



THE TRANSMITTER

January 2021

Article Reviews

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Comparison of efficacy of deep brain stimulation and focused ultrasound in parkinsonian tremor: a systematic review and network meta-analysis

The authors note that MRI-guided focused ultrasound (MRIgFUS) was an efficacious intervention for improving parkinsonian tremor and presented indirect evidence in identifying that MRIgFUS is not inferior to DBS in parkinsonian tremor suppression.

In addition, DBS excluding PPN-DBS can effectively relieve tremor in patients with PD regardless of stimulation target. The authors set out to compare the efficacy of deep brain stimulation (DBS) and MRI-guided focused ultrasound (MRIgFUS) in parkinsonian tremor. A network meta-analysis based on a Bayesian framework was performed and a literature search was done for articles published between January 1990 and October 2020 using three databases: PubMed, Embase and Cochrane Library (The Cochrane Database of Systematic Reviews). A total of 24 studies were included in our analysis, comprising data from 784 participants.

The authors findings revealed similar efficacy of DBS and MRIgFUS in parkinsonian tremor suppression. Compared with internal globus pallidus (GPi)- MRIgFUS, GPi-DBS -1.84 (-6.44, 2.86), pedunculopontine nucleus (PPN)_DBS -3.28 (-9.28, 2.78), PPN and caudal zona incerta (cZI)-DBS 0.40 (-6.16, 6.87), subthalamic nucleus (STN)_DBS 0.89 (-3.48, 5.30), STN and cZI-DBS 1.99 (-4.74, 8.65), ventral intermediate nucleus (VIM)_DBS 1.75 (-2.87, 6.48), VIM_FUS 0.72 (-5.27, 6.43), cZI-DBS 0.27 (-4.75, 5.36) were no significantly difference. Compared with VIM-MRIgFUS, GPi-DBS -2.55 (-6.94, 2.21), GPi-FUS -0.72 (-6.43, 5.27), PPN_DBS -4.01 (-9.97, 2.11), PPN and cZI-DBS -0.32 (-6.73, 6.36), STN_DB 0.16 (-3.98, 4.6), STN and cZI-DBS 1.31 (-5.18, 7.87), VIM-DBS 1.00 (-3.41, 5.84) and cZI-DBS -0.43 (-5.07, 4.68) were no significantly difference.

With respect to the results for the treatment of motor symptoms, GPi-DBS, GPi-MRIgFUS, STN-DBS and cZI-DBS were significantly more efficacious than baseline (GPi-DBS 15.24 (5.79, 24.82), GPi -MRIgFUS 13.46 (2.46, 25.10), STN-DBS 19.62 (12.19, 27.16), cZI-DBS 14.18 (1.73, 26.89).

The results from the surface under the cumulative ranking results showed that STN-DBS ranked first, followed by combined PPN and cZI-DBS, and PPN-DBS ranked last. MRIgFUS, an efficacious intervention for improving parkinsonian tremor, has not demonstrated to be inferior to DBS in parkinsonian tremor suppression. Hence, clinicians should distinguish individual patients' symptoms to ensure that the appropriate intervention and therapeutic approach are applied.

Lin F, et al. Comparison of efficacy of deep brain stimulation and focused ultrasound in parkinsonian tremor: a systematic review and network meta-analysis. *Neurol Neurosurg Psychiatry* 2021;0:1–10. doi:10.1136/jnnp-2020-323656

Why People with Parkinson's Disease Experience Near-Drowning—and How to Prevent It

The authors note that exercise is regarded as helpful for persons with Parkinson's disease (PD) and swimming is a popular activity. However, in a survey (n=309) of persons with PD, 87.7% noticed a deterioration of their swimming ability and 49.1% reported a near-drowning experience. In this case study, the authors report on a 56 yo male swimmer who initially noticed left leg lag and progressive problems until inability to swim two years later. At that point bradykinesia and poor interlimb coordination combined to produce poor propulsive force as well as inability to remain horizontal. With supplied videos, the authors record the swimmer's abilities in both the off and on (levodopa/carbidopa 187.5 mgs tid) state. A third video shows the added advantage of using swim fins and internal cueing techniques. The authors maintain that impaired corticostriatal input is likely responsible for the bradykinesia and poor interlimb coordination. They further maintain that the medication can reduce bradykinesia but has little impact on limb coordination. Finally, they discuss the beneficial effect of swim aids on the ability to swim. The researchers stress that persons with PD should be warned about the potential hazards of swimming and the benefit of using medication and swimming aids.

