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

THE TRANSMITTER

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Article Reviews

Prepared by: Fariha Jamal, MD & George Jackson, MD, PhD ~ Houston PADRECC

Long-term Outcomes (15 Years) After Subthalamic Nucleus Deep Brain Stimulation in Patients With Parkinson Disease

In patients with advanced Parkinson disease (PD), deep brain stimulation of the subthalamic nucleus (STN-DBS) is a well-recognized effective treatment in both short- and long-term follow up. The improvement of several motor and non-motor signs has been reported up to 11 years after STN-DBS. Outcomes beyond first decade after surgery are largely missing. The overall objective of this study was to evaluate the effects of STN-DBS beyond 15 years after surgery, mainly focusing on PD motor complications changes. Moro et al. retrospectively retrieved data on motor complications, quality of life, activities of daily living, Unified Parkinson's Disease Rating Scale motor scores, dopaminergic treatment, stimulation measures, and side effects of STN-DBS and compared before surgery, at 1 year, and beyond 15 years after bilateral STN-DBS. Fifty-one patients with 17.06 ± 2.18 years STN-DBS follow-up were recruited. Compared to baseline, the time spent with dyskinesia and the time spent in the "off" state was reduced by 75% ($p < 0.001$) and by 58.7% ($p < 0.001$), respectively. Moreover, dopaminergic drugs were reduced by 50.6% ($p < 0.001$). Parkinson's Disease Quality of Life Questionnaire total score and the emotional function and social function domains improved 13.8% ($p = 0.005$), 13.6% ($p= 0.01$), and 29.9% ($p < 0.001$), respectively. Few and mostly manageable device-related adverse events were observed during the follow-up. The authors concluded that STN-DBS is effective beyond 15 years from the intervention, notably with significant improvement in motor complications and stable reduction of dopaminergic drugs. Furthermore, despite the natural continuous progression of PD with worsening of levodopa-resistant motor and nonmotor symptoms over the years, patients undergoing STN-DBS could maintain an improvement in QoL. This study provides Class IV evidence that, for patients with PD, STN-DBS remains effective at treating motor complications 15 years after surgery.

Bove F, Mulas D, Cavallieri F, Castrioto A, Chabardès S, Meoni S, Schmitt E, Bichon A, Di Stasio E, Kistner A, Pélissier P, Chevrier E, Seigneuret E, Krack P, Fraix V, Moro E. Long-term Outcomes (15 Years) After Subthalamic Nucleus Deep Brain Stimulation in Patients With Parkinson Disease. ***Neurology. 2021*** Jun 2:10. Epub ahead of print
DOI: 10.1212/WNL.0000000000012246

Genome-Wide Association Study Meta-Analysis for Parkinson Disease Motor Subtypes

Parkinson disease (PD) is a clinically heterogenous disorder. PD subtypes, tremor dominant (TD) and postural instability/gait difficulty (PIGD), are based on phenotypic features. These subtypes have implications for clinical progression and prognostication. Exact mechanisms underlying these phenotypic differences remain largely unclear. A strong genetic contribution to PD etiology is well established, including several rare, monogenic forms of the disease and many common variant PD risk alleles identified in genome-wide association studies (GWASs). Shulman at al performed a GWAS meta-analysis for PD motor subtype in 3,212 subjects, examining potential associations for 71 established PD risk alleles and further testing for novel

modifiers of TD vs PIGD motor phenotypes. Among 71 established PDrisk variants, multiple suggestive associations with PD motor subtype were identified, including GPNMB (rs199351, *p*subtype = 0.01, *p*ratio = 0.03), SH3GL2 (rs10756907, *p*subtype = 0.02, *p*ratio = 0.01), HIP1R (rs10847864, *p*subtype = 0.02), RIT2 (rs12456492, *p*subtype = 0.02), and FBRSL1 (rs11610045, *p*subtype = 0.02). A PD genetic risk score integrating all 71 PD risk variants was also associated with subtype ratio (p = 0.026, ß = -0.04, 95% confidence interval = -0.07–0).

Based on top results of GWAS, authors were able to identify a novel suggestive association at the STK32B locus (rs2301857, *p*ratio = 6.6 × 10-7), which harbors an independent risk allele for essential tremor. This suggests a possible overlap between genetic risk for essential tremor and tremor-dominant PD. It was concluded that multiple PD risk alleles may also modify clinical manifestations to influence PD motor subtype. These data provide insights into the role of genetic variants in the PD clinical course, whether motor manifestations, rate of progression, medication response, or some combination.

