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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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Effects of COVID-19 on Parkinson's disease clinical features: a community-based case-control study

With the emergence of the COVID-19 pandemic, acquiring data on the effects of COVID-19 on our patients with Parkinson's disease (PD) has been of paramount importance to guide management. Patients with PD may be more susceptible to COVID-19 because of PD-related factors as well as age-related co-morbidities. Cilia and colleagues recently published the first observational, community-based, case-control study on the effects of COVID-19 on the motor and non-motor symptoms in a cohort of patients with idiopathic PD (iPD) and COVID-19 as compared to a control population with iPD over a 3 month period (i.e between the pre-outbreak period to the end of lockdown in Italy). 1092 records of residents with iPD in the Lombard region of Northern Italy. Of the 141 patients who consented to be remotely interviewed, 12 patients were found to be affected by COVID-19 and of the remaining 129 controls, 36 patients matched for sex, age and disease duration (± 1 year). Of the 12 affected patients, 3 (25%) had mild COVID-19 illness, 8 (66.7%) had moderate illness and only 1 needed to be hospitalized with pneumonia. No mortalities were reported. Between-group case-control analysis revealed greater motor disability, motor fluctuations, and non-motor complaints in the group affected by COVID-19. This study highlights that patients with PD may experience substantial worsening of motor and non-motor symptoms during mild-to-moderate COVID-19 illness, independent of age and disease duration. Further studies in larger populations with PD are warranted to clarify the etiology of the clinical changes which currently seems to be related to a systemic inflammatory response due to the COVID-19 illness rather than direct invasion of the virus into the central nervous system.

*Cilia R, Bonvegna S, et al. Effects of COVID-19 on Parkinson's disease clinical features: a community-based case-control study. **Mov Disord.** 2020; doi: 10.1002/mds.28170.*

REM sleep without atonia is associated with increased rigidity in patients with mild to moderate Parkinson's disease.

Abnormally elevated muscle activity during rapid eye movement (REM) sleep is present in approximately 40% of people with Parkinson's disease (PD). This is diagnosed by polysomnography electromyogram showing increased phasic or tonic muscle activity and is termed REM sleep without atonia (RSWA). Rigidity, a cardinal motor symptom of PD, is also characterized by increased muscle activity. Prior studies have shown that patients with akinetic-rigid phenotype of PD have increased prevalence of RSWA. Researchers at the University of Minnesota and Massachusetts General Hospital sought to test the hypotheses that PD patients with RSWA would have more severe and symmetric rigidity compared to patients with PD but without RSWA. The study

had 61 participants, of which 41 had PD and 20 were age-matched, healthy controls without PD. Participants underwent an overnight polysomnography, which was analyzed by a blinded rater. PD participants were further stratified into those with RSWA positive or negative (normal) groups. Rigidity was quantitatively measured using a robotic manipulandum, a device that passively supinates and pronates the forearm. The study found that the levodopa daily equivalent (LDE) was significantly higher in PD patients with RSWA, but there was no significant difference in MDS-UPDRS Part III total scores or rigidity subscores between PD participants with and without RSWA. Quantitative forearm rigidity measures were significantly higher PD patients with RSWA group compared to the control group and was more symmetric compared to those with PD without RSWA. In conclusion, RSWA is associated with an increased and more symmetric upper limb rigidity in patients with mild to moderate PD. The findings from this study suggest that synucleinopathy affecting the areas of brainstem that control muscle tone during REM sleep contributes to parkinsonian rigidity outside of sleep.

*M. E. Linn-Evan et al., REM sleep without atonia is associated with increased rigidity in patients with mild to moderate Parkinson's disease, **Clinical Neurophysiology**, <https://doi.org/10.1016/j.clinph.2020.04.017>*

Relationship of Cerebrospinal Fluid Vitamin B12 Status Markers With Parkinson's Disease Progression.

