



THE TRANSMITTER

May 2017

Article Reviews

Prepared by: Dr. Sneha Mantri, MD, MS & Dr. Delaram Safarpour, MD, MSCE~Philadelphia PADRECC

Evaluating the performance of the Montreal Cognitive Assessment in early stage Parkinson's disease.

Cognitive dysfunction is common in PD; up to 20% of patients manifest PD-MCI at the time of diagnosis, and up to 80% of PD patients will go on to develop dementia over time. The Montreal Cognitive Assessment (MoCA) is commonly used to assess cognitive function and has been shown to be both sensitive and specific to the range of cognitive difficulties affecting PD patients. However, the validity and difficulty level of individual questions are not well understood. This study was a Rasch analysis of the MoCA to assess construct validity, unidimensionality, and differential item functioning with prespecified covariates (gender, age, education, depression, and medication use), which have been shown to impact performance in other populations. The authors queried the PPMI cohort for baseline and follow-up MoCA scores, as well as demographic variables, functional status, and several motor scales (e.g. motor UPDRS subscore, Hoehn and Yahr stage). They found that the most difficult MoCA items were word recall (52-74% correct answers), and that the easiest items were orientation and confrontational naming (99% correct answers). There was a large ceiling effect, with 11% of assessments achieving a perfect score. Subgroups did perform differentially on individual items (e.g. women performed better on calculation and visuospatial function while men performed better on delayed recall) but overall scores were not different between groups. The authors conclude that while the MoCA remains a valid screening test for cognitive impairment in PD, it may not be complex enough for early-stage PD. They suggest replacing some of the easiest items in this cohort with more challenging items, or developing an adaptive approach to cognitive screening that can more accurately and efficiently assess a patient's global cognitive function.

Kletzel et al. *Parkinsonism and Related Disorders* 37 (2017) 58-64.

The influence of vascular risk factors on cognitive function in early Parkinson's disease.

Previous studies have shown the impact of hypertension, dyslipidemia, diabetes, and obesity on cognitive impairment and dementia in older adults. This study aimed to assess the effect of these risk factors on cognitive function in patients with Parkinson Disease (PD). A total of 367 untreated and non-demented patients aged 50 years and older with early PD (measured by Hohn and Yahr, a scale commonly used in research and clinical practice for assessment of motor function in PD) underwent a comprehensive clinical and neuropsychological assessment at baseline and 24 months later. A longer history of hypertension and a higher pulse pressure were significant predictors of lower scores on immediate and delayed free recall, recognition, and verbal fluency tests. The effects were independent of age, education, disease duration, motor impairment, medication, and depressive symptoms. On average, every 10 mmHg increase in pulse pressure was associated with a 0.08 reduction on the cognitive function after 24 months. Researchers concluded that hypertension exerts an important effect on memory and verbal fluency in early PD and therefore, management of blood pressure and cardiovascular risk factors including use of medications and routine exercise may reduce risk of cognitive decline in PD.

<https://www.ncbi.nlm.nih.gov/pubmed/28509343>

Rotigotine Effects on Bladder Function in Patients with Parkinson's Disease

Urinary disturbances, such as urgency, are present in two-thirds of patients with Parkinson's disease (PD) and cause disability that is typically not responsive to dopaminergic replacement therapy with carbidopa/levodopa. Previous studies have shown over activity of the bladder smooth muscle that leads to irritative symptoms like urinary frequency. This study examined 20 patients with diagnosis of PD (who were not on dopaminergic therapy) and had urinary symptoms (day/night time frequency) were started on Rotigotine patch. All subjects reported subjective urinary symptoms and underwent urodynamic evaluation prior to treatment and after three months of treatment with rotigotine patch. Rotigotine improved sensation of bladder filling and increased bladder contraction threshold and capacity. Patients also reported decreased irritative sense of filling after treatment with rotigotine. The researchers concluded that Rotigotine patch can improve lower urinary tract symptoms along with motor symptoms in Parkinson disease perhaps owing to rotigotine's action at D1 receptors in the anterior cingulate cortex and insula, which regulate bladder function.

Movement Disorders Clinical Practice, 19 April 2017, e-pub ahead of print

<http://onlinelibrary.wiley.com/doi/10.1002/mdc3.12488/full>

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 April/May. 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. The management of orthostatic hypotension including the role of the newly FDA-approved agent droxidopa (Northera).
 2. 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
 3. The prevalence of vitamin D deficiency in Parkinson's disease and the need to monitor and adequately replete levels for bone and cognitive health.
 4. Practical aspects regarding the use of DAT scans; applications and pitfalls, including the issue of drug interference
 5. Continued discussion on the use of Pimavaserin (Nuplazid) in the treatment of psychosis associated with PD, compared to quetiapine and clozaril.

