



# THE TRANSMITTER

November 2015

## Article Review

Prepared by: Dr. Indu Subramanian, West LA PADRECC

### **Electroencephalogram slowing predicts neurodegeneration in rapid eye movement sleep behavior disorder.**

A large proportion of patients with idiopathic rapid eye movement sleep behavior disorder (iRBD) develop a synucleinopathy, mostly Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy. Therefore, identifying markers of neurodegeneration in iRBD could have major implications. The authors aimed to assess the usefulness of electroencephalography (EEG) spectral analysis performed during wakefulness for predicting the development of a neurodegenerative disease in iRBD. Fifty-four iRBD patients, 28 of whom developed Parkinson's disease, multiple system atrophy, or dementia with Lewy bodies (mean follow-up: 3.5 years), and 30 healthy controls underwent at baseline a resting-state waking EEG recording, neurological exam, and neuropsychological assessment. Absolute and relative spectral powers were analyzed for 5 frequency bands in frontal, central, parietal, temporal, and occipital regions. The slow-to-fast  $[(\delta + \theta)/(\beta_1 + \beta_2)]$  power ratio for each of the 5 cortical regions and the dominant occipital frequency were calculated as an index of cortical slowing. Patients who developed disease showed higher absolute delta and theta power in all 5 cortical regions compared to disease-free patients and controls. The slow-to-fast power ratio was higher in all regions in patients who developed disease than in the 2 other groups. Moreover, patients who developed disease had a slower dominant occipital frequency compared to controls. The only significant difference observed between disease-free iRBD patients and controls was higher absolute delta power in frontal and occipital regions in iRBD patients. Specific EEG abnormalities were identified during wakefulness in iRBD patients who later developed a synucleinopathy. The authors concluded that EEG slowing is a promising marker of neurodegeneration in iRBD patients.

*Neurobiol Aging*. 2015 Oct 23. pii: S0197-4580(15)00496-0. doi: 10.1016/j.neurobiolaging.2015.10.007. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/26545633>

### **Incident impulse control disorder symptoms and dopamine transporter imaging in Parkinson disease.**

The authors hoped to describe the incidence of, and clinical and neurobiological risk factors for, new-onset impulse control disorder (ICD) symptoms and related behaviors in early Parkinson disease (PD). The Parkinson's Progression Markers Initiative is an international, multicenter, prospective study of de novo patients with PD untreated at baseline and assessed annually, including serial dopamine transporter imaging (DAT-SPECT) and ICD assessment (Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease short form, QUIP). Participants were included if they screened negative on the QUIP at baseline. Kaplan-Meier curves and generalised estimating equations examined frequency and predictors of incident ICD symptoms.

Participants were seen at baseline (n=320), year 1 (n=284), year 2 (n=217) and year 3 (n=96). Estimated cumulative incident rates of ICD symptoms and related behaviors were 8% (year 1), 18% (year 2) and 25% (year 3) and increased each year in those on dopamine replacement therapy (DRT) and decreased in those not on DRT. In participants on DRT, risk factors for incident ICD symptoms were younger age (OR=0.97, p=0.05), a greater decrease in right caudate (OR=4.03, p=0.01) and mean striatal (OR=6.90, p=0.04) DAT availability over the first year, and lower right putamen (OR=0.06, p=0.01) and mean total striatal (OR=0.25, p=0.04) DAT availability at any post-baseline visit.

The authors concluded that , the rate of incident ICD symptoms increases with time and initiation of DRT in early PD. In this preliminary study, a greater decrease or lower DAT binding over time increases risk of incident ICD symptoms, conferring additional risk to those taking DRT.

*J Neurol Neurosurg Psychiatry.* 2015 Nov 3. pii: jnnp-2015-311827. doi: 10.1136/jnnp-2015-311827. [Epub ahead of print

<http://www.ncbi.nlm.nih.gov/pubmed/26534930>

### **Preladenant as an Adjunctive Therapy With Levodopa in Parkinson Disease: Two Randomized Clinical Trials and Lessons Learned.**

Preladenant is an adenosine 2A receptor antagonist that reduced "off" time in a placebo-controlled phase 2b trial in patients with Parkinson disease (PD). We sought to confirm its efficacy in phase 3 trials. The authors set out to evaluate preladenant as an adjunct to levodopa in patients with PD and motor fluctuations.

Two 12 week, phase 3, randomized, placebo-controlled, double-blind trials were performed from July 15, 2010, to April 16, 2013. The setting included neurology clinics, clinical research centers, and hospitals in the Americas, the European Union, Eastern Europe, India, and South Africa. Participants included patients with moderate to severe PD taking levodopa who were experiencing motor fluctuations. In trial 1, a total of 778 eligible patients were randomized to the addition of preladenant (2 mg, 5 mg, or 10 mg twice daily), placebo, or rasagiline mesylate (1 mg/d) in a 1:1:1:1:1 ratio. In trial 2, a total of 476 eligible patients were randomized to the addition of preladenant (2 mg or 5 mg twice daily) or placebo in a 1:1:1 ratio.

The primary outcome measure was change in off time from baseline to week 12.

