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**NATIONAL VA PARKINSON'S DISEASE
CONSORTIUM**
Education · Collaboration · Advocacy

THE TRANSMITTER

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Article Reviews

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Closed-loop programming using external responses for deep brain stimulation in Parkinson's disease

This single center, randomized, double blind crossover study assessed whether an external motion sensor can be used to guide DBS programming in a 'closed-loop' algorithmic fashion. The authors recruited 12 patients who had DBS implantation at least 6 months prior, and who had demonstrated at least 30% improvement in UPDRS Part 3 with DBS programming during routine clinical care. Participants were assessed in the medication OFF state without DBS and after programming with standard and closed loop algorithmic approaches. Standard programming was a monopolar review with pulse width(PW) of 60us and frequency 130 Hz, where the stimulation was gradually increased to determine therapeutic window and the best stimulation contact and amplitude was selected, with the option to adjust pulse width or frequency if satisfactory benefit was not achieved. Closed loop programming was conducted using an algorithm which initially explored the amplitude and contact numbers available, and then gradually focused on the areas leading to the better clinical scores. PW and frequency were fixed. The clinician only changed the stimulation as suggested by the algorithm and evaluated for side effects but did not guide parameter selection. The authors report that both standard and closed loop algorithmic programming improved motor function similarly: Median UPDRS-3 with DBS off was 37.5, after standard programming was 22.0 ($p=0.006$ vs baseline) and after algorithmic programming was 23.5 ($p=0.006$ vs baseline, $p=0.30$ vs SOC). Closed loop algorithmic programming required fewer programming steps than standard programming (20.5 vs 55.5, $p<0.0001$). Limitations include small sample size, use of DBS system by a single manufacturer, lack of use of PW and frequency in the algorithm, and assessment after only short duration on selected DBS settings. This small study demonstrates the feasibility of the use of external biometric sensors and algorithmic approaches in DBS programming and suggests that similar clinical benefit may be achieved with shorter programming time.

Sasaki F, Oyama G, Sekimoto S, et al. Closed-loop programming using external responses for deep brain stimulation in Parkinson's disease. *Park Relat Disord.* 2021;84(March):47-51.

doi:10.1016/j.parkreldis.2021.01.023

Fracture Risk Assessment in Atypical Parkinsonian Syndromes

The authors of this study recognize the high risk of falls and fractures among patients with atypical parkinsonism (AP), but note that there is relatively little in the way of evidence-based recommendations

regarding management of bone health in this patient population. In Parkinson's Disease (PD), however, there is guidance suggesting the use of the QFracture to assess the ten-year risk of major osteoporotic fracture as a means to trigger empirical bone protection treatment. This study sought to evaluate the use of this scale in the AP population to evaluate outcome and management decisions as compared to the PD population. They did this as a cross-sectional study where they recruited both PD and AP patients, collecting information about ongoing treatment for bone health (calcium, vitamin, bisphosphonates, denosumab) and calculated their 10 year fracture risk using QFracture and FRAX. They were able to recruit 71 patients with AP and 267 with PD. Patients with AP were more likely to have fallen in the last year. QFracture and FRAX scores were similar between the two groups for patients more than 70 years old, but AP patients less than 70 years old had higher scores compared to the PD population. For management, 54 (76%) of AP vs 167 (63%) of PD patients met criteria for bone-sparing treatment. There was no significant difference in treatment between the groups except for a higher percentage (56.3% vs 38.2%) of AP patients on calcium supplementation. There were 18 (33% of those indicated) on oral bisphosphonates in the AP group. Ultimately the researchers conclude that the main difference between the two populations was the higher fall incidence amongst patients with AP and higher predicted fracture risk for younger patients. Based on this they recommend early screening for fracture risk and increased efforts to ensure patients are prescribed appropriate bone sparing treatments with positive screening.

Kobylecki C, Glasse H, Amin J, Gregson C, Lyell V, Henderson E. Fracture risk assessment in atypical parkinsonism syndromes. *Movement Disorders Clinical Practice*. 2021; 8 (3): 385-389.

Parkinson Disease–Related Brain Metabolic Patterns and Neurodegeneration in Isolated REM Sleep Behavior Disorder

It has been shown that 74-91% of the patients with iRBD convert to Lewy body disease within 15 years after symptom onset. Therefore, iRBD patients are a good candidate for disease-modifying treatment.

In Parkinson's disease (PD), brain metabolic covariance pattern is characterized by increased activity in globus pallidus, thalamus, pons and reduced activity in premotor and posterior parietal area. This can differentiate parkinsonian subjects from healthy controls. Currently, there are three major PD-related metabolic patterns derived: PD-RP, derived from long-standing PD patients with chronic levodopa therapy regardless of having RBD symptoms; dPD-RP, from drug naïve PD patients; and the dnPDRBD-RP, from de novo PD patients with prolonged RBD symptoms preceding parkinsonism.

