. A 28% increase in incidence of PD was found among patients with IBD compared with unaffected matched controls, after adjusting for age and sex. A significantly lower PD incidence rate (0.08 per 1000 patient-years) was noted among IBD patients who were exposed to anti-TNF therapy as compared to those who were not exposed (0.76 per 1000 patient-years). These results add to the growing notion that systemic inflammation plays a role in the pathogenesis of both diseases. A potential role for anti-TNF treatment in reducing PD risk was suggested, requiring larger studies to confirm.

*JAMA Neurol.* 2018. Aug; 75(8): 939.

**Tauopathy-associated PERK alleles are functional hypomorphs that increase neuronal vulnerability to ER stress.** Progressive supranuclear palsy (PSP) is an important “Parkinson’s plus” disorder seen in VA populations. The H1 tau haplotype is an established risk factor for PSP, but other genetic factors predisposing to the disorder remain relatively uncharacterized. In 2011, a genome-wide association study of PSP identified protein kinase R-like endoplasmic reticulum kinase (PERK; also known as eukaryotic translation initiation factor 2 alpha kinase 3/EIF2AK3) in PSP pathogenesis. PERK is an ER stress sensor. Variants in PERK also are implicated in Wollcot-Rallison syndrome, an autosomal recessive metabolic disorder. In a tour de force analysis, Shauna Yuan at UCSD, as well as other collaborators from various institutions, used techniques including PSP patient-derived induced pluripotent stem cell cultures to analyze the effect that PSP-associated PERK variants have on the protein’s function. Unlike the Wollcot-Rallison variants, which either abrogate protein expression or interfere with kinase function, the PSP-associated variants either (1) interfere with PERK signaling without directly affecting the kinase domain, or (2) increase PERK turnover. This study adds to our understanding of PSP pathogenesis and supports the notion that pharmacologic activators of PERK might provide new hope for PSP therapeutics.

*Hum. Mol. Genet.* epub before print Aug. 29, 2018.

## **Committee Activities**

### **Clinical Care Committee**

- Rotation of Committee Chair: Leadership for the clinical care committee rotates amongst the PADRECCs. The West LA PADRECC leads the committee for September/October. 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. Clinical experience with recently introduced medications for Parkinson’s disease, Huntington’s disease, and tardive dyskinesia including Rytary, Extended Release Amantadine, Pimavanserin, deutetrabenazine, valbenazine, etc.
  2. Continued discussion about referrals, outcomes and target selection trends regarding deep brain stimulation surgery for PD, ET, and dystonia.
  3. Continued discussion focused on clinical experience sharing among the group regarding DUOPA™ (carbidopa/levodopa) enteral suspension for the treatment of motor fluctuations in advanced Parkinson's disease
  4. Discussion about newer avenues of delivering tele-health within the VA healthcare system including video-connect
  5. Discussion about newer clinic models to provide focused treatment for non-motor symptoms of PD (Palliative Care Clinics) and to improve overall health of our patient population (Wellness Clinics)
  6. Discussion about the role of kinesiotherapy in Parkinson’s disease
  7. Strategies to minimize the impact of reduced workforce at the PADRECC, innovative ideas to improve performance and deliver care

8. Discussion about collaborative research, including involvement in industry supported projects like Apomorphine subcutaneous infusion study.
9. The prevalence of vitamin D deficiency in Parkinson's disease , the need to monitor and strategies and outcomes of current replacement strategies.
10. Discussion about management of psychogenic/functional movement disorders

