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

THE TRANSMITTER

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Article Reviews

Prepared by: Jeff Kraakevik, MD-Attending Neurologist, Zachery Rosensweet, DO-Fellow, & Hae-Young Hawong, DO-Fellow ~ Northwest PADRECC

Efficacy and Tolerability of Vesicular Monoamine Transporter Type 2 Inhibitors in the Treatment of Tic Disorders

This is a meta-analysis of all randomized, controlled trials of vesicular monoamine transporter type 2 (VAMT2) inhibitors in the treatment of tic disorders. Tic disorder treatments currently include treatment with medications with negative side effect profiles like the neuroleptics. VAMT2 inhibitors have been proven to be useful in other hyperkinetic movement disorders like chorea and tardive dyskinesia, so there was interest in seeing if the VMAT2 inhibitors would help with tics. This group looked at double-blinded randomized controlled trials of VMAT2 inhibitors for acute treatment of tics (up to 12 weeks) which were published through October 2021. The meta-analysis identified 178 potential references of which 5 met criteria for inclusion. Three of these studies used valbenazine and two used deutetrabenazine, and ranged from 6-12 weeks in length. Numbers of study subjects ranged from 98 to 158, but only one study included adults (n= 124, mean age 35.1), and the others were focused on pediatric populations (mean age 11.5 to 12.3). Unfortunately, the primary outcome of tic symptom severity reduction did not show significant difference between pooled VMAT2 inhibitor and placebo groups as measured by the YGTSS (k=8; N=585; MD=-0.71; 95% CI, -1.93 to 0.50; P=0.24). Similarly, the secondary endpoints looking at subgroup anaylsis to see if there were treatment effects looking at pediatric vs adults, and valbenazine vs deutetrabenzine also failed to show statistically significant differences. Also additional end point measures including a global impression score did not have a significant treatment effect either (TS-CGI). Interestingly, the meta-analysis did not show an increase in depression or suicidality in the treatment arm groups of all trials, which has been a concern with VMAT2 inhibitors in prior trials. Overall, this provides relatively strong evidence that VAMT2 inhibitors are not helpful in the treatment of tic disorders. This study did look only at acute treatment, and did not assess whether there could be effects seen outside of the 12 week maximum treatment window of these trials. Continued research is needed to search for additional medical options to treat tic disorders in both adults and in the pediatric populations.

Behling, et al. Meta-analysis: Efficacy and Tolerability of Vesicular Monoamine Transporter Type 2 Inhibitors in the Treatment of Tic Disorders. **Mov Dis.** 22 Feb 2022. Epub.
https://movementdisorders.onlinelibrary.wiley.com/doi/10.1002/mds.28957

Do patients with Progressive Supranuclear Palsy have episodic memory impairment? A systematic review.

Progressive supranuclear palsy (PSP) is the most common atypical parkinsonism and has executive dysfunction as a core feature. The magnitude of episodic memory disturbance in PSP is yet to be defined. The authors goal was to investigate how impaired episodic memory in PSP compares to healthy controls and other

neuropsychiatric disorders. A systematic review of the literature found that PSP patients had lower scores on episodic memory compared to healthy controls, but that PSP does not differ from Parkinson's disease and from atypical parkinsonism in terms of episodic memory performance. The same relationship appeared to be supported between PSP and frontotemporal dementia. Conversely, episodic memory impairment seems to be greater in typical Alzheimer's disease compared to PSP. Neuroimaging findings indicated that striatofrontal structures may be involved in PSP episodic memory dysfunction, while no associations with mesial structures (including hippocampi) were found. Whether this amnesia refers to executive dysfunction remains controversial.

Macedo, A.C., Mariano, L.I., Martins, M.I., Friedlaender, C.V., Ventura, J.M., Rocha, J.V.d.F., Camargos, S.T., Cardoso, F.E.C., Caramelli, P. and de Souza, L.C. (11 March 2022), **Mov Disord Clin Pract.** Accepted Author Manuscript. https://doi.org/10.1002/mdc3.13435

Novel anti-apoptotic L-DOPA precursors SuperDopa and SuperDopamide as potential neuroprotective agents for halting/delaying progression of Parkinson's disease

The hallmark pathology of Parkinson disease (PD) is nigrostriatal dopaminergic neuronal (NSDA) degeneration and accumulation of intracytoplasmic inclusion, α-synuclein. Levodopa is able to alleviate motor symptoms of PD but does not halt progression of NSDA degeneration. In this study, Dr. Wiesen and Dr. Atlas injected rats with a SuperDopa (SD) and SuperDopamide (SDA) - levodopa merged with an antioxidant N-acetylcysteine (NAC) into a single molecule. In rats injected with SuperDopa, protective effect was seen on motor disability caused by rotenone. Rotenone is a mitochondrial complex I inhibitor, which causes NSDA degeneration. In addition, in human cell culture study, there was reduced rotenone-induced-α-synuclein (α-syn) expression and α-syn oligomerization with SD and SDA in α-syn-overexpressing cells. Also, SD and SDA showed attenuation of oxidative stressed-induced mitogen-activated kinase (MAPK) signaling which is involved in inflammatory/apoptotic pathway. Therefore, the researcher suggested that a single molecule, levodopa precursor fused with NAC able to cross blood brain barrier and have neuroprotective effect on dopaminergic neurons via antioxidant/apoptotic/inflammatory activity and provide a “potential disease-modifying treatment” for PD.

Wiesen T, Atlas D. Novel anti-apoptotic L-DOPA precursors SuperDopa and SuperDopamide as potential neuroprotective agents for halting/delaying progression of Parkinson's disease. **Cell Death Dis.** 2022 Mar 11;13(3):227.

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The San Francisco PADRECC leads the committee for March/April. 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:

    1. Discussion regarding COVID 19 pandemic-clinical challenges and solutions.

2. 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

3. Discussion around challenges of DBS evaluations/programming with patients remotely (live to far from a PADRECC) i.e. using a Medtronic or Boston Scientific Rep to assist local neurologist, sending a PADRECC neurologist to another VA to do a DBS clinic etc.

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

5. Discussion around extended billing and coding with fellows

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. 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
  - **Movement Disorders Series Part 1-Webinar** was held on **February 10th.** Topics included: PD 101, Whole Health, Beyond PD and Exercise. Thank you to all who attended, we had a fantastic turn out!

  - **Nursing Care Across the Parkinson's Disease Spectrum: An Introduction**- April 27th This knowledge-based, live virtual training will provide nurses an overview of the different nursing roles (i.e. LPN, RN, APRN, PA) across the PD spectrum. Registration is now open: VA employees click here

- **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
    - Motor Symptoms
    - Non-Motor Symptoms
    - Agent Orange and Toxic Exposures and PD
  - **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 Initiating Therapy* is available on the National Website:
  https://www.parkinsons.va.gov/Consortium/PocketCard/PocketCard19.pdf

Dates to Remember

April 2-7, 2022

American Academy of Neurology - Annual Meeting

Seattle, Washington

Annual Meeting: World's Premier Neurology Meeting | AAN

April 27th, 2022

Webinar: Nursing Care Across the Parkinson's Disease Spectrum: An Introduction

Virtual

Click here to register

April 28th, 2022

VHA/PADRECC/ Parkinson's Foundation Joint Webinar: Understanding Parkinson's Disease and Mental Health in the Veteran Community
Virtual
Click here to register

October 17-20, 2022

Parkinson's Foundation Fall 2022 Team Training

Kansas City, KS

Click here to learn more

July 4-7, 2023

6th World Parkinson Congress

Barcelona, Spain

World Parkinson Congress (wpc2023.org)