



THE TRANSMITTER

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Article Reviews

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Southeast PADRECC

A Comparison Study of Cognitive and Neuropsychiatric Features of Essential Tremor and Parkinson's Disease

Little information exists comparing the cognitive/personality features of individuals with ET and those with PD. Thirty-two ET patients (mean age 67.7), 32 non-demented patients (mean age 67.7) with PD and 32 healthy controls (mean age 67.9) were administered comprehensive neuropsychological batteries and the Personality Assessment Inventory (PAI). Multivariable linear regression analyses were performed, adjusted for age, sex, years of education, medications that potentially affect cognitive function, number of medications, and the 17-item Hamilton Depression Rating Scale Total Score. Scores were similar in the PD and ET groups. Controls were superior to both PD/ET groups in attention, executive functioning, memory and naming. The authors conclude that the disease groups were similar in those functions thought to rely on the integrity of the prefrontal cortex and the frontocerebellar circuits. The authors further conclude that ET is not a benign and monosymptomatic disorder.

Tremor and Other Hyperkinetic Movements. Published: December 15, 2016

<http://www.tremorjournal.org/index.php/tremor/article/view/431/html>

Predicting First Fall in Newly Diagnosed Parkinson's Disease: Insights from a Fall-Naïve Cohort

This is the first study done for the newly diagnosed Parkinson's disease patients. It is a prospective study on newly diagnosed, falls-naïve patients. Risk of falling was about 8 times higher in people with slow gait speed, decreased stance time, and H&Y III. Evidence suggested beneficial effects of exercise in reducing the falls rate in mild cases. Despite targeted interventions, falls are a persistent clinical feature. This study revealed that motor features dominate their model although disease severity, age, and attention did not emerge as significant predictors. It also suggested that first fall occurs soon after the diagnosis, highlighting the need for early intervention. The strongest predictor was the gait speed followed by the stance time and H&Y stage.

Movement Disorders, Vol. 31, No. 12, 2016, P1829-1836

<https://dx.doi.org/10.1002/mds.26742>

Nigral and striatal connectivity alterations in asymptomatic LRRK2 mutation carriers: A magnetic resonance imaging study

The study of functional connectivity by means of magnetic resonance imaging (MRI) in asymptomatic LRRK2 mutation carriers could contribute to the characterization of the pre-diagnostic phase of LRRK2-associated Parkinson's disease (PD). The objective of this study was to characterize MRI functional patterns during the resting state in asymptomatic LRRK2 mutation carriers. The authors acquired structural and functional MRI data of 18 asymptomatic LRRK2 mutation carriers and 18 asymptomatic LRRK2 mutation non-carriers, all first-degree relatives of LRRK2-PD patients. Starting from resting-state data, the functional connectivity of the striatocortical and the nigrocortical circuitry was analyzed. Structural brain data were analyzed by voxel-based morphometry, cortical thickness, and volumetric measures. Asymptomatic LRRK2 mutation carriers had functional connectivity reductions between the caudal motor part of the left striatum and the ipsilateral precuneus and superior parietal lobe. Connectivity in these regions correlated with subcortical gray-matter volumes in mutation carriers. Asymptomatic carriers also showed increased connectivity between the right substantia nigra and bilateral occipital cortical regions (occipital pole and cuneus bilaterally and right lateral occipital cortex). No intergroup differences in structural MRI measures were found. In LRRK2 mutation

carriers, age and functional connectivity correlated negatively with striatal volumes. Additional analyses including only subjects with the G2019S mutation revealed similar findings. The authors concluded that asymptomatic LRRK2 mutation carriers showed functional connectivity changes in striatocortical and nigrocortical circuits compared with noncarriers. These findings support the concept that altered brain connectivity precedes the onset of classical motor features in a genetic form of PD.

Movement Disorders Journal. Published: December 2016.

<http://onlinelibrary.wiley.com/doi/10.1002/mds.26799/full>

MicroRNAs in Cerebrospinal Fluid as Potential Biomarkers for Parkinson's Disease and Multiple System Atrophy