## Education Committee

- **PADRECC/EES Movement Disorder Series:** The final audioconference for FY 18 was held on September 13th, 2018, “**Neurotoxin Use for Treating PD Symptoms**” by Adrienne Keener, 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 FY19 audioconferences and mark your calendars.
- **National VA PD Newsletter:** The newsletter is currently being assembled and will be emailed electronically once completed.
- **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. Monthly flyers will be emailed to all Consortium Members, please advertise to your PD patients.
- **Updating PADRECC Pocket Card:** Committee is exploring updating the pocket card which includes the treatment algorithm and medication list as it is out of date. Project request submitted and approved by EES to help with design and distribution. Prospective project start date, January 2019.
- **National Website Maintenance:** The committee performs 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.
- **Resources available on the National Website-** *Please share with your patients*
  - **Patient Education Brochures-** <https://www.parkinsons.va.gov/patients.asp>
    - Exercise and Physical Activity
    - Fall Prevention
    - PD Medications
    - Motor Symptoms
    - Non-Motor Symptoms
    - Agent Orange and Toxic Exposures and PD
  - **My Parkinson's Story-**<https://www.parkinsons.va.gov/patients.asp>  
A series of short videos prepared by the VA PADRECCs addressing various aspects of Parkinson's disease.
  - **Suggested Education Essentials for Veterans with PD** <https://www.parkinsons.va.gov/patients.asp>
  - **PADRECC Support Group Listings** <https://www.parkinsons.va.gov/patients.asp>
  - **Updated Resource Request Form-**PADRECC staff and consortium members can order bulk supply of FREE educational materials from PF and APDA. Please click on the following website and complete the **Resource Request Form** and mail or fax to address listed:  
<https://www.parkinsons.va.gov/clinicians.asp>

# Houston PADRECC Service Area Updates

## Houston PADRECC

Michael E. DeBakey VA Medical Center

### **Director: Aliya Sarwar, MD**

Houston's Parkinson's Disease Research, Education and Clinical Center (PADRECC) housed in the Michael E DeBakey VA Medical Center provides state of the art medical and surgical services to Veterans with Parkinson's disease and related movement disorders who reside in the South Central and Mid-Western United States. The area served by the Houston PADRECC includes all or parts of the following states: Texas, Louisiana, Mississippi, Oklahoma, Arkansas, Alabama, Florida, Kansas, Missouri, Indiana, Illinois, Wisconsin, and Kentucky (Houston PADRECC Consortium).

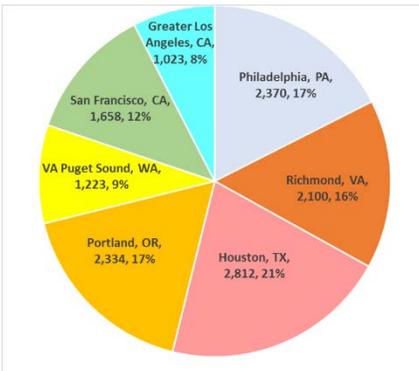
### **Consortium update:**

Houston PADRECC has added the following new consortium sites and members in FY 18:

Juebin Huang, MD,PhD, at the G.V. (Sonny) Montgomery VA Medical Center in Jackson, MS

Padma Kumar MD, at the Central Texas Veterans Health Care System/Austin Outpatient Clinic in Austin, TX

### **Clinical Update:**



Dr. Paolo Moretti, a Houston PADRECC neurologist and movement disorder specialist, relocated to Utah at the beginning of FY18. Our nurse supervisor and clinic coordinator nurse positions remain un-filled due to SCS hiring freeze. Despite these limitations, Houston PADRECC has maintained its leadership position with respect to patient encounters amongst all 6 PADRECCs.

There have been a total of 2812 patient encounters in FY18 to date, approximately 91% of those seen to date in FY17.

### **New Initiatives:**

Houston PADRECC 's Suzanne Moore spearheaded the development of Movement Disorders Clinical Case Registry. This registry would be an invaluable resource for our clinics both in operational and research purposes.

- The New and Follow up patient evaluation templates were revised to incorporate the AAN criteria.
- A New Clinic Initiative – focused on preventive and corrective measures to improve brain and overall health of the patients called “the BRAIN HEALTH Clinic” has been incorporated in our current clinics.
- Initiated the process to begin Video Connect service with PADRECC patients.