6. Continued discussion of Rytary and conversion and titration dosing strategies. Consensus that often more than a three times/day dosing is needed.
7. Discussion of the possible role for levodopa-induced hyperhomocystinemia in Parkinson's disease and the strategies to monitor and manage this problem

Education Committee

- **PADRECC/EES Movement Disorder Series:** The 4th audioconference for FY 17 was held on **May 11, 2017** "*Creativity and Parkinson's Disease*" by Dr. Michele York, PhD, ABPP-CN, Houston 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 17 audioconferences and mark your calendars.
- **National Newsletter:** Currently accepting articles for the **2017 VA Parkinson Report**. Articles should preferably cover, one or more of the following:
 1. Latest Research (Clinical or basic science) pertaining to PD
 2. Rehabilitation strategies pertaining to PD
 3. Discussion regarding management of certain clinical aspects of PD
 4. New diagnostic tools pertaining to movement disorders

Any other interesting topics can be considered, if discussed in advance. Contributors should review the previous VA Reports and avoid duplicating the topics covered in the last 2 years (unless it is an update). Previous newsletter can be found at: <https://www.parkinsons.va.gov/Consortium/Newsletter.asp>

If you are interested in submitting an article for the newsletter please email Glennys Asselin-Cavey (Glennys.Asselin@va.gov) and Suzanne Moore (Suzanne.Moore@va.gov).

Deadline for submission has been extended to **June 1st, 2017**

- **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.
- **“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 available on TMS:

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

*Please note CME credit will no longer be available as of **July 30, 2017**

- **PADRECC Transmitter:** This committee continues to assemble and distribute this e-newsletter every other month.

Dates to Remember

June 4-8, 2017

21st International Congress of Parkinson's Disease and Movement Disorders

Vancouver, BC

<http://www.mdscongress2017.org/Congress-2017.htm>

September 14, 2017

EES/PADRECC Movement Disorders Series

Topic: Cognition and Exercise

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

Philadelphia PADRECC Service Area Updates

Philadelphia PADRECC

Corporal Michael J. Crescenz VAMC

Director: John Duda, MD

- **Brain Wellness Clinic**

This innovative clinic was developed by Dr. John Duda and Heidi Watson, BSN, RN in 2016 and 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.

- **Exercise As Medicine-Patient Education Program**

This program was held on **April 24, 2017** to educate attendees about the benefits of exercise in treating Parkinson's disease. In a 3 hour program, participants were provided with practical information on the benefits of exercise in treating PD as well as an opportunity to try out different types of exercises shown to be beneficial to the PD population such as Tai Chi, Yoga, Rock Steady Boxing and LSVT BIG. It was a fun morning that got participants moving and realizing exercise can be enjoyable as well as beneficial.

- **10th PADRECC/MIRECC Symposium on Neurodegenerative Diseases:**

Preclinical and Prodromal Stages of Neurodegenerative and Neurodevelopmental Disorders

The Philadelphia PADRECC in collaboration with the Philadelphia MIRECC hosted this CME program to continue the practice of delivering an informative symposium for clinicians and clinical researchers. With the development and testing of disease-modifying therapies, as opposed to purely symptomatic therapies, the need to identify patients with neurodegenerative diseases as early as possible becomes increasingly

important, as early identification and treatment with such therapies has the potential to prevent or delay onset of these diseases (such as Alzheimer's disease, Parkinson's disease, dementia with Lewy bodies, frontotemporal dementia, and schizophrenia). This symposium focused on cutting edge, ongoing research to identify patients at-risk (pre-clinical) or manifesting early signs of disease (prodromal). The results of these research studies have the potential to dramatically alter how clinicians screen and manage patients in the general population at increased risk for these disease.

- **Duopa Therapy**

The Philadelphia PADRECC, in partnership with the local VA Gastroenterology department, developed a local standard operating procedure for the initiation of Duopa therapy. Philadelphia was the first VA in the country to start Duopa on site. To date, two Veteran patients have started the treatment at the Philadelphia PADRECC.

- **Current Research**

- ❖ **Drug-induced Parkinsonism (DIP): A canary in the coal mine?**

DIP associated with dopamine receptor blocking drugs (most often antipsychotics) is the second most common cause of Parkinsonism and can be clinically indistinguishable from PD. In some cases, when symptoms persist after drug withdrawal, DIP may represent “unmasking” of prodromal PD-with the offending drugs acting as a “stress test” for dopaminergic pathways.

We previously reported that olfactory impairment (a non-motor feature that often precedes motor symptoms of PD) was more common in patients with persistent DIP (Morley *et al. Park Rel Dis*, 2015). Dr. Morley received a VISN 4 Pilot Award to study the relationship of DIP to PD using DAT-SPECT, olfactory testing and other biomarkers of PD. As part of that study, we have reviewed DAT-SPECT studies for 33 subjects with suspected DIP. DAT-SPECT was abnormal in 7/33 (21%) of suspected DIP cases. Objective olfactory testing was available for 30 subjects and was concordant with the DAT-SPECT result in 27/30 (Odds Ratio=63, 95% CI 4.8-820). Subjects with abnormal scans also had higher scores on the validated PD Non-Motor Symptom Questionnaire. Additionally, subjects with abnormal scans were, on average, treated with lower dose/potency antipsychotics suggesting that the appearance of Parkinsonism with low-intensity dopamine blockers may raise concern for underlying neurodegeneration. This study was recently published in *Movement Disorders: Clinical Practice* and we are continuing to study the relationship between DIP and underlying PD.