Recent investigations of vitamin B12 levels in untreated early Parkinson's disease (PD) found that those patients with low B12 levels had greater annual declines in gait and balance. In particular, participants from the DATATOP study with B12 levels in the lowest one-third had significant annual worsening of their ambulatory capacity score. B12 is known to have a role in supporting the myelination of nerves in the central and peripheral nervous system, and low B12 levels are associated with sensory and gait impairments. Recent studies have also shown that B12 inhibits the abnormal accumulation of α -synuclein, which is one of the key pathological features in neurons of patients with PD. B12 is also known to modulate the function and shape of a key enzyme (LRRK2) implicated in PD pathogenesis. Genetic variants of the *LRRK2* gene account for the majority of all known heritable PD. While the previous studies looked at B12 levels in the blood of PD patients, cerebrospinal fluid (CSF) is considered the preferred fluid to assess central nervous status. Thus, the current study sought to determine whether baseline CSF levels of B12 corresponded with previously obtained measures from blood and their effect on gait and balance over time. 570 CSF samples from the DATATOP study were analyzed in comparison to their corresponding blood samples. It was found that the levels of B12 and other analytes (holoTC, tHcy, and MMA) in the serum and CSF were directly associated with one another. While there was worsening in the ambulatory capacity score of patients with the lowest one-third of CSF B12 levels, this change in score was not statistically significant compared to those with the higher CSF B12 levels. There was a statistically significant worsening of 1 of the 5 sub-items of that score – the annualized UPDRS “walking score“. But in general, the results did not support the hypothesis that CSF B12 might be a more sensitive predictor of PD progression. The analysis does support prior work that lower blood B12 levels predict greater declines in ambulatory capacity.

*Christine CW et al. Relationship of Cerebrospinal Fluid Vitamin B12 Status Markers With Parkinson's Disease Progression. **Mov Disord.** 2020; May 14. doi: 10.1002/mds.28073.*

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. 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. Update on the CSP #468 Trial, kick off meeting will likely occur in December or early 2021
 3. Discussion about Cala Trio Device for the management of essential tremor. This device is now available upon request through the Prosthetics Service.
 4. Updates on clinical experience with newer medications – Nourianz (Adenosine Receptor antagonist), Gocovri and Imbrija Inhaler
 5. Discussion about involvement with ongoing Levodopa Pump study – NeuroDerm
 6. Clinical experience with Boston Scientific DBS

Education Committee

- **National VA PD Consortium Bi-Annual Meeting-** due to Covid 19 pandemic meeting is being changed to a virtual meeting. Date and additional details will follow as they are known.
- **New Partnership-VHA/PADRECC and The Parkinson's Foundation:** 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 will be spearheading many of the projects planned for this partnership
- **PADRECC/EES Movement Disorder Series:** The third audioconference for FY 20 was held on May 14th, 2020 “**Web-based Resources for Parkinson's Disease Patients, Caregivers and Health Care Providers**” by Dr. John Duda, National PADRECC Director, Philadelphia PADRECC Director, and Chair of the National PD Consortium. Please see the **Dates to Remember** section below for a listing of upcoming audioconferences and mark your calendars.
- **National VA PD Newsletter:** Currently accepting articles for the **2020 VA Parkinson Report**. Articles should focus on cutting edge research or treatment pertaining to PD. If you are interested in submitting an article for the newsletter please email Eileen Hummel (Eileen.Hummel@va.gov) or Gretchen Glenn (Gretchen.Glenn@va.gov). Deadline for submission is **June 19th, 2020**.
- **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.
- **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
 - **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>
 - **PADRECC Support Group Listings** <https://www.parkinsons.va.gov/patients.asp>
 - **Updated 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>

San Francisco PADRECC Service Area Updates

Welcome Dr. Zuzuárregui and Dr. Dietiker



Jose Rafael Zuzuárregui, MD is board certified in Neurology, he completed his fellowship in Movement Disorders at Boston University School of Medicine and fellowship in Sleep Disorders at Stanford University. He earned his medical degree from Boston, came to UC-Fresno for his internship, returning to complete his residency at Boston University School of Medicine where he was Chief Resident.

Dr. Zuzuárregui has an interest in the treatment of Parkinson's and various sleep disorders, as well as the use of Botox and Deep Brain Stimulation (DBS) for treatment of movement disorders. His research has focused on the intersection between movement and sleep disorders with particular focus with the impact of DBS on various sleep parameters. He also has a strong interest in medical education.

