



THE TRANSMITTER

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Article Reviews

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Slow-wave sleep and motor progression in Parkinson disease

There is little known about the effect of slow-wave sleep (SWS) and the progression of Parkinson's Disease (PD) motor symptoms. This retrospective study sought to provide evidence that SWS, or deep non-rapid eye movement (NREM) sleep, plays a role in the progression of PD motor symptoms. The study subjects were 129 people diagnosed with PD who had one-night video-polysomnography in the in-house sleep lab, which was already part of the routine diagnostic workup in their clinic for all patients with parkinsonism. The subjects also had routine follow up of their PD every 3 to 6 months over at least 2 years. The researchers determined slow-wave activity (SWA) and slow-wave energy (SWE), or accumulated SWA, using polysomnography data. They estimated motor progression of PD through analysis of total UPDRS score, axial UPDRS III (arising from chair, posture, gait, postural stability, and body bradykinesia—motor symptoms thought to be less levodopa responsive) and levodopa equivalent daily dose (LED). Increases in axial UPDRS III, total UPDRS III, and LED demonstrated a progression of motor symptoms and the increase in doses of medication over time. Their results showed that the patients with high SWE were found to have significantly slower progression of axial UPDRS III. The authors acknowledged that there were limitations with the study design, such as data variability, inter-rater variability, and not accounting for PD-related non-motor issues that can affect sleep, i.e. depression or nighttime off-time. Additionally, SWE for each patient was obtained only through one night of polysomnography data. This preliminary data shows an area of opportunity for more studies to further explore the relationship between SWS and neurodegeneration, specifically Parkinson's disease.

Ann Neurol 2019 May. 85: 765-770.

PMID: 30887557

Is lowering stimulation frequency a feasible option for subthalamic deep brain stimulation in Parkinson's disease patients with dysarthria?

Speech impairment can present after subthalamic nucleus deep brain stimulation (STN-DBS). Short-term benefit of low-frequency stimulation (LFS) for speech has been reported in the past. The objective of this study was to confirm the effect of LFS on speech in STN-DBS PD patients and investigate if the benefit of LFS could be maintained over time. In this cohort study, 10 PD patients with severe speech impairment and 10 PD patients with mild speech impairment were included. All patients were submitted to STN-DBS and were tested in all

“ON/OFF” combinations of medication and stimulation using assessments of voice, speech, and motor performance (MDS-UPDRS-III). LFS significantly improved speech, among patients with severe speech impairment in the absence of l-dopa as compared to no stimulation and high-frequency stimulation (HFS). Speech benefit was maintained with adjustment of DBS settings after six months. Five patients with severe speech impairment opted to maintain LFS after the study. The study concluded that LFS may offer both an immediate and long-lasting improvement of speech in a subgroup of STN-DBS patients with severe speech impairment during HFS. However, its effect on motor symptoms may not be preserved over time.

Parkinsonism Relat Disord. 2019 Apr 28. doi: 10.1016/j.parkreldis.2019.04.018.

<https://www.ncbi.nlm.nih.gov/pubmed/31060986>

Mapping of apparent susceptibility yields promising diagnostic separation of progressive supranuclear palsy from other causes of parkinsonism.

Differentiating Parkinson’s disease from atypical parkinsonism remains a challenge for clinicians. Structural MRI is commonly performed to obtain supporting information distinguishing these, however can be unrevealing early in the disease course. Susceptibility weighted imaging is an MRI sequence that is sensitive to iron deposition, a common feature in numerous neurodegenerative disorders. The goal of this study was to corroborate and expand on previously noted differences in characteristic susceptibility patterns between parkinsonian disorders. The researchers evaluated patients with a clinical diagnosis of Parkinson’s disease (N=134, mean disease duration 6 years), Progressive Supranuclear Palsy (PSP, N=11, mean disease duration 5.5 years), Multiple System Atrophy (MSA, N=10, mean disease duration, 4.7 years) and 44 healthy controls (HC). A 3T MRI was used to obtain SWI images, and quantitative susceptibility mapping was then performed to create maps of apparent susceptibility. Imaging analysis was blinded. ANOVA analysis was used to compare groups. ANCOVA was then used to analyze differences in susceptibility, with post hoc pairwise comparisons to determine group differences in each region of interest (ROI). Subjects with PSP had increased apparent susceptibility in the red nucleus compared to all other groups, and increased apparent susceptibility in the globus pallidus, putamen, substantia nigra, and dentate nucleus compared to PD and controls. Discriminant analysis was used between the three patient groups and the controls, using all of the ROIs to develop a classifier model. In classifying PSP v. PD, the model revealed a sensitivity of 100%, a specificity of 97%, and 97.2% of cases correctly classified. In subjects with MSA, there was higher putaminal susceptibility compared to PD and HC. There was also higher susceptibility in substantia nigra and dentate nucleus compared to PD. In classifying PSP v. MSA, the authors report a sensitivity of 90.9%, a specificity of 90%, with 90.5% of cases correctly classified. The authors conclude that “susceptibility in the deep nuclei could play a role in the diagnosis of atypical parkinsonism, especially PSP”, although further research is warranted.