Tosserams A, Nijkrake MJ, Voet NB, Bloem BR, Nonnekes J. Why people with Parkinson's disease experience near-drowning—and how to prevent it. *Movement disorders clinical practice*. 2020 Jul;7(5):573.

A Comparative Study of the Behavioral Profile of the Behavioral Variant of Frontotemporal Dementia and Parkinson's Disease Dementia

The authors note that executive dysfunction is commonly seen both in pure cortical dementia (e.g., the behavioral variant of frontotemporal dementia (bvFTD)) and subcortical dementia (e.g., Parkinson's disease dementia (PDD)) but observe that the behavioral symptoms differentiating these 2 conditions are still not well known and set out to find which behavioral symptoms can differentiate between the two. Twenty consecutive patients with bvFTD (>1 year after diagnosis) and 20 PDD patients were recruited according to standard diagnostic criteria. Exclusion criteria included patients with overlapping features of both degenerative and vascular dementia, patients with such severe dementia that they could not be assessed, and patients with incomplete clinical evaluation and brain imaging data. Behavioral symptoms were collected from reliable caregiver by means of a set of questionnaires and then compared between the 2 groups. Results revealed bvFTD patients had more severe disease and more behavioral symptoms than PDD. bvFTD patients had significantly greater: loss of basic emotion ($p < 0.001$, odds ratio [OR] 44.33), loss of awareness of pain ($p < 0.001$, OR 44.33), disinhibition ($p < 0.001$, OR 35.29), utilization phenomenon ($p = 0.008$, OR 22.78), loss of taste discrimination ($p < 0.001$, OR 17), neglect of hygiene ($p = 0.001$, OR 13.22), loss of embarrassment ($p = 0.003$, OR 10.52), wandering ($p = 0.004$, OR 9.33), pacing ($p = 0.014$, OR 9), selfishness ($p = 0.014$, OR 9), increased smoking ($p = 0.014$, OR 9), increased alcohol consumption ($p = 0.031$, OR 7.36), social avoidance ($p = 0.012$, OR 6.93), mutism ($p = 0.041$, OR 5.67), and failure to recognize objects ($p = 0.027$, OR 4.33). The bvFTD patients were also significantly less suspicious ($p = 0.001$, OR 0.0295), less inclined to have a false belief that people were in their home ($p = 0.014$, OR 0.11) and had fewer visual illusions/hallucinations ($p = 0.004$, OR 0.107) than PDD patients. Limitations include lack of pathology results, small sample size, and cross-sectional

design limitations, The authors conclude that behavioral symptoms are a helpful tool to distinguish bvFTD from PDD.

*Saini D, Mukherjee A, Roy A, Biswas A. A Comparative Study of the Behavioral Profile of the Behavioral Variant of Frontotemporal Dementia and Parkinson's Disease Dementia. **Dementia and Geriatric Cognitive Disorders Extra.** 2020;10(3):182-94.*

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Southeast PADRECC leads the committee for January & February. 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, including the need for enhanced assessment and aggressive treatment of depression using tele-technology amongst the home confined patients across the nation.
 2. Discussion about Cala Trio Device for the management of essential tremor. This device is now available upon request through the Prosthetics Service.
 3. Discussion regarding the use of VVC for PM&R therapies during the pandemic for Veterans unable to come in for face to face visits.
 4. Discussion regarding the experience and use of Focused Ultra Sound versus Thalamotomy for Essential Tremor.
 5. Updates on clinical experience with newer medications – Nourianz (Adenosine Receptor antagonist), Gocovri and Imbrija Inhaler
 6. Clinical experience with newer DBS systems including Boston Scientific's "Vercise" and Abbott's " St. Jude Medical Infinity DBS".
 7. CSP # 2015 Trial, planning and trial initiation related matters.