In trial 1, neither preladenant nor rasagiline was superior to placebo in reducing off time from baseline to week 12. The differences vs placebo were -0.10 hour (95% CI, -0.69 to 0.46 hour) for preladenant 2 mg twice daily, -0.20 hour (95% CI, -0.75 to 0.41 hour) for preladenant 5 mg twice daily, -0.00 hour (95% CI, -0.62 to 0.53 hour) for preladenant 10 mg twice daily, and -0.30 hour (95% CI, -0.90 to 0.26 hour) for rasagiline mesylate 1 mg/d. In trial 2, preladenant was not superior to placebo in reducing off time from baseline to week 12. The differences vs placebo were -0.20 hour (95% CI, -0.72 to 0.35 hour) for preladenant 2 mg twice daily and -0.30 hour (95% CI, -0.86 to 0.21 hour) for preladenant 5 mg twice daily. Preladenant was well tolerated, with the most common adverse event that showed an increase over placebo in both trials being constipation (6%-8% for preladenant vs 1%-3% for placebo). The authors concluded that in these phase 3 trials, preladenant did not significantly reduce off time compared with placebo. That the active control rasagiline also failed to demonstrate a significant reduction in off time suggests that issues of study design or conduct may have affected these trials.

## **Committee Activities**

### **Clinical Care Committee**

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Portland PADRECC leads the committee for November/December. Committee meets via conference call the first Tuesday of the month at 12pm (EST)
- **Standardize and Optimize Clinical Care:** Continues to discuss a variety of clinical issues to improve patient care and outcomes. The committee continues to provide clinical support to the consortium network, and works on measures to standardize clinical care across the PADRECC network. Recent agenda items have included new and ongoing discussion on:
  - 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. Discussion focused on development of standardized protocol for this therapy across the PADRECC network, logistical issues, education and support aspects.
  - 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.
  - Practical aspects regarding the use of DAT scans; Applications and pitfalls, including the issue of drug interference
  - Palliative Care: Review of palliative care resources and practices in the PADRECCs
  - 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 1<sup>st</sup> audioconference for FY 2016 was held on **November 12, 2015**- "*Drugs and Movement Disorders: Truths, Myths and More,*" by Jessica Lehoist, DO-Richmond 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 16 audio conferences.

- **National Newsletter:** The **2015 VA Parkinson Report** is now available on the National PADRECC & VA Consortium Website: [www.parkinsons.va.gov](http://www.parkinsons.va.gov)
- **“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](https://www.tms.va.gov/learning/user/deeplink_redirect.jsp?linkId=ITEM_DETAILS&componentID=14771&componentTypeID=VA&revisionDate=1343926380000)

- **National Website Maintenance:** The committee will perform 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.

## **West LA PADRECC Service Area Update**

### **West LA PADRECC**

**Director: Indu Subramanian, MD**

### **SW PADRECC Welcomes New Director!**

**Dr. Indu Subramanian** is excited to transition to her new role as PADRECC Director. She has been the Clinical Director at the SW PADRECC since her fellowship in 2002. Dr. Subramanian is interested in the non-motor aspects of PD and palliative care issues in movement disorders. She is also yoga teacher certified and is designing a program for PD patients that includes yoga, breathing techniques and mindfulness. Dr. Subramanian just finished the MBSR course for the healthcare provider at the VA and hopes to get trained to teach mindfulness to Veterans. Please reach out to Dr. Subramanian if you have shared interests in palliative care and complementary approaches in PD.

### **SW PADRECC Clinical and Research Update**

The SW PADRECC provides a multi-interdisciplinary, comprehensive evaluation and management of Veterans with movement disorders including deep brain stimulation and botulinum therapy for dystonia and blepharospasm. In our effort to reach Veterans across the region, a network of eight sites are located in Southern California; Las Vegas, Nevada; New Mexico, and Arizona. Teleneurology has been established at various sites, including a new program for care of Veterans at a Californian non-VA facility. A telephone-based monthly, education and support group for Veterans with PD and caregivers is available VA-wide.

There are multiple research studies being done at various sites that include: cost analysis of DBS, detection of pre-symptomatic parkinsonism, evaluation of how PD persons make decisions which may shed information on impulse control disorders in PD, investigating novel therapies for PD and several translational projects, effects of singing on speech and swallowing, transcranial magnetic stimulation and dystonia, a nurse-led care management versus usual care, studying the cortical physiology of dystonia, studying the effect of DBS on non-movement PD symptoms; and investigating neuropathologic changes in brains of those with PD and other dementing illness.

## **Dates to Remember**

**January 14<sup>th</sup>, 2016**

**EES/PADRECC Movement Disorder Series**

Topic: Nutrition and PD

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

**February 20-March 2, 2016**

**2016 PAN Forum**

Washington, DC

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

**March 10<sup>th</sup>, 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](http://www.ann.com)

**May 12<sup>th</sup>, 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](http://www.mdsccongress2016.org)

**September 8<sup>th</sup>, 2016**

**EES/PADRECC Movement Disorders Series**

Topic: Palliative Care and PD

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

**September 20-23, 2016**

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

Portland, Oregon

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