Scientific Reports volume 9, Article number: 6079 (2019).

<https://www.nature.com/articles/s41598-019-42565-4.pdf>

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Philadelphia PADRECC leads the committee for May/June. 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 and discussion on obtaining baseline EKG with QTc monitoring on patients on anti-psychotics and Pimavanserin
2. Continued discussions and progress towards delivering Telehealth to our veterans using Video Connect.
3. VA Tele-Mental Health Parkinson's Disease Expert Consultation Program was developed to assist providers with managing PD patients with complex mental health diagnostic or psychopharmacological questions
4. Discussion about the use of St. Jude, Medtronic or Boston Scientific device for deep brain stimulation.
5. 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.
6. Continued discussion about referrals, outcomes and target selection trends regarding deep brain stimulation surgery for PD, ET, and dystonia.
7. 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
8. 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 (Brain Wellness Clinics)
9. Strategies to minimize the impact of reduced workforce at the PADRECC, innovative ideas to improve performance and deliver care
10. Discussion about collaborative research, including involvement in industry supported projects like Apomorphine subcutaneous infusion study
11. The prevalence of vitamin D deficiency in Parkinson's disease, the need to monitor and strategies and outcomes of current replacement strategies
12. Discussion about management of psychogenic/functional movement disorders

Education Committee

- **PADRECC/EES Movement Disorder Series:** The fourth audioconference for FY 19 was held on May 9, 2019 “**Sleep Issues in Parkinson's Disease**” by Dr. Amie Hiller, Director of Fellowship at Northwest PADRECC, Assistant Professor Oregon Health Services University. 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 audioconferences and mark your calendars.
- **Updating PADRECC Pocket Card:** Committee is in the final stages of updating the pocket card which includes the treatment algorithm and medication list as it was out of date. The pocket card will be available electronically with limited print copies available.

- **PD at Home:** Monthly PD telephone education/support group conference for patients and caregivers available nationwide on the 2nd 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.
- **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.
- **Promoting PADRECCs Nationally:** Established relationship with Patient Care Services-Communications Manager- to further promote the PADRECCS throughout VHA 10P, Patient Care Services and Neurology.
- **PADRECC is now on VA PULSE-** We invite you to follow us: <https://www.vapulse.net/community/care-topics/parkinsons-disease/overview>

On this page you can view notices of upcoming Movement Disorders Series presentations, links to all recorded webinars and our 20-video VA Parkinson's playlist on YouTube. Also available are a wealth of resources for VA Professionals and Veterans/families, research publications, informational newsletters, and more.

- **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 link and complete the **Resource Request Form** and mail or fax to address listed:
<https://www.parkinsons.va.gov/clinicians.asp>

Philadelphia PADRECC Service Area Updates

Philadelphia PADRECC

Corporal Michael J. Crescenz VAMC

Director: John Duda, MD

Clinical Update

- **Expansion of Telehealth**

- **Telemental Health:** Psychiatric symptoms in patients with PD have a large impact on quality of life. Managing these symptoms can be difficult and should be managed by a subject matter expert. Luckily, Philadelphia PADRECC has such an expert who is sharing his expertise with other VA Medical Centers. Dr. Dan Weintraub in collaboration with the National Telemental Health Center is providing psychiatric consult services via telehealth to the Bronx, White Plains, Northport, New Mexico, and San Diego VAMCs for patients with Parkinson's disease (PD) and psychiatric symptoms. Both providers and Veterans are happy with the service and Dr. Weintraub is in the process of expanding the service to other VAMCs.
- The Philadelphia PADRECC currently provides telehealth services to 7 VA Medical Centers and 16 CBOCs within VISN's 2 and 4 and this year added the Delaware Valley Veteran State Home to the list. Telehealth is used to provide consultative services, follow up care, DBS stimulation adjustments, and medication management. *VA Video Connect* into the home is a modality used to reach Veterans who find traveling to a VAMC or a CBOC too difficult and is a great tool for clinicians to follow up on the most vulnerable Veterans.