Alfradique-Dunham I, Al-Ouran R, von Coelln R, Blauwendraat C, Hill E, Luo L, Stillwell A, Young E, Kaw A, Tan M, Liao C, Hernandez D, Pihlstrom L, Grosset D, Shulman LM, Liu Z, Rouleau GA, Nalls M, Singleton AB, Morris H, Jankovic J, Shulman JM. Genome-Wide Association Study Meta-Analysis for Parkinson Disease Motor Subtypes. ***Neurol Genet***. ***2021*** Jan 28;7(2):e557. DOI: 10.1212/NXG.0000000000000557

Functional Connectomics and Disease Progression in Drug-Naïve Parkinson's Disease Patients

Resting-state functional magnetic resonance imaging (RS fMRI) provides consistent evidence to categorize PD patients from controls and can help to unravel neural correlates of motor and non-motor symptoms. Converging evidence has suggested that brain network organization shapes the expression and course of both psychiatric and neurodegenerative diseases. Moreover, functional dysconnectivity may be detectable even before the occurrence of neuronal death or brain atrophy, indicating its potential as a sensitive and early marker of pathological processes. Most previous fMRI studies have been performed in PD patients under chronic dopamine replacement therapy, which has been shown to variably influence functional connectivity. Following these observations, authors sought to determine the whole-brain network topologic organization of the functional connectome in a large cohort of drug-naïve early PD patients. They hypothesized that specific and subtype-related functional architecture changes may be detected even at clinical early disease.
One hundred and forty-seven drug-naïve, cognitively unimpaired PD patients were enrolled in the study at baseline and compared to 38 age- and gender matched controls. Non-hierarchical cluster analysis using motor and non-motor data was applied to stratify PD patients into two subtypes: 77 early/mild and 70 early/severe. Graph theory analysis and connectomics were used to assess global and local topological network properties and regional functional connectivity at baseline. Stepwise multivariate regression analysis investigated whether baseline functional imaging data were predictors of clinical progression over 2 years. At baseline, widespread functional connectivity abnormalities were detected in the basal ganglia, sensorimotor, frontal, and occipital networks in PD patients compared to controls. Decreased regional functional connectivity involving mostly striato-frontal, temporal, occipital, and limbic connections differentiated early/mild from early/severe PD patients. Connectivity changes were found to be independent predictors of cognitive progression at 2-year follow-up. These findings revealed that functional reorganization of the brain connectome occurs early in PD and underlies crucial involvement of striatal projections.
De Micco R, Agosta F, Basaia S, Siciliano M, Cividini C, Tedeschi G, Filippi M, Tessitore A. Functional Connectomics and Disease Progression in Drug-Naïve Parkinson's Disease Patients. Mov Disord. 2021 Jul;36(7):1603-1616.

DOI: 10.1002/mds.28541

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Southeast/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. Discussion regarding COVID 19 pandemic-clinical challenges and solutions.

  2. Exploring new diagnostic procedures especially Syn-One test – evidence review and use in the PADRECC/VA

  3. Clinical experience and comparative use of three available DBS systems including Boston Scientific's "Vercise", Abbott's "Infinity", and Medtronic's "Percept" within the six PADRECCs

  4. Updates on clinical experience with newer medications – Nourianz (Adenosine Receptor antagonist), Gocovri and Imbrija Inhaler

  5. CSP # 2015 Trial, planning and trial initiation related matters.

Education Committee

- **PADRECC/EES Movement Disorder Series-Webinar:** knowledge-based webinars to provide VHA healthcare professionals with current practice standards and emerging trends in the treatment of Parkinson's disease and other movement disorders. CEs are typically provided for the live webinars. The next MDS webinar will be held on November 4th **"Military Exposures in Parkinson's Disease"** at 12pm and 3pm EST**.** Registration link will be coming soon**.**

  Check out the following link for a list of past webinars and if you are interested in receiving a recording of a past webinar please email Gretchen.glenn@va.gov and list the date/topic of interest: https://www.parkinsons.va.gov/Consortium/Presentations/Audio_Conference/MDS.asp

  Planning is underway for the **FY 22 MDS Webinar Series** which will have a new format to include 2 webinar sessions that are 3-4 hours long. **Save the Date** for the 1st webinar which will include topics on: PD 101, Whole Health, Beyond PD and Exercise. Date: **February 10th** time to be determined.

- **National VA PD Newsletter:** The **VA Parkinson Report** newsletter was completed and disseminated via email to all PADRECC and Consortium Members and is available for viewing on the national website: Fall_2021_VAParkinsonReport.pdf

- **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** 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

November 4th, 2021
EES/PADRECC Movement Disorders Series- Webinar
Topic: Military Exposures and Parkinson's Disease

April 2-7, 2022
American Academy of Neurology - Annual Meeting

Seattle, Washington

Annual Meeting: World's Premier Neurology Meeting | AAN

July 4-7, 2023

6th World Parkinson Congress

Barcelona, Spain

World Parkinson Congress (wpc2023.org)