- ❖ **Exercise in PD**

Identifying early or prodromal PD that has been “unmasked” by DIP offers opportunities for intervention at the earliest stages of disease. Exercise is known to improve symptoms in PD and some evidence suggests aerobic exercise could influence disease progression. In 2016, Dr. Morley received a VA Rehabilitation R&D service Career Development Award entitled “**Effect of exercise on recovery in drug-induced Parkinsonism and Parkinson disease.**” In this study, subjects with suspected DIP who also have abnormal DAT-SPECT are randomized to exercise (aerobic walking) or no intervention. We are examining the short term effects of exercise using the UPDRS and quantitative gait testing after 8 weeks. A potential disease modifying effect of exercise will be assessed using serial DAT-SPECT and biochemical markers after 52 weeks. We will continue to recruit for this study over the next 3 years and plan to eventually expand this intervention into the wider population of patients with early PD.

If exercise can benefit our PD patients, how can we make sure they are getting enough? Dr. Sneha Mantri, PADRECC fellow, is conducting a study to better understand exercise and activity levels in PD. She is examining PD patients’ attitudes and barriers to exercise and comparing them to activity levels using both a self-reported survey and objective monitoring in the community using wearable devices. Dr. Mantri hopes to use this information to identify potential interventions to increase exercise and activity levels in PD patients.

❖ **Balance and Parkinson's Disease**

Dr. Delaram Safarpour, PADRECC Movement Disorders Fellow, and Dr. James Morley, are studying whether a balance vest, Balance Based Torso Weighting (BBTW), can improve walking and balance in patients with PD and related conditions. The weighted vest has been shown to improve walking and balance in patients with other neurological conditions, but it is unknown whether the vest could help patients with PD. Dr. Safarpour is using a sham-controlled randomized crossover design to test the effect of BBTW on walking as measured by clinical impression and quantitative gait and balance assessments. It is hoped that the BBTW can offer a non-pharmacological approach for improvement of balance and walking in this population of patients.

❖ **Traumatic Brain Injury**

Dr. John Duda, PADRECC Director, and his colleagues, Drs. Kacy Cullen 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 develop animal models of Chronic Traumatic Encephalopathy (CTE) that sometimes develops years later in people such as football players and war fighters who have had traumatic brain injuries. The goal of these studies is to develop models of these changes in the brains of animals so that novel treatments and preventive strategies can be tested. It is hoped that these studies will lead to treatments to prevent the development of these neuro-degenerative diseases in Veterans and others who have suffered head injuries.

❖ **Neurorestoration in Parkinson's disease and other causes of Brain Injury**

Drs. Cullen, Duda and Wolf were awarded a two-year grant from the Michael J. Fox Foundation for Parkinson's Research to investigate experimental reconstitution of the nigrostriatal pathway (the pathway that degenerates in PD and causes the motor symptoms) in animal models of PD in a grant entitled, '**Restoring the nigrostriatal pathway with living micro-tissue engineered axonal tracts**'. This project involves growing cellular constructs in culture, comprised of dopaminergic neurons and the long axonal projections necessary to recapitulate the nigrostriatal pathway. These constructs will then be transplanted into animals that have had lesions of the nigrostriatal pathway to see if these cells can functionally replace the damaged cells. In addition, Dr. Isaac Chen, who is also from the department of Neurosurgery at the University of Pennsylvania and is mentored by Dr. Duda, was recently awarded a Career Development Award from the Rehabilitation R&D Service to try to grow complete cortical structures in culture and transplant them into animal models. It is hoped the lessons learned from all of these studies will one day lead to breakthroughs in our ability to restore function in Veterans suffering from many disorders that affect the brain.

❖ **Bacteria and Parkinson's Disease**

Dr. Michelle Fullard and 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.

West Haven, CT

VA Connecticut Healthcare System-West Haven Campus

Director: Diana Richardson, MD

The West Haven Parkinson's Disease Consortium remains active in promoting good health, well-being and fitness for our Veteran patient with Parkinson's disease. Currently we in our 9th year of offering an annual **PD Lecture & Support series**. This year we have added boxing workshops to a mixed program of Wii Sport Fitness, Dance, Yoga and Music therapy. This spring we have launched an Agent Orange Information Research and Education (AO-IRE) support group which has been well attended. In the Fall we are working to expand the AO-IRE group to VISN wide tele-conferencing or audio-conferencing. Lastly, April's celebration of Parkinson Awareness was marked several Special events. The **Annual Parkinson Fair** provided opportunity to distribute educational materials and to discuss nutrition, pharmacy, physical therapy, occupational therapy, neurology and speech pathology with specialist in an open format style. The **2017 Parkinson's Disease Symposium** which focused on Dysautonomia in Parkinson Disease included formal lectures from Cardiology, Speech Pathology and Urology. And, team representation at the **Parkinson's Unity Walk** held in NYC central Park.