- **Brain Wellness Clinic**

The Brain Wellness Clinic developed by Dr. John Duda and Heidi Watson, BSN, RN in 2016 is still thriving at the Philadelphia PADRECC. This clinic provides patients the opportunity to focus in-depth on brain wellness. Current brain wellness risks are assessed and explored by looking at different lifestyle factors including sleep, nutrition, exercise, mindfulness/spiritual, cognitive and social interaction. During the visit, a thorough interview, several short written or web-based assessment of patients health status, and lab work (if appropriate) are completed. Clinicians discuss wellness goals important to the patient and together develop an individualized plan with realistic and achievable goals, and provide support to implement them. Patients' progress is followed either in person or through telehealth.

- **Staff Update**

Eileen Hummel, MSN, CRNP: Eileen Hummel-PADRECC Clinical Nurse Coordinator completed her Master of Science in Nursing program and is now a licensed Nurse Practitioner! Eileen will function in the role of a Nurse Practitioner in The Philadelphia PADRECC and will continue to collaborate with the Attending Neurologists.

Education Update

- **11th PADRECC/MIRECC Symposium on Neurodegenerative Diseases:**

The Philadelphia PADRECC in collaboration with the Philadelphia MIRECC hosted this CME program on **March 29, 2019** to continue the practice of delivering an informative symposium for clinicians and clinical researchers. Movement disorders represent a key intersection of psychiatry and neurology, with psychiatric and cognitive disorders common in disorders such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB), and movement disorders common in patients with primary psychiatric disorders treated with psychotropic medications. Both psychiatric and cognitive disorders in PD and DLB remain under-recognized and under-treated in routine clinical care, which represents a major unmet need in terms of long-term outcomes, quality of life and caregiver burden. This symposium provided an update on key psychiatric and cognitive disorders in PD and DLB, as well as medication-induced movement disorders in psychiatric patients. Information imparted in this symposium will improve clinicians' abilities to identify and manage

complex neurological and psychiatric disorders. The target audience for this symposium was physicians, nurses, psychologists, social workers and other healthcare professionals providing care to patients with Parkinson's disease, dementia, and psychiatric disorders. There were approximately 92 VA and Non-VA healthcare professionals who attended this symposium

- **Veterans Empowered Through Art: The Six Week Selfie Project**

On April 24, 2019, the Corporal Michael J. Crescenz VAMC presented *Veterans Empowered Through Art: The Six Week Selfie Project*, an exhibit by the Philadelphia Museum of Art in partnership with the Veterans Empowerment Center and the Philadelphia VA Parkinson's Disease Research, Education and Clinical Center (PADRECC). This exhibit chronicled the work of 18 Veterans who were part of *The Six Week Selfie Project*, a class where students explored artistic expression through tours of the museum as well as workshops in visual arts and writing. Highlights of the exhibition included preliminary portraits with no instruction, completed self portraits done in about 12 hours, samples of creative writing and poetry, and personal photos of the Veterans during their time of service. There was also a video presentation where participants talked about their experience as well as a live presentation of a group poem and a personal poem. Nine PADRECC Veterans participated in this exhibition. The art work will be on display in the Crescenz VA Medical Center Auditorium for the month of May. Efforts are underway to have the PADRECC self-portraits moved to the clinic waiting area indefinitely.

- **April PD Awareness Month Activities**

The Philadelphia PADRECC participated in several patient and professional education/outreach programs during the month of April to continue to raise awareness of PD and the PADRECC program both in the VA and the community.

- Dr. Duda presented at the Crescenz VAMC Medical Grand Rounds on April 8, 2019-**Differential Diagnosis and Assessment of Mild Parkinsonism**
- Display in the PADRECC waiting area promoting April as PD Awareness Month and highlighting PD educational materials and both PADRECC and community PD programs available to Veterans and families
- PD Awareness table set up in the Crescenz VAMC Canteen on 4/17/19 providing PADRECC educational materials to Veterans
- Attended a PD Health Fair at a local community medical center sharing PADRECC educational materials.
- E-blast included in Crescenz VAMC Weekly Pulse electronic newsletter acknowledging April as PD Awareness Month and reminding staff of the PADRECC program.

- **Walk to Stamp Out Parkinson's**

Last October, members of the Philadelphia PADRECC Team and their families joined the local Parkinson's community in **The Parkinson's Council's: Walk to Stamp out Parkinson's**. The walk was held at The Philadelphia Zoo and was a fun day had by all raising awareness for Parkinson's disease. We are excited to walk again this October!

Research Update

- **Exercise and Parkinson’s Disease**

Dr. Morley is conducting a study supported by the VA Rehabilitation R&D service to study exercise as a therapy to improve symptoms and, potentially, slow disease progression in PD. Patients with early PD are randomized to exercise or control groups. The exercise group is asked to perform aerobic walking up to 5 times per week. Effects on motor symptoms and cardiovascular fitness are tested after 8 and 52 weeks while brain scans to measure PD progression are measured at baseline and after 52 weeks. This study will continue to recruit new patients through the end of 2020.