He is currently researching the relationship between toxicant exposures during Gulf War deployment and prodromal Parkinson's disease; the impact of Globus Pallidus Deep Brain Stimulation on Sleep Disorders in Parkinson's Disease.



Cameron Dietiker, MD has returned to the San Francisco PADRECC! She is a graduate of University of California San Diego (UCSD), followed by two years research for the Collaborative Study on the Genetics of Alcoholism (COGA) under the Veterans Medical Research Foundation. She acquired her medical degree from NYMC, completed her neurology residency training at UCSF, and in 2017, the PADRECC movement disorders fellowship at UCSF and San Francisco VAHCS. Dr. Dietiker is Assistant Clinical Professor in Neurology at UCSF. She treats people with movement disorders in the SFVA PADRECC and the

Movement Disorders & Neuromodulation Center at the UCSF Mt. Zion campus as well as the Memory and Aging Center at the Mission Bay campus.

As a movement disorders specialist, Dr. Dietiker's clinical practice encompasses Parkinson's disease, Huntington's disease, ataxia, tremor, and dystonia, among other disorders. She is knowledgeable in the administration of botulinum toxin as well as deep brain stimulation (DBS) programming. Her current research endeavors include clinic trials in Parkinson's disease, Huntington's disease, multiple system atrophy, and essential tremor.

PADRECC recent Publications

Brown EG, Bledsoe IO, Luthra NS, Miocinovic S, Starr PA, Ostrem JL. Cerebellar Deep Brain Stimulation for Acquired Hemidystonia. *Mov Disord Clin Pract*. 2020;7(2):188-193. Published 2020 Jan 8. doi:10.1002/mdc3.12876

Caroff SN, Yeomans K, Lenderking WR, Cutler AJ, Tanner CM, Shalhoub H, Pagé V, Chen J, Franey E, Yonan C.J *RE-KINECT: A Prospective Study of the Presence and Healthcare Burden of Tardive Dyskinesia in Clinical Practice Settings*. *Clin Psychopharmacol*. 2020 May/Jun;40(3):259-268. doi: 10.1097/JCP.0000000000001201.PMID: 32332461

Chen W, de Hemptinne C, Miller AM, Leibbrand M, Little SJ, Lim DA, Larson PS, Starr PA. *Prefrontal-Subthalamic Hyperdirect Pathway Modulates Movement Inhibition in Humans*. *Neuron*. 2020 Feb 26:S0896-6273(20)30135-5. doi: 10.1016/j.neuron.2020.02.012. Online ahead of print. PMID: 32155442
<https://pubmed.ncbi.nlm.nih.gov/32155442/>

Dietiker C, Kim S, Zhang Y, Christine CW. Characterization of Vitamin B12 Supplementation and Correlation with Clinical Outcomes in a Large Longitudinal Study of Early Parkinson's Disease. *J Mov Disord*. 2019 May; 12(2):91-96. PMID: 31158942.

Luo M, Larson PS, Martin A, Miga MI. *Accounting for Deformation in Deep Brain Stimulation Surgery with Models: Comparison to Interventional Magnetic Resonance Imaging*. IEEE Trans Biomed Eng. 2020 Feb 14. doi: 10.1109/TBME.2020.2974102. Online ahead of print. PMID: 32078527

Luthra NS, Marcus AH, Hills NK, Christine CW. (2020) Vitamin B12 measurements across neurodegenerative disorders. Journal of Clinical Movement Disorders. 7:3. doi: 10.1186/s40734-020-00085-8

Pahwa R, Dhall R, Ostrem J, Gwinn R, Lyons K, Ro S, Dietiker C, Luthra N, Chidester P, Hamner S, Ross, E and Delp S. (2019). An acute randomized controlled trial of non-invasive peripheral nerve stimulation in essential tremor. Manuscript accepted for publication in Neuromodulation: Technology at the Neural Interface.

Zuzuárregui JR, Ostrem, JL. The Impact of Deep Brain Stimulation on Sleep in Parkinson's Disease: An update. J Parkinsons Dis. 2020;10(2):393-404. doi: 10.3233/JPD-19182

Dates to Remember

September 10, 2020

EES/PADRECC Movement Disorders Series

Topic: Palliative Care Needs in Parkinson's Disease

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