Education Committee

- **National VA PD Consortium Bi-Annual Meeting-** due to Covid 19 pandemic meeting is being held virtually on **January 29th, 2021**.
- **PADRECC/EES Movement Disorder Series-Webinar:** The 2nd audioconference for FY 21 was held on January 14th "**Microbiome and the Gut Brain Axis**" presented by Dr. Jasmohan S. Bajaj, MD, MS, FACG, AGAF, Associate Professor of Medicine, Division of Gastroenterology, Hepatology and Nutrition at Virginia Commonwealth University & McGuire VAMC, Richmond VA

- **FY 2021 Education Needs Assessment-** Designed to determine education needs of consortium members, usefulness of current programs/resources offered (Transmitter, MDS, Newsletter, Website, patient resources etc.) and guide future education initiatives. In the final stage of development, due to contracting issues on EES side dissemination has been delayed, keep an eye out for it in February. Your feedback is important to us!
- **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. Call information: 1-800-767-1750 enter code #54321
- **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. This committee is spearheading 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*)
 - **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>

Southeast PADRECC Service Area Updates

Southeast PADRECC

Hunter Holmes McGuire VAMC

Director: Jessica Lehosit, DO

Clinical/Education News

Southeast/PADRECC has become efficient in delivering care via VVC to home in lieu of face to face visit during the COVID-19 Pandemic. In the beginning of the Pandemic, we were experiencing difficulty with our veterans connecting using VVC which resulted in many visits being converted to telephone visits. Our PADRECC team developed a plan involving TCTs from our area who began reaching out to the veterans prior to their appointments to work out any issues and answer questions. Our connectivity issues were mostly resolved leading to an increase in veteran and provider satisfaction and an increase in the number of VVC visits.

Southeast/PADRECC has prescribed the Cala Trio Device for five patients with Essential Tremor that were either refractory to medications, not interested in DBS surgery or trialing medications. Awaiting results.

Southeast/PADRECC has trialed the Balance Wear vests on two patients with Ataxia. The Balance Vest aims to improve balance, postural control and alignment. Currently, two patients have been evaluated by a physical therapist trained using BalanceWear technology. Awaiting results.

Southeast PADRECC is collaborating with Philadelphia PADRECC to offer a virtual PD support group via WebEx (VA approved) starting March 2021. With the COVID pandemic, both PADRECC support groups were being held via telephone and participation decreased dramatically. We are currently working out the logistics but plan to alternate months with each PADRECC finding speakers and moderating the meeting. Our goal is to be able to reach more veterans including those that live remotely.

Neurosurgery/DBS Update

CVHCS DBS Program Overview

Deep brain stimulation (DBS) procedures including lead implantation and battery replacement are performed by Drs. Kathryn Holloway and Paul Koch at the Central Virginia VA Health Care System (CVHCS) in Richmond, VA. These highly trained functional neurosurgeons have performed DBS on nearly 700 people. Careful assessment by the Richmond PADRECC interdisciplinary team is conducted to determine eligibility for DBS and if so, what surgery is most appropriate.

DBS is performed in a variety of ways depending on the patient's symptoms, medication response, and side effects, as well as the neurosurgeon's and movement disorder neurologist's preference and surgical facility resources. DBS surgical decisions include unilateral vs bilateral, staged vs simultaneous, target selection and implant choice. DBS surgery can be done with the patient awake or asleep, using a stereotactic head frame or a frameless approach. Leads can be placed using technologies such as neuronal recordings to help identify the targeted brain structures, test stimulation to determine efficacy and side effects, and intraoperative imaging such as computerized tomography (CT) and magnetic resonance imaging (MRI) to help visualize lead location. There are three manufacturers of DBS systems including Abbott, Boston Scientific and Medtronic. Surgical centers can vary widely in their approach to performing DBS surgery.