### **Education Update:**

Houston PADRECC 's Associate Director for Education position remains unfilled due to SCS hiring freeze.

We have continued our 16 educational programs geared towards patients/caregivers, medical trainees and practicing healthcare providers.

These include 1) Clinic based patient/caregiver education, 2) Patient's monthly educational support group, 3) Patient and Caregiver educational conference (Educational Forums), 4) Collaborative Patient Educational Programs with Community groups, 5) Patient and Caregiver based educational newsletter (PADRECC Pathways), 6) Medical Staff's weekly educational conference, 7) Medical staff's monthly journal club, 8) Physicians' monthly Clinical Case Conference, 9) Medical staff's monthly inter-disciplinary surgical case discussion series, 10) Monthly Consortium based tele- educational meeting, 11) PADRECC based BCM neurology residents monthly elective rotation, 12) PADRECC's joint educational venture with Pharmacy residency training program, 13) In-patient medical student and medical residents hands on educational experience, 14) PADRECC physicians' lectures (including grand rounds, invited lectures) at the VA, BCM, national and international locations, 15) Production of National PADRECC newsletter (VA Report), 16) Nurse lecture series.

### **New Initiatives:**

- Initiation of formal PADRECC clinic based educational rotation for Baylor College of Medicine students.
- Nurse clinic based "Fall Prevention", educational initiative
- Nurse clinic based bilingual (English and Spanish) caregiver "Stress Reduction" educational initiative

### **Research:**

We currently have 13 active research projects. In FY18, we have continued recruitment in our Circadian Rhythm/ Sleep Study and began screening subjects for a collaborative project with the GI department entitled "High Resolution Manometric Abnormalities of the Esophagus and Clinical Features of Gastroesophageal Reflux in Patients with Parkinson's Disease".

Renewal for our collaborative traumatic brain injury project has been submitted.

A P50 NIH grant. "P50 NS108720: Baylor College of Medicine Udall Center for Parkinson's Disease Research" was submitted and scored, but not funded. A future re-submission is planned.

### **New Initiatives:**

- Protocol for an industry research project which is a "Phase 3, Open-Label Study of the Safety, Efficacy, and Tolerability of Apomorphine Administered by Continuous Subcutaneous Infusion in Advanced Parkinson's Disease Patients with Unsatisfactory Control on Available Therapy" has been approved by the IRB and R&D committees. The site initiation visit has been completed.
- A new collaborative protocol with Neurosurgery entitled "Analysis of Human Basal Ganglia Electrophysiological Recordings and Targeted Stimulation for Optimization of Deep Brain Stimulation" has been approved
- A new project to study the clinical characteristics of tremor in Veterans has been approved by the IRB and R&D committees and will utilize the Movement Disorders Clinical Case Registry to supplement a chart review for Essential tremor patients seen at the Houston PADRECC.

### **Publications and other research presentations:**

Abstracts/posters = 7 (4 presented, 1 submitted, 2 in development)

Papers = 10 (6 published, 2 submitted, 2 in development)

## **Dates to Remember**

### **October 5-9, 2018**

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

Hong Kong

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

### **November 8<sup>th</sup>, 2018**

*EES/PADRECC Movement Disorders Series*

Topic: Lewy Body Dementia

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

### **January 10, 2019**

*EES/PADRECC Movement Disorders Series*

Topic: DBS

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

### **March 14, 2019**

*EES/PADRECC Movement Disorders Series*

Topic: Pain in PD

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

### **May 4-10, 2019**

*American Academy of Neurology (AAN) Annual Meeting*

Philadelphia, PA

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

### **May 9, 2019**

*EES/PADRECC Movement Disorders Series*

Topic: Sleep and PD

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

### **June 2-7, 2019**

**5<sup>th</sup> World Parkinson Congress**

Kyoto, Japan

<https://www.worldpdcoalition.org/default.aspx>

**September 12, 2019**

*EES/PADRECC Movement Disorders Series*

Topic: PD 101

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