This study aimed to elucidate the role of PD-related brain metabolic patterns as a potential biomarker in iRBD for future disease conversion. It is a prospective cohort study consisting of 100 subjects divided into four age-matched groups of 30 iRBD patients, 25 de novo PD patients with a premorbid history of RBD, 21 long-standing PD patients on stable treatment and 24 healthy controls. iRBD group was longitudinally followed up at 3-month intervals over a mean of 3 years. All participants were evaluated with olfaction, cognition and MDS-UPDRS at baseline, and underwent FDG-PET scans. From these, the authors derived metabolic patterns from the long-standing PD group (PD-RP) and de novo PD group with RBD (dnPDRBD-RP), and calculated the PD-RP and dnPDRBD-RP scores in iRBD patients. A separate cohort of 14 iRBD patients were also included in this study to validate brain metabolic patterns.

From the iRBD group (n=44), 12 patients converted to neurodegenerative disease during the follow-up (7 PD, 1 MSA and 4 DLB). Both PD-RP and dnPDRBD-RP and scores at baseline were significantly higher in disease converters than non-converters, with baseline dnPDRBD-RP show higher discriminability of future converters than PD-R. MDS-UPDRS scores were significantly correlated with PD-RP, while dnPDRBD-RP was significantly correlated with olfactory function.

Overall, the authors concluded that dnPDRBD-RP better reflects prodromal clinical features of PD and better predicts future phenoconversion in iRBD, and therefore, can be an efficient biomarker individually applicable in iRBD.

Jung Hwan Shin, Jee-Young Lee, Yu-Kyeong Kim, Eun Jin Yoon, Heejung Kim, Hyunwoo Nam, Beomseok Jeon. Parkinson Disease–Related Brain Metabolic Patterns and Neurodegeneration in Isolated REM Sleep Behavior Disorder. *Neurology* May 2021, 10.1212/WNL.0000000000012228; DOI: 10.1212/WNL.0000000000012228

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. Discussion regarding COVID 19 pandemic-clinical challenges and solutions.
 2. Exploring the **VA Annie App** and ways it can be used with PADRECC patients, i.e. medication and exercise reminders, monitor blood pressure etc. <https://mobile.va.gov/app/annie-app-veterans>
 3. Discussion regarding genetic testing for PD patients and how this is ordered: genetic clinic at local VA vs. Parkinson’s Foundation PD GENERation
 4. Updates on clinical experience with newer medications – Nourianz (Adenosine Receptor antagonist), Gocovri and Imbrija Inhaler
 5. Clinical experience with newer DBS systems including Boston Scientific’s “Vercise” and Abbott’s “ St. Jude Medical Infinity DBS”.
 6. CSP # 2015 Trial, planning and trial initiation related matters.

Education Committee

- **PADRECC/EES Movement Disorder Series-Webinar:** The 5th webinar for FY 21 was held on May 13th, 2021: “*Update on Deep Brain Stimulation in PD: Trends in Candidacy & New Technology*”

presented by Dr. Nicolas Galifianakis, San Francisco PADRECC. Please check the **Dates to Remember** section for upcoming webinars.

- **National VA PD Newsletter:** Currently accepting articles and updates for the **2021 VA Parkinson Report**. Articles should preferably cover, one or more of the following:
 - Highlight-current research (clinical or basic science) pertaining to PD
 - Rehabilitation strategies pertaining to PD
 - Treatment and management of certain clinical aspects of PD
 - New diagnostic tools pertaining to movement disorders
 - National VA Consortium Centers at a Glance- brief Consortium Center updates (clinic, research, education activities in the last year)

All articles and updates should be **double spaced, Times New Roman, 11 pt font**. Please send pictures as well. If you are interested in submitting an article for the newsletter please email Gretchen.Glenn@va.gov your topic by **June 4th**. **Deadline for final submission: July 23rd**

- **VHA/PADRECC & The Parkinson's Foundation Partnership:** Goal of the partnership is to improve the care and quality of life for Veterans living with PD through collaborative education, research and services. We are now one year into the partnership and much of the foundational work has been done. This committee continues to spearhead many of the projects for this partnership.
- **National Website Maintenance:** The committee performs periodic 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:**
 - **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 (*recently updated*)
 - **PADRECC Support/Education Groups:** The PADRECCs are now holding virtual groups open to Veterans and care partners interested in attending. Please check out the National Website for listing of dates/times and contact person to register for the groups and please share with your patients/care partners: <https://www.parkinsons.va.gov/patients.asp>
 - **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** (*recently updated*)
<https://www.parkinsons.va.gov/patients.asp>
 - **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 fax or email to address listed:

<https://www.parkinsons.va.gov/clinicians.asp>

- **PADRECC Pocket Card:** *Parkinson's Disease Quick Reference Guide for Imitating Therapy* is available on the National Website:

<https://www.parkinsons.va.gov/Consortium/PocketCard/PocketCard19.pdf>

Dates to Remember

September 9, 2021

EES/PADRECC Movement Disorders Series-Webinar

Topic: Military Exposures & Movement Disorders

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

September 17 - 22, 2021

International Parkinson's and Movement Disorder Society

Location: Virtual

<https://www.mdscongress.org/Congress-2021.htm>