For the past two decades, the CVHCS DBS team has provided interdisciplinary assessment and coordinated care, using a patient centered approach. Both surgeons perform frameless DBS surgery utilizing Medtronic's Nexframe system and more recently FHC's STarFix frameless platform. We perform microelectrode recording and macrostimulation during surgery as well as intraoperative CT scanning. Most patients are awake during some portions of surgery but for some, it can be done with the patient asleep for the entire procedure. DBS devices from all three manufactures are used for implantation as each offer unique features such as segmented (directional) vs non-segmented leads, re-chargeable vs non-rechargeable batteries and brain sensing ability. Which implant is chosen' for each patient is determined by such factors as type of movement disorder, one vs both sides of the brain being treated, and brain target? Some veterans are offered a rechargeable battery option. This battery minimizes the need for battery replacement for 15 years. This option is appropriate for those who are capable and feel comfortable with charging the system several times per week and who have a caregiver

who can offer support with this in case he/she becomes incapacitated. This is just one example of how the needs and preferences of each veteran must be taken into consideration to ensure best outcome and patient satisfaction.

CVHCS DBS Research Highlights

Dr. Kathryn Holloway, neurosurgical director for the Central Virginia VA Health Care System PADRECC, and a team of researchers are involved in several projects aimed at improving the lives of people with Parkinson's disease. Of interest is the utility of deep brain stimulation (DBS) for the treatment of dementia in Parkinson's disease (PD) and the use of quantitative electroencephalography (QEEG) in DBS programming.

The number of people living with dementia doubles every five years creating ever-growing health, social, and economic challenges. Thus, it is crucial to develop a better understanding of this disease and more effective treatments. DBS has resulted in improved quality of life and survival rates in people living with PD. The electrical stimulation of diseased circuits in the brain corrects deficiencies in those areas with resultant motor symptom improvement. For the dementia that occurs in Alzheimer's disease (AD) and PD, we are looking at another circuit in the brain, the nucleus basalis of Meynert (NBM). We hope that with stimulation, this cognitive circuit can reactivate one's memory and even regenerate this circuit. The NBM also plays an important role in the regulation of sleep which is disrupted in people with dementia. We are carefully exploring the effects of stimulation on sleep, learning, and the regenerative process in animal models, before proceeding to human trials.

DBS is a proven and effective treatment for PD, essential tremor (ET), and dystonia. DBS programming is currently a qualitative, iterative process that is growing more complex with newer DBS implants. Thus, a rapid, repeatable, objective, physiologic measure of response could be an invaluable aid in DBS programming. Preliminary data has demonstrated that high density QEEG may be useful. This brain mapping technology utilizes neurophysiologic signatures between the subcortical and cortical structures involved in PD, ET and dystonia. We are using machine learning (ML) to aid in identifying biomarkers of stimulation in two specific brain targets, the ventral intermediate (VIM) and the globus pallidus interna (GPi) and to differentiate these from stimulation in adjacent areas. Our study consists of recording dense array EEG in patients with implanted DBS leads in GPI or VIM, using different stimulation configurations and compare the corresponding spatiotemporal modulations in the EEG spectrum.

Other DBS related research projects conducted at the CVHCS include but are not limited to Registry for the Advancement of Deep Brain Stimulation in Parkinson's Disease (RAD-PD) sponsored by the Michael J Fox Foundation, Physiological Brain Atlas Development sponsored by Vanderbilt University Medical Center/National Institutes of Health and investigator sponsored projects including Accuracy of Targeting Subthalamic Nucleus vs Globus Pallidus and Clinical Implications.

Research/ Grants/Awards

- George Gitchel PhD - collaborating with nQ medical (a small startup company) to develop a protocol for FDA device designation for a remote PD monitoring tool. IRB submission is pending.