Dr. Sneha Mantri, former PADRECC Movement Disorders Fellow, and Dr. James Morley continue to study physical activity habits and attitudes about exercise of people with Parkinson’s disease (PD). Participants were asked to complete a series of questionnaires to assess exercise and activity habits, attitudes about exercise, sleep, mood, memory, and other symptoms. Interim analysis of the first sixty participants shows that one in five meet American Heart Association recommended physical activity (20-30 minutes of moderate to vigorous activity, 2-3 times per week). Active Veterans score higher on cognitive tests, have fewer PD-related symptoms, and enjoy a better quality of life. By understanding a veteran’s physical activity habits, we can better design an exercise program that meets their needs to remain physically active. An extension of this study is examining the use of wearable technologies (Fitbit) to measure and improve physical activity levels in PD patients

- **Medication-Induced Parkinsonism**

Dr. Morley is conducting studies to understand how Parkinson’s-like symptoms caused by medications are related to PD. Symptoms of PD can be mimicked by certain medicines that block dopamine—the major brain chemical missing in PD. Not everyone’s symptoms improve after the medicines are switched or stopped, so it is possible that the medicines uncover very early PD in some cases. Dr. Morley’s team is comparing medication-exposed patients with and without Parkinson’s symptoms using questionnaires, physical exam, blood tests and a brain scan in addition to following patients with symptoms after the medication is switched or stopped. Initial analyses published recently demonstrated that more than 20% of patients with drug-induced symptoms actually had underlying PD or a related disorder that was “unmasked” by the dopamine blocking drugs. Loss of the sense of smell (as is seen in most PD patients) was the strongest predictor of an abnormal brain scan. Appearance of PD-like symptoms after treatment with a low dose of antipsychotic medication also predicted an abnormal scan suggesting that dopamine blocking drugs can act like a “stress test” for the brain.

- **The Immune System and Parkinson’s Disease**

Dr. Morley and the PADRECC are collaborating with a local biotech company (Longevity Biotech) on a project recently funded by the Michael J. Fox Foundation to study whether the immune system plays a role in PD. The team will recruit *pairs of patients and their caregivers* to study whether immune cells and other blood markers are different in PD and are associated with disease severity or other PD characteristics. This study has recruited 40% of its goal and will continue enrolling through the end of 2019

- **Bacteria and Parkinson’s Disease**

Dr. Duda, in collaboration with Dr. Noam Cohen from the Ear Nose and Throat Department, continue to study how bacteria that colonize our body might contribute to the risk of Parkinson's disease. It has been shown that these bacteria are different in people with Parkinson's disease compared to people without

Parkinson's disease. This study is trying to understand if there are genetic reasons why some people have certain types of bacteria in the hopes of developing new therapies in the future. Preliminary results confirm prior studies showing that participants with Parkinson's disease were more likely to be non-tasters of bitter compounds compared to participants without Parkinson's disease. Once recruitment is complete, they will examine differences in the genetics of the taste receptors and in the bacteria of the nose and gut between those with Parkinson's disease and those without.

- **Traumatic Brain Injury**

Dr. Duda and his colleagues, Drs. Kacy Cullen, Isaac Chen and John Wolf, from the Department of Neurosurgery at the University of Pennsylvania, continue studies funded by the Rehabilitation Research and Development Service of the Department of Veterans Affairs to study the relationship between brain trauma and neurodegeneration. The researchers have published several studies that have shown how the brain reacts to trauma and how that could possibly lead to chronic neurodegenerative disease development. It is hoped that these studies will lead to treatments to prevent the development of these neurodegenerative diseases in Veterans and others who have suffered head injuries.

- **Neurorestoration in Parkinson's Disease**

Dr. Duda and his colleagues Dr. Kacy Cullen and Isaac Chen from the Center for Neurotrauma, Neurodegeneration, and Restoration (CNNR) at the Crescenz VA Medical Center, continue to investigate whether one of the main brain pathways affected in Parkinson's disease, the nigrostriatal pathway, can be generated in a petri dish and transplanted in animal models to reverse the motor symptoms in PD. The success of their efforts to date have led to several publications and special recognition at several different scientific meetings and additional research grants to continue these studies. The team has been successful in implanting these bioengineered pathways into a rat model of PD and are now funded to do the same in pigs, which more closely resemble what would need to be achieved to begin trying this approach in humans.

Dates to Remember

June 2-7, 2019

5th World Parkinson Congress

Kyoto, Japan

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

September 12, 2019

EES/PADRECC Movement Disorders Series

Topic: Parkinson's 101

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

September 22-26, 2019

International Parkinson and Movement Disorder Society Congress

Nice, France

<https://www.movementdisorders.org/MDS/All-Congress-Sites.htm>