Parkinson's Disease (PD) and Multiple System Atrophy (MSA) are both α -synucleinopathies that appear similar early in their course, are difficult to differentiate, and have profoundly different future outlooks for the patient. At present, there are no quantitative measures that would reliably differentiate MSA from PD at initial presentation to a specialist. MicroRNA's (miRNA) regulate messenger RNA and have the ability to downregulate numerous genes. Recent studies have found specific miRNA in the brain tissue of PD and MSA subjects at autopsy, and more recently it was discovered that miRNA are found circulating in many bodily fluids, including CSF. This study investigates the ability to detect specific miRNA in the CSF of living patients, and its possible utility as a clinical biomarker. CSF was collected from 28 PD's, 17 MSA's, and 30 controls; further processed for quantification, and then analyzed for the presence of 10 specific miRNA that had been previously detected in autopsy. Two miRNA were associated with PD, with one upregulated and one downregulated compared to controls. In MSA subjects, 4 miRNA were downregulated compared to control subjects, one of which was also the downregulated miRNA in PD subjects. Utilizing these combinations of miRNA, and a ROC and AUC analysis, the team was able to achieve a sensitivity/specificity of detecting PD of 96%/92%, and a sensitivity/specificity of detecting MSA of 94%/64%. The authors suggest that these 5 miRNA may be useful in differential diagnoses of MSA and PD patients, early in the course of their disease, and further go on to say that one miRNA in particular that was downregulated in both PD and MSA (miR-24) should be studied further for its potential role in the pathology of α -synucleinopathies.

Mol Neurobiol (2016). doi:10.1007/s12035-016-0253-0

<https://www.ncbi.nlm.nih.gov/pubmed/27844283>

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 December/January. 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. New PD treatments in the pipeline, including ND0612, which is a proprietary formulation of levodopa and carbidopa continuously administered subcutaneously and extended release Amantadine formulation. Discussions focused on reviewing the safety, tolerability and clinical efficacy data, presented at recent scientific meetings.
 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 and Rytary

(carbidopa/levodopa IR/SA combination oral medication). Recent discussions have focused on learning optimal titrating schedules, strategies to manage complication, logistical and support issues

3. Continued experience sharing regarding the use of various Neurotoxins across the PADRECC network with the objective to improve this specialized clinical practice and develop neurotoxin selection criteria for various conditions in the Veteran population.
4. Practical aspects regarding the use of DAT scans; applications and pitfalls, including the issue of drug interference
5. Palliative Care: Review of palliative care resources and practices in the PADRECCs
6. Veteran's Choice Program: re-distribution of resources, optimal use of the program, impact on VA based sub-specialty care.
7. Consortium Sites: Strategies to improve communications, enhance educational and clinical support and develop research projects with the consortium sites.
8. New MRI body scanning protocols for DBS implanted patients
9. Discussed the FDA-approved antipsychotic for PD, pimavanserin. PBM review scheduled for Fall 2016. In the interim, local P/T committee review/approval required. PADRECCs have circulated their applications to streamline individual on-boarding. Discussed likely indication and criteria for use.
10. Continued discussion of Rytary and dosing strategies. Consensus that often more than a three times/day scheduled is needed.

Education Committee

- **PADRECC/EES Movement Disorder Series:** The 2nd audioconference for FY 17 was held on **January 12, 2017** "*Yoga & Mindfulness*" by Dr. Indu Subramanian, Southwest 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.
- **Patient Education Brochures:** In response to the 2016 National VA PD Consortium Education Needs Assessment, the existing patient education brochures are in the process of being updated. Once completed they will be made available on the National Website for download.
- **2016 National Consortium Conference:** Presentations from this conference are available for viewing on the National Website:
http://www.parkinsons.va.gov/Consortium/Presentations/2016_Consortium_Meeting_esp.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
- **PADRECC Transmitter:** The committee continues to assemble and distribute this e-newsletter every other month.

Southeast PADRECC Service Area Updates

Gainesville, FL

North Florida/South Georgia VAMC

Director: Christopher Hess, MD

Phone: (352) 374-6058

The North Florida/South Georgia (NF/SG) Consortium provides care to veterans with Parkinson's disease as well as a variety of other movement disorders, including atypical parkinsonism, tremor disorders, myoclonus, chorea, dystonia, ataxia, and functional movement disorders. They provide EMG-guided botulinum toxin injections for movement disorders, as well as patient selection, programming, and follow-up care for patients requiring deep brain stimulation. A movements disorders physiology laboratory provides computerized tremor analysis and EMG-EEG back-averaging when indicated. Dr. Hess was recently a guest on C-SPAN's *Washington Journal* discussing Parkinson's disease in the US following the death of Muhammad Ali.

Nashville, TN

VA Tennessee Valley Healthcare System – Nashville Campus

Director: John Fang, MD

Phone: (615) 873-7510

Operational since 2002, the Movement Disorders clinic at the Nashville Campus of the VA Tennessee Valley Healthcare System treats patients with Parkinson's disease and other movement disorders. The focus is on optimizing medications and working with primary care providers and other specialists. Botulinum toxin therapy and deep brain stimulation programming are supported. Dolores Otto, neurology department secretary provides administrative support for the clinic. In 2011, Clinical Video Telehealth (CVT) was added linking select Community-Based Outpatient Clinics (CBOCs).

Orlando, FL

Orlando VA Medical Center

Director: Ramon L Rodriguez Cruz, MD

Phone: (407) 631-1050

The Orlando VAMC Movement Disorders Clinic provides specialty care for those veterans affected by Parkinson's disease, Dystonia, Tremors, Huntington's disease, Parkinson Plus syndromes and other movement disorders in Central Florida. The Clinic operates under the supervision of Dr. Ramon Rodriguez, fellowship trained Movement Disorders Specialist. The clinic provides access to the latest medical and surgical procedures for patients suffering from movement disorders. Our center has a large experience in managing patients with DBS and Duopa, and provides specialized services like Physical therapy, Occupational Therapy and Speech therapy by providers experienced in the management of Parkinson's disease. In addition, Dr. Khizar Malik, Fabian Rossi, Aunali Khaku, Nina Tsakadze, Umesh Sharma and Michael Hoffmann provide their neurological expertise, creating a comprehensive center that covers all the aspects of neurological care of this population. For more information, please contact the number provided for appointments.

Lexington, KY

Lexington VAMC

Director: John T. Slevin, MD

Phone: 859-281-4920

Established in 2000, The Movement Disorders Clinic at the Lexington VAMC is staffed by Dr. Slevin, a nurse practitioner, nurse manager, a movement disorders fellow and Pharm. D. It provides subspecialty consultations, patient selection and management services for DBS surgery, carbidopa-levodopa enteral suspension, and botulinum toxin injections. Dr. Slevin is affiliated with the University of Kentucky Medical Center and Director of Clinical Research for the UKMC Parkinson's Disease Research Center of Excellence, is the PI or Co-PI on 4 industry, 1 investigator initiated and 1 NIH-sponsored clinical/translational studies, four of which are currently recruiting subjects.

Recent Publications:

- Lang, A.E., Rodriguez, R.L., Boyd, J.T., Chouinard, S., Zadikoff, C., Espay, A.J., **Slevin, J.T.**, Fernandez, H.H., Lew, M.F., Stein, D.A., Odin, P., Fung, V.S.C., Klostermann, F., Fasano, A., Draganov, P., Schmulewitz, N., Robieson, W.Z., Eaton, S., Chatamra, K., Benesh, J.A., Dubow, J. *Long-term Integrated Safety of Levodopa-Carbidopa Intestinal Gel from Prospective Clinical Trials.* Movement Disorders 31(4):538-546, 2016. PMID: 26695437
- Antonini, A., Fung, V.S.C., Boyd, J.T., **Slevin, J.T.**, Hall, C., Chatamra, K., Eaton, S., Benesh, J.A. *Effect of Levodopa-Carbidopa Intestinal Gel on Dyskinesia in Advanced Parkinson's Disease Patients.* Movement Disorders 31(4):530-537, 2016. PMID: 26817533
- Van Horne, C.G., Quintero, J.E., Gurwell, J.A., Wagner, R.P., **Slevin, J.T.**, Gerhardt, G.A. *Implantation of Autologous Peripheral Nerve Grafts Into the Substantia Nigra of Subjects With Idiopathic Parkinson's Disease Treated With Bilateral STN DBS: A Report of Safety and Feasibility.* J Neurosurgery. 2016 May 6:1-8. PMID: 27153166
- Gash, D.M., Gerhardt, G.A. and **Slevin, J.T.** GDNF (Including Neurturin). In: Reference Module in Neuroscience and Biobehavioral Psychology, Elsevier, Oxford, UK, 2017. ISBN 9780128093245

Tampa, FL

James A. Haley (JAH) Tampa VAMC
Parkinson's Disease and Movement Disorders Center
Director: Theresa A. Zesiewicz, MD FAAN
Phone: (813) 972-7633

The Parkinson's Disease and Movement Disorders Center at the JAH in Tampa, Florida specializes in Parkinson's disease, Essential Tremor, Dystonia, Ataxia, and Huntington's disease. We also specialize in evaluations for surgical treatment of movement disorders. At the University of South Florida (USF) in Tampa, Dr. Zesiewicz is the Director, as well as heading The Frances J. Zesiewicz Center and Foundation for Parkinson's Disease and the USF Ataxia Research Center. Dr. Zesiewicz is a professor at USF and is involved with clinical trials in movement disorders. Please contact Melinda Anello at the number provided for appointments at the JAH Tampa VAMC.

Recent Publications:

- [Practice guideline summary: Treatment of restless legs syndrome in adults: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology.](#)
Winkelman JW, Armstrong MJ, Allen RP, Chaudhuri KR, Ondo W, Trenkwalder C, Zee PC, Gronseth GS, Gloss D, **Zesiewicz T.** *Neurology.* 2016 Dec 13;87(24):2585-2593. PMID: 27856776
- [The Initial Symptom and Motor Progression in Spinocerebellar Ataxias.](#)
Luo L, Wang J, Lo RY, Figueroa KP, Pulst SM, Kuo PH, Perlman S, Wilmot G, Gomez CM, Schmahmann JD, Paulson H, Shakkottai VG, Ying SH, **Zesiewicz T,** Bushara K, Geschwind M, Xia G, Subramony SH, Ashizawa T, Kuo SH. *Cerebellum.* 2016 Nov 15. [Epub ahead of print] PMID: 27848087
- [Progression of brain atrophy in PSP and CBS over 6 months and 1 year.](#)
Dutt S, Binney RJ, Heuer HW, Luong P, Attygalle S, Bhatt P, Marx GA, Eloffson J, Tartaglia MC, Litvan I, McGinnis SM, Dickerson BC, Kornak J, Waltzman D, Voltarelli L, Schuff N, Rabinovici GD, Kramer JH, Jack CR Jr, Miller BL, Rosen HJ, Boxer AL; AL-108-231 investigators.. *Neurology.* 2016 Nov 8;87(19):2016-2025. PMID: 27742814
- [Progression of Friedreich ataxia: quantitative characterization over 5 years.](#)
Patel M, Isaacs CJ, Seyer L, Brigatti K, Gelbard S, Strawser C, Foerster D, Shinnick J, Schadt K, Yiu EM, Delatycki MB, Perlman S, Wilmot GR, **Zesiewicz T,** Mathews K, Gomez CM, Yoon G, Subramony SH, Brocht A, Farmer J, Lynch DR. *Ann Clin Transl Neurol.* 2016 Jul 25;3(9):684-94. doi: 10.1002/acn3.332. PMID: 27648458

- [Comorbid Medical Conditions in Friedreich Ataxia: Association With Inflammatory Bowel Disease and Growth Hormone Deficiency.](#)
Shinnick JE, Schadt K, Strawser C, Wilcox N, Perlman SL, Wilmot GR, Gomez CM, Mathews KD, Yoon G, **Zesiewicz** T, Hoyle C, Subramony SH, Yiu EM, Delatycki MB, Brocht AF, Farmer JM, Lynch DR. J Child Neurol. 2016 Aug;31(9):1161-5. doi: 10.1177/0883073816643408. PMID: 27071470
- [Emerging therapies in Friedreich's ataxia.](#)
Aranca TV, Jones TM, Shaw JD, Staffetti JS, Ashizawa T, Kuo SH, Fogel BL, Wilmot GR, Perlman SL, Onyike CU, Ying SH, **Zesiewicz** TA. Neurodegener Dis Manag. 2016;6(1):49-65. doi: 10.2217/nmt.15.73. Review. PMID: 26782317
- [Depression and clinical progression in spinocerebellar ataxias.](#)
Lo RY, Figueroa KP, Pulst SM, Perlman S, Wilmot G, Gomez C, Schmahnmann J, Paulson H, Shakkottai VG, Ying S, **Zesiewicz** T, Bushara K, Geschwind M, Xia G, Yu JT, Lee LE, Ashizawa T, Subramony SH, Kuo SH. Parkinsonism Relat Disord. 2016 Jan;22:87-92. doi: 10.1016/j.parkreldis.2015.11.021. PMID: 26644294
- [A Randomized Controlled Exploratory Pilot Study to Evaluate the Effect of Rotigotine Transdermal Patch on Parkinson's Disease-Associated Chronic Pain.](#)
Rascol O, **Zesiewicz** T, Chaudhuri KR, Asgharnejad M, Surmann E, Dohin E, Nilius S, Bauer L. J Clin Pharmacol. 2016 Jul;56(7):852-61. doi: 10.1002/jcph.678. PMID: 26626320

Dates to Remember

March 9, 2017

EES/PADRECC Movement Disorders Series

Topic: Exercise as Medicine

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

April 22-28, 2017

American Academy of Neurology: Annual Meeting

Boston, MA

<https://www.aan.com/conferences/2017-annual-meeting/submit-your-abstract/>

May 11, 2017

EES/PADRECC Movement Disorders Series

Topic: Creativity and Parkinson's Disease

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

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/>