VA Career Development Award

P. Koch, PI (Mark Baron Primary Mentor)

Sponsor: Dept of Veterans Affairs

Post-traumatic epileptogenesis: role of neocortical-hippocampal interactions

Request for 5 yrs, 9/11/20 resubmission

- **Value and Efficiency Teaching and Research (VETAR) Award**

Mark Baron, PI; 11/20-10/21

Sponsor: VCU Office of Research and Innovation

Safety and Efficacy of State-of-the-Art Exoskeleton Technology to Improve Mobility in Parkinson's Disease

- **BrightFocus Foundation**

Kumbhare, PI (Mark Baron and Kathryn Holloway Mentors)

Postdoctoral Fellowship Program in Alzheimer's disease research

Basal nucleus of Meynert and neocortex coupling in memory and dementia

Request for 2 yrs, 11/17/20 submission

- **Diseases Research Award Fund (ARDRAF)**

Kathryn Holloway, PI (VCU/VA); 07/01/2020 –6/30/2021

Supporting Agency: Virginia Center on Aging- Alzheimer's and Related

McGuire research Institute - Amount awarded \$45,000

Title: Deep Brain Stimulation of the Nucleus Basalis of Meynert: Using electricity to regenerate and restore cognitive function in dementia rodent model.

% Effort: 5%

The project objective is to assess the effect of duration and timing of NBM stimulation within the sleep/wake cycle on the restoration of learning ability, neurogenesis, and cholinergic cell survival in demented rats.

Manuscripts

Carmona C.A., Kumbhare, D., Baron, M.S., Hadimani R.L., Quintuple AISI 1010 Carbon Steel Core Coil for Transcranial Magnetic Stimulation. AIP Advances, accepted for publication.

Carmona C.A., Kumbhare, D., Baron, M.S., Hadimani R.L., Space-varying E-field Vector Modulation with Oriented Control Using Quintuple Core Coil for TMS. IEEE Intermag 2021 Conference (submitted).

Publications:

Matthew Moser, Paul Koch, Harsh P. Shah, Alen Docef, Kathryn Holloway. Brief Report: The poised cannula technique reduces the stereotactic error of the fiducial-less frame-less DBS procedure. *In Press in Stereotactic and Functional Neurosurgery.*

Conference Abstracts

Stamenkovic A., Cloud L.J., Baron, M.S., Hand R.O, Van Der Veen, S., Thomas, J.S, Perceptions to a novel virtual reality intervention to improve trunk control in Parkinson's disease: a pilot study. UNC regional conference, April 2020.

Kumbhare, D., Weistroffer, G., Baron, M.S., A novel phasic and restricted basal ganglia thalamocortical subcircuitry model. Movement Disorders Virtual Congress 2020, Sept 13-17, 2020.

Carmona, C., Kumbhare D., Baron M.S., Hadimani R.L. A Quadruple Silicon Steel Core Coil for Highly Focused Transcranial Magnetic Stimulation in Small Animals. 2020 MMM Conference, Las Vegas, Nevada, Nov, 2020.

Carmona C.A., Kumbhare, D., Baron, M.S., Hadimani R.L., Space-varying E-field Vector Modulation with Oriented Control Using Quintuple Core Coil for TMS. IEEE InterMag 2021 Conference (submitted).

Dates to Remember

January 29, 2021

National VA PD Consortium Meeting

Philadelphia, PA

February 25, 2021

EES/PADRECC Movement Disorders Series-Webinar

Topic: Managing Telehealth for Movement Disorders: Tips & Tricks

Click here to register: [Managing Telehealth for Movement Disorders-Tips and Tricks](#)

March 11, 2021

EES/PADRECC Movement Disorders Series-Webinar

Topic: Rehabilitation Strategies for Parkinson's Disease: What is Rehabilitation?"

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

April 17-23, 2021

American Academy of Neurology - Annual Meeting

San Francisco, CA (in person) & Virtual Component

<https://www.aan.com/conferences-community/annual-meeting/>

May 13, 2021

EES/PADRECC Movement Disorders Series-Webinar

Topic: DBS

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

September 9, 2021

EES/PADRECC Movement Disorders Series-Webinar

Topic: TBD

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

September 19, 2021 - September 23, 2021

International Congress of Parkinson's Disease and Movement Disorders

Location: Copenhagen, Denmark

<https://www.mdscongress.org/Congress/Program--Abstracts/View-Past--Future-